Current issue date: 22 June 2021
Expiry date: 21 June 2024
Certificate identity number: 10361225

Original approval(s):
ISO 13485 - 9 June 2019

Certificate of Approval

This is to certify that the Management System of:

ELITechGroup B.V.

Van Rensselaerweg 4, 6956 AV Spankeren, The Netherlands

Digitally signed by Ceaicovschi Tudor
Date: 2021.11.26 18:26:52 EET
Reason: MoldSign Signature
Location: Moldova

has been approved by Lloyd's Register to the following standards:

ISO 13485:2016

Approval number(s): ISO 13485 – 00020722

This certificate is valid only in association with the certificate schedule bearing the same number on which the locations applicable to this approval are listed.

The scope of this approval is applicable to:

Design, development and manufacturing of clinical chemistry analyzers, contract manufacturing of erythrocyte sedimentation rate analyzers and warehousing of erythrocyte sedimentation rate tubes for the in vitro diagnostic investigation of samples of human origin.

Paul Graaf

Chief Operating Officer, Management Systems, MSIS

Issued by: Lloyd's Register Nederland B.V.

for and on behalf of: Lloyd's Register Quality Assurance Limited

UKAS MANAGEMENT SYSTEMS
001

Certificate Schedule

Location	Activities
ELITechGroup B.V. Van Rensselaerweg 4, 6956 AV Spankeren, The Netherlands	**ISO 13485:2016** Design, development and manufacturing of clinical chemistry analyzers, contract manufacturing of erythrocyte sedimentation rate analyzers and warehousing of erythrocyte sedimentation rate tubes for the in vitro diagnostic investigation of samples of human origin.
ELITechGroup B.V. Kanaaldijk 90, 6956 AX Spankeren, The Netherlands	**ISO 13485:2016** Design, development and manufacturing of clinical chemistry analyzers, contract manufacturing of erythrocyte sedimentation rate analyzers and warehousing of erythrocyte sedimentation rate tubes for the in vitro diagnostic investigation of samples of human origin.

UKAS MANAGEMENT SYSTEMS
001

ELITech Clinical Systems
Zone industrielle
61500 Sées - France
Tél : +33 (0)2 33 81 21 00 Fax : +33 (0)2 22 28 77 51
www.elitechgroup.com

ELITechGroup
EMPOWERING IVD

DECLARATION DE CONFORMITE CE

Nous, ELITech Clinical Systems SAS, zone industrielle 61500 SEES France, déclarons sous notre seule responsabilité que les réactifs référencés dans la liste ci-jointe (2 pages), sont conformes aux exigences essentielles des annexes I et III de la Directive Européenne 98/79/CE relative aux dispositifs médicaux de diagnostic *in vitro* et au code de la santé publique.

Ces dispositifs sont classés dans la catégorie « autre dispositif » puisqu'ils n'appartiennent ni à la liste A et liste B de l'annexe II et ni à la classe des autotests.

Cette déclaration est basée sur le contenu de chaque dossier technique et s'appuie sur la certification de notre système qualité selon la norme NF EN ISO 13485 : 2016 (Certification valable jusqu'au 27 juillet 2023).

DECLARATION OF EC CONFORMITY

We, ELITech Clinical Systems SAS, Zone Industrielle 61500 SEES France, hereby certify, under our own responsibility, that the reagents such as listed attached (2 pages) , conform to the essential requirements of appendices I and III of European Directive 98/79/EC, relating to in vitro diagnostic medical devices and to the public health code.

These devices are classified in the "other device" category since they do not belong neither to list A or list B of annex II nor to self-testing class.

This declaration is based on the contents of each technical file and is supported by the certification of our quality system according to the standard NF EN ISO 13485 : 2016 (Certification valid until July 27th , 2023).

DECLARACIÓN CE DE CONFORMIDAD

Nosotros, ELITech Clinical Systems SAS, Zone Industrielle 61500 SEES France, declaramos bajo nuestra única responsabilidad que los reactivos referenciados en la lista adjunta (2 páginas), son conformes con los requisitos esenciales de los anexos I y III de la Directiva Europea 98/79/CE sobre dispositivos médicos para diagnóstico in vitro y el código de salud pública.

Estos dispositivos se clasifican en la categoría "otro dispositivo", ya que no pertenecen a la lista A ni a la lista B del anexo II, tampoco a la clase de autodiagnóstico.

Esta declaración se basa en el contenido de cada expediente técnico y está respaldado por la certificación de nuestro sistema de calidad según la norma NF EN ISO 13485 : 2016 (Certificación válida hasta el 27 de Julio 2023).

Sées, le 12 Mai 2021

Valérie LAMBERT,
Responsable des Affaires Réglementaires
Regulatory Affairs Manager
Responsable de los Asuntos Reglementarios

ELITech Clinical Systems SAS
Zone Industrielle
61500 SEES - France
Tél. : +33(0)2 33 81 21 00 - Fax : +33(0)2 33 28 77 51
SIRET 318 365 228 00036

Cécile GOUBAULT,
Directeur Général Délégué
Managing Director
Directora General

REACTIFS - REAGENTS - REACTIVOS	RÉFÉRENCES - REFERENCES - REFERENCIAS	Code GMDN
Metabolites divers / Miscellaneous metabolites		
ALBUMIN	ALBU-0600/0700/0250/M830	53597
ALBUMIN ENVOY	ALBU-0850	
BILIRUBIN DIRECT 4+1	BIDI-0600/0250	53233
BILIRUBIN TOTAL 4+1	BITO-0600/0250	53229
BILIRUBIN TOTAL & DIRECT 4+1	BITD-0600	53229/53233
CREATININE ENVOY	CRSL-0850	53250
CREATININE JAFFE	CRCO-0600/0700	53251
CREATININE PAP	CRSL-M490	53250
CREATININE PAP SL	CRSL-0630/0250	
DIRECT BILIRUBIN	BIDI-M430	53233
DIRECT BILIRUBIN ENVOY	BIDV-0850	53233
GLUCOSE ENVOY	GPSL-0850	53301
GLUCOSE HK	GHSL-M490	
GLUCOSE HK SL	GHSL-0600/0250	
GLUCOSE PAP	GPSL-M690	
GLUCOSE PAP SL	GPSL-0507/0500/0707/0700/0250/0455/0497	
LACTATE	LACT-0100	53342
MICROPROTEIN PLUS	PRTU-0600/0250	53481
PHOSPHORUS	PHOS-0600/0230/M430	59123
PHOSPHORUS ENVOY	PHOS-0850	
TOTAL BILIRUBIN	BITO-M430	53229
TOTAL BILIRUBIN ENVOY	BITV-0850	53229
TOTAL PROTEIN	PROB-M830	53985
TOTAL PROTEIN ENVOY	PROB-0850	
TOTAL PROTEIN PLUS	PROB-0600/0700/0250	
UREA	URSL-M830	53587
UREA ENVOY	URSL-0850	
UREA UV SL	URSL-0427/0420/0500/0507/0250/0455	
URIC ACID	AUML-M830	53583
URIC ACID ENVOY	AUVD-0850	
URIC ACID MONO SL	AUML-0497/0427/0420/0500/0507/0707/0250	
URIC ACID SL	AUSL-0250	
URINE PROTEIN	PRTU-M230	53481
Enzymes / Enzymes		
ALP (DEA) SL	PASL-0400/0420/0230	52928
ALP ENVOY	PIVD-0850	
ALP IFCC	ALPI-0230	
ALT ENVOY	ALSL-0850	52923
ALT/GPT	ALSL-M490	
ALT/GPT 4+1 SL	ALSL-0410/0430/0510/0250/0455	
AMYLASE	AMSL-M430	52940
AMYLASE ENVOY	AMSL-0850	
AMYLASE SL	AMSL-0390/0400/0230	
AST/GOT	ASSL-M490	52954
AST ENVOY	ASVD-0850	
AST/GOT 4+1 SL	ASSL-0410/0430/0510/0250/0455	
CHOLINESTERASE	CHES-0053	52971
CK ENVOY	CKSL-0850	53003
CK-MB ENVOY	CMSL-0850	52994
CK-MB SL / CKMB	CMSL-0410/0430/0230	
CK NAC	CKSL-M230	53003
CK NAC SL	CKSL-0410/0430/0230	
GAMMA-GT	GISL-M230	53027
GAMMA-GT PLUS SL	GISL-0400/0420/0250	
GGT ENVOY	GISL-0850	
LDH ENVOY	LLSL-0850	53072
LDH IFCC	LLSL-M230	
LDH-L SL	LLSL-0400/0420/0230	
LIPASE	LPSL-0250	53108
LIPASE ENVOY	LPSL-0850	
LIPASE SL	LPSL-0230	
Electrolytes / Oligo-élements / Electrolytes / Trace-elements		
CALCIUM ARSENAZO	CALA-0600/0250/M430	45789
CALCIUM ENVOY	CALA-0850	
CHLORIDE	CHLO-0600/0250	60037
IRON ENVOY	FEFE-0850	54758
IRON FERENE	FEFE-0230/0600/M230	
MAGNESIUM ENVOY	MAGX-0850	46795
MAGNESIUM XB	MGXB-0250/0600/M430	
MAGNESIUM XYLIDYL	MAGX-0230/0600	
Lipides / Lipids		
CHOLESTEROL	CHSL-M690	53359
CHOLESTEROL ENVOY	CHSL-0850	
CHOLESTEROL HDL SL 2G	HDLL-0230/0380/0390	53391
CHOLESTEROL LDL SL 2G	LDLL-0230/0380/0390	53395
CHOLESTEROL SL	CHSL-0507/0500/0700/0707/0250/0455/0497	53359
HDL CHOLESTEROL	CHDL-0250/0600/M330	53391
HDL CHOLESTEROL ENVOY	HDLL-0850	
LDL CHOLESTEROL	CLDL-0250/M330	53395
LDL CHOLESTEROL ENVOY	LDLL-0850	
TRIGLYCERIDES	TGML-M690	53460
TRIGLYCERIDES ENVOY	TGML-0850	
TRIGLYCERIDES MONO SL NEW	TGML-0427/0425/0515/0700/0517/0707/0497	
TRIGLYCERIDES SL	TGML-0250/0455	

V10
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REACTIFS - REAGENTS - REACTIVOS	RÉFÉRENCES - REFERENCES - REFERENCIAS	Code GMDN
Contrôles-Calibrants-Standards / Controls-Calibrators-Standards		
CHOLESTEROL HDL 2G CALIBRATOR	HDLL-0011/0041	44696
CHOLESTEROL LDL 2G CALIBRATOR	LDLL-0011/0041	41728
CHOLESTEROL Standard 200 mg/dL	CHOL-0055	44698
CK-MB CONTROL	CKMB-0900	44693
ELICAL 2	CALI-0550	47868
ELITROL I	CONT-0060	47869
ELITROL II	CONT-0160	
GLUCOSE Standard 100 mg/dL	GLUP-0055	41818
HDL LDL CALIBRATOR	HLCA-0041	47868
ISE CONTROL I	ISCT-0046	47869
ISE CONTROL II	ISCT-0047	
MICROPROTEIN PLUS Standard 100 mg/dL	PRTU-0022	53482
TRIGLYCERIDES Standard 200 mg/dL	TRIG-0055	44702
UREA Standard 50 mg/dL	URUV-0055	53588
URIC ACID Standard 6 mg/dL	ACUR-0055	44704
Protéines spécifiques / Specific proteins		
ANTI-STREPTOLYSIN O	ASLO-0250	59055
CRP IP	ICRP-0400/M230	53705
CRP IP CALIBRATOR SET	ICRP-0043	41838
CRP IP CONTROL I	ICRP-0046	41839
CRP IP CONTROL II	ICRP-0047	
CRP WR	CRPW-0230	53705
CRP WR CALIBRATOR SET	CRPW-0043	41838
CRP WR CONTROL	CRPW-0045	41839
CRP WR ENVOY	CRPW-0850	53705
FERRITIN	IFRT-0230	53718
FERRITIN CALIBRATOR	IFRT-0042	41927
HAPTOGLOBIN IP	IHAP-0400	53737
HbA1c	HBAC-0240	59090
HbA1c CALIBRATOR SET	HBAC-0043	53315
HbA1c CONTROL L + H	HBAC-0049	44435
IgA IP	IIGA-0400	53760
IgG IP	IIGG-0400	53787
IgM IP	IIGM-0400	53795
µALBUMIN IP	IMAL-0400	53475
µALBUMIN IP CALIBRATOR SET	IMAL-0043	53477
µALBUMIN IP CONTROL I	IMAL-0046	53478
µALBUMIN IP CONTROL II	IMAL-0047	
OROSOMUCOID IP	IORO-0400	53606
PREALBUMIN IP	IPAL-0400	53957
PROTEIN IP CALIBRATOR SET	IPRO-0043	53593
RF CALIBRATOR	IRFA-0042	42230
RHEUMATOID FACTOR	IRFA-0230	55111
RHEUMATOLOGY CONTROL I	IRCT-0046	47869
RHEUMATOLOGY CONTROL II	IRCT-0047	
TRANSFERRIN IP	ITRF-0400	59041
Vitamines/Vitamins		
VITAMIN D	VITD-0250	54476
VITAMIN D CALIBRATOR SET	VITD-0043	54474
VITAMIN D CONTROL SET	VITD-0049	54475
ISE Solutions pour électrodes selectives d'ions / ISE Solutions for ion-selective electrodes		
ISE BASELINE SOLUTION ENVOY	ISBA-0850	59238
ISE CALIBRATORS	ISCA-0250	52867
ISE CALIBRATOR ENVOY	ISCV-0850	
ISE CLEANER/CONDITIONER	ISCC-0280	59058
ISE DILUENT	ISDI-0250	58237
ISE DILUENT ENVOY	ISDV-0850	
ISE REFERENCE SOLUTION	ISRS-0800	59238
ISE REFERENCE SOLUTION ENVOY	ISRS-0850	
Solutions de lavage pour les équipements ELITech Clinical Systems / Cleaning solutions for ELITech Clinical Systems Equipments		
ACID SOLUTION for ELITech Clinical Systems Analyzers	SLHC-5900	59058
SYSTEM CLEANING SOLUTION for ELITech Clinical Systems Analyzers	SLNA-5900	59058
SYSTEM SOLUTION	SLSY-5905	58236
SYSTEM SOLUTION for ELITech Clinical Systems Analyzers	SLSY-5900	
WASH SOLUTION A	SOLA-M163	59058
WASH SOLUTION B	WASH SOLUTION B	59058
Tests d'agglutination / Agglutination tests		
CRP LATEX	LXCR-0112	53707

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CG

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To: Whom it May Concern

Regulatory status of parts & accessories

As mentioned on the current Declarations of Conformity of our Clinical Chemistry Analyzers also the accessories conform to the provisions of the EU Directive on In Vitro Diagnostic Medical Devices (98/79/EC). This applies to the parts and accessories as mentioned in the attached list.

'IVD accessory' means an article which, whilst not being an IVD medical device, is intended specifically by its manufacturer to be used together with an IVD device to enable that IVD device to be used in accordance with its intended purpose.

ELITechGroup B.V.

Adriaan P. Intveld
Manager Quality Assurance & Regulatory Affairs

Part number	Description	IVD medical device	IVD accessory	general laboratory use	spare part	supporting part
1540-001	Anti-Slip sheet					✓
2206-007	Cooling Liquid (1 L)					✓
3062-021	Sample cup (1000 pcs)		✓			
3062-033	Sample tube 6 ml (500 pcs)					✓
3062-040	Water container 10 L					✓
3062-041	Water container 5 L					✓
3066-155	Syringe 100 µl		✓			
3066-156	Syringe 1 ml		✓			
3069-040	Keyboard Dust cover					✓
3069-047	Keyboard Dust cover					✓
3070-518	Cap holder					✓
3070-538	Cap rotor Left					✓
3070-539	Cap rotor right					✓
3201-002	Dichromate 8 Abs (25ml)		✓			
3365-192	USB Stick					✓
3374-003	Mains cable (USA)					✓
3374-059	Pumpunit cable		✓			
3374-066	Mains cable					✓
3374-097	Serial Null-modem cable					✓
3374-286	USB Extension cable					✓
4804-038	Reagent identification Disc					✓
6001-826	Diluted Waste container		✓			
6001-827	Concentrated Waste container		✓			
6001-860	Water container		✓			
6001-861	Tube assy (analyser)		✓			
6001-872	Tube assy (cooling unit)		✓			
6002-102	Assorter unit				✓	
6002-386	System software on CD		✓			
6002-706	Reaction Rotor set (3 pcs)		✓			
6002-726	System Disc		✓			
6002-817	Bottle 30 ml (20 pcs)		✓			
6002-818	Bottle 15 ml (20 pcs)		✓			
6002-904	Water container 5 L		✓			
6002-910	Assorter unit				✓	
6002-913	External tubing		✓			
6003-074	System software on USB stick		✓			
6003-444	Diluted Waste Container 5 L		✓			
6003-466	Keyboard Support option					✓
6003-797	CW Waste Container 2 L		✓			
6003-808	Assorter unit				✓	

ELITechGroup VITAL SCIENTIFIC

Instrument Training

Vital Scientific BV hereby declares that the participant has attended a four days seminar for service engineers and the participant is now a certified engineer for the declared instruments.

Participant: Mr. S. Sorocovici

Company: Global Biomarketing Group-Moldova SRL
Moldova

Instrument: Vitalab: XL Series
E Series
Junior Series
Dry ISE
Micro Series
ProXS

Date of training: April 20th – April 23rd, 2010

System Support Manager:
Jan Oostendorp

System Support Engineer:
Frank v.d. Korput

ELITechGroup
EMPOWERING IVD

ELICAL 2

CALI
CALI-0550 : 4 x 3 mL

FTCE-CALI2-5-v6 (05/2021)

Français - FR

USAGE PRÉVU

Ce dispositif de diagnostic *in vitro* est destiné à la calibration des tests quantitatifs ELITech Clinical Systems listés dans la fiche de valeurs.
Ce dispositif de diagnostic *in vitro* est uniquement destiné aux professionnels.

COMPOSITION

- Produit sous forme lyophilisée préparé à partir de sérum humain contenant des additifs chimiques et biologiques.
- Azide de sodium < 0.1 % (p/p)
- Les concentrations pour chaque analyte à doser sont spécifiques à chaque lot.

MATÉRIELS REQUIS MAIS NON FOURNIS

- Réactifs ELITech Clinical Systems listés dans la fiche de valeurs.
- Equipement général de laboratoire.

TRACABILITE

La traçabilité est indiquée dans la fiche de valeurs incluse dans le coffret.

PRÉCAUTIONS D'EMPLOI ET MISES EN GARDE

- Chaque unité de sang humain utilisée pour la fabrication de ces produits a été testée et trouvée négative/non-réactive pour la présence d'HBsAg, HCV et HIV1/2. Les méthodes utilisées étaient approuvées par la FDA ou autorisées en conformité à la Directive Européenne 98/79 / CE, Annexe II, liste A. Cependant le risque d'infection ne pouvant être exclu avec certitude par aucune méthode, ces produits doivent être manipulés comme étant potentiellement infectieux. En cas d'exposition, suivre les directives des autorités sanitaires compétentes.
- Prendre des précautions lors de la manipulation de flacons de verre brisés, car les bords tranchants peuvent blesser l'utilisateur.
- Ces produits contiennent de l'azide de sodium qui peut réagir avec le plomb ou le cuivre et former des azides métalliques potentiellement explosifs. Lors de l'élimination de ces réactifs toujours rincer abondamment avec de l'eau pour éviter l'accumulation d'azides.
- Respecter les précautions d'usage et les bonnes pratiques de laboratoire.
- Utiliser du matériel de laboratoire propre ou à usage unique afin d'éviter toute contamination.
- Consulter la fiche de données de sécurité (FDS) pour une manipulation appropriée.

TRAITEMENT DES DÉCHETS

L'élimination de tous les déchets doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales (veuillez-vous référer à la fiche de données de sécurité (FDS)).

PRÉPARATION

- Ouvrir avec précaution le flacon en évitant la perte de poudre lyophilisée.
- Ajouter **précisément 3 mL d'eau distillée ou désionisée**.
- Reboucher le flacon avec soin et dissoudre le contenu complètement dans les 30 minutes en remuant délicatement le flacon et en évitant la formation de mousse.

DÉTÉRIORATION DU PRODUIT

- Le produit peut présenter un aspect légèrement trouble après reconstitution. Cela n'a aucun effet sur les performances du produit. Toute présence de particules serait le signe d'une détérioration.
- Ne pas utiliser le produit s'il y a des signes évidents de détérioration biologique ou chimique (ex : particules après reconstitution).
- Un flacon endommagé peut avoir un impact sur les performances du produit. Ne pas utiliser le produit si les flacons présentent des signes physiques de détérioration (par exemple, fuite).

STABILITÉ

Avant reconstitution :
- Stocker à 2-8 °C et à l'abri de la lumière.
- Ne pas utiliser après la date d'expiration indiquée sur l'étiquette du flacon.

Après reconstitution :
- Ces produits doivent être immédiatement et correctement refermés afin d'éviter toute contamination ou évaporation.

- Stabilité des constituants :
<u>Entre 15 et 25 °C</u> : 8 heures
<u>Entre 2 et 8 °C</u> : 2 jours
<u>Entre -25 et -15 °C</u> : 4 semaines (ne congeler qu'une seule fois)

Exceptions :
- Stabilité de la bilirubine totale (à conserver à l'abri de la lumière) :
<u>Entre 15 et 25 °C</u> : 6 heures
<u>Entre 2 et 8 °C</u> : 1 jour
<u>Entre -25 et -15 °C</u> : 2 semaines (ne congeler qu'une seule fois)
- Stabilité de la bilirubine directe (à conserver à l'abri de la lumière) :
<u>Entre 15 et 25 °C</u> : 3 heures
<u>Entre 2 et 8 °C</u> : 8 heures
<u>Entre -25 et -15 °C</u> : 2 semaines (ne congeler qu'une seule fois)

***Note** : Conserver les flacons bien fermés et à l'abri de la lumière.*

PROCÉDURE

Pour utiliser ELICAL 2, suivre la procédure décrite dans la fiche technique du réactif ELITech Clinical Systems utilisé.

LIMITATIONS

L'utilisation de ELICAL 2 a été validée avec les systèmes ELITech (Automates et réactifs listés dans la fiche de valeurs).
L'utilisation sur un autre système doit être validée par le laboratoire.

VALEURS

Les concentrations sont indiquées dans la fiche de valeurs incluse dans le coffret.
Pour les utilisateurs d'automates Selectra permettant l'import de tests, de calibrants et de contrôles, utiliser le code barre correspondant, disponible sur la fiche de valeurs.

DECLARATION DES INCIDENTS GRAVES

Veuillez notifier au fabricant (par l'intermédiaire de votre distributeur) et à l'autorité compétente de l'Etat membre de l'union européenne dans lequel l'utilisateur et/ou le patient est établi, les cas d'incident grave survenu en lien avec le dispositif.
Pour les autres juridictions, la déclaration d'incident grave doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales.
En signalant les incidents graves, vous contribuez à fournir davantage d'informations sur la sécurité des dispositifs médicaux de diagnostic *in vitro*.

TECHNICAL ASSISTANCE

Contacter votre distributeur local ou ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

English - EN

INTENDED USE

This *in vitro* diagnostic device is intended for the calibration of ELITech Clinical Systems quantitative tests listed in the value sheet.
This *in vitro* diagnostic device is for professional use only.

COMPOSITION

- Lyophilized product prepared from human serum spiked with chemical and biological additives.
- Sodium azide < 0.1 % (w/w)
- Concentrations for each analyte to test are lot-specific.

MATERIALS REQUIRED BUT NOT PROVIDED

- ELITech Clinical Systems reagents listed in the value sheet.
- General Laboratory equipment.

TRACEABILITY

The traceability is indicated in the value sheet enclosed in the kit.

PRECAUTIONS FOR USE AND WARNINGS

- Each unit of human blood used in the manufacture of these products was tested and found to be negative/non-reactive for the presence of HbsAg, HCV and HIV1/2. The methods used were FDA approved or cleared in compliance with European Directive 98/79/EC, Annex II, List A. Nevertheless, since the risk of infection cannot be fully excluded these products must be handled as potentially infectious. In case of exposure, follow the guidelines of the competent health authorities.
- Take precautions when handling broken glass vials as sharp edges can injure the user.
- These products contain sodium azide which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of these reagents always flush with copious amounts of water to prevent azide buildup.
- Take normal precautions and adhere to good laboratory practice.
- Use clean or single use laboratory equipment only to avoid contaminations.
- Consult Safety Data Sheet (SDS) for a proper handling.

WASTE MANAGEMENT

Disposal of all waste material should be in accordance with local, state and federal regulatory requirements (please refer to the Safety Data Sheet (SDS)).

PREPARATION

- Carefully open the vial, avoiding the loss of lyophilizate.
- Add **in exactly 3 mL of distilled or deionized water**.
- Carefully close the vial and dissolve the contents completely within 30 minutes by occasional gentle stirring avoiding the formation of foam.

PRODUCT DETERIORATION

- The product may present a slightly hazy appearance after reconstitution. This has no effect on the performances of the product. All presence of particules would indicate deterioration.
- Do not use the product if there is visible evidence of contamination or damage (e.g. particle matter after reconstitution).
- Damage to the container may impact on product performance. Do not use the product if there is physical evidence of deterioration (e.g. leakages).

STABILITY

Prior to reconstitution :
- Stored at 2-8 °C and protected from light.
- Do not use after expiration date indicated on the vial label.

After reconstitution :
- These products should be immediately and tightly capped to prevent contamination and evaporation.

- Stability of the components:
<u>Between 15 and 25 °C</u> : 8 hours
<u>Between 2 and 8 °C</u> : 2 days
<u>Between -25 and - 15 °C</u> : 4 weeks (when frozen once)

Exceptions:
- Stability of total bilirubin (when stored protected from light):
<u>Between 15 and 25 °C</u> : 6 hours
<u>Between 2 and 8 °C</u> : 1 day
<u>Between -25 and -15 °C</u> : 2 weeks (When frozen once)
- Stability of direct bilirubin (when stored protected from light):
<u>Between 15 and 25 °C</u> : 3 hours
<u>Between 2 and 8 °C</u> : 8 hours
<u>Between -25 and -15 °C</u> : 2 weeks (when frozen once)

***Note**: Store vials tightly capped and protected from light.*

PROCEDURE

To use ELICAL 2, follow the procedure described in the instructions for use of the ELITech Clinical Systems reagent used.

LIMITATIONS

Using ELICAL 2 has been validated with the ELITech systems (Analyzers and reagents listed in the value sheet).
Using any other system should be validated by the laboratory.

VALUES

The concentrations are indicated in the value sheet enclosed in the kit.
For users of Selectra instruments allowing data import for tests, calibrators and controls, use corresponding barcode, available on the value sheet.

DECLARATION OF SERIOUS INCIDENT

Please notify the manufacturer (through your distributor) and competent authority of the Member State of the european union in which the user and/or the patient is established, of any serious incident that has occurred in relation to the device. For other jurisdictions, the declaration of serious incident should be in accordance with local, state and federal regulatory requirements.
By reporting a serious incident, you provide information that can contribute to the safety of *in vitro* medical devices.

ASSISTANCE TECHNIQUE

Contact your local distributor or ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

Español - ES

USO PREVISTO

Este dispositivo de diagnóstico *in vitro* está diseñado para la calibración de las pruebas cuantitativas ELITech Clinical Systems listadas en la hoja de valores.
Este dispositivo de diagnóstico *in vitro* esta destinado unicamente para los profesionales.

COMPOSICIÓN

- Producto liofilizado preparado a partir de suero humano enriquecido con aditivos químicos y biológicos.
- Azida sódica < 0.1 % (p/p)
- Las concentraciones de cada analito a analizar son específicas a cada lote.

MATERIALES REQUERIDOS PERO NO INCLUIDOS

- Reactivos ELITech Clinical Systems listados en la hoja de valores.
- Equipo de laboratorio de uso general.

TRAZABILIDAD

La trazabilidad se indica en la ficha de valores incluida en el kit.

PRECAUCIONES DE USO Y ADVERTENCIAS

- Cada unidad de sangre humana utilizada en la fabricación de estos productos fue analizada y resultó ser negativa / no reactiva ante la presencia de HbsAg, VHC y VIH1/2. Los métodos utilizados fueron aprobados de conformidad por la FDA y con la Directiva Europea 98/79 / CE, Anexo II, Lista A. Sin embargo, dado que el riesgo de infección no puede excluirse por completo, estos productos deben manejarse como potencialmente infecciosos. En caso de exposición, siga las indicaciones de las autoridades sanitarias competentes.
- Tenga precauciones al manipular viales de vidrio roto, ya que los bordes afilados pueden dañar al usuario.
- Los productos contienen azida sódica que puede reaccionar con el plomo o el cobre de la tubería y potencialmente formar azidas metálicas explosivas. Cuando se eliminen los reactivos, enjuague con agua abundantemente para prevenir la acumulación de azidas.
- Respetar las precauciones de uso y las buenas prácticas de laboratorio.
- Para evitar contaminaciones utilizar equipo nuevo o completamente limpio.
- Consulte la Hoja de Datos de Seguridad (SDS) para un manejo adecuado.

TRATAMIENTO DE LOS RESIDUOS

Todos los materiales de desecho deben eliminarse de acuerdo con los requisitos regulatorios locales, estatales y federales (dirijase a la hoja de seguridad (SDS)).

PREPARACIÓN

- Destapar cuidadosamente el frasco con el fin de evitar la pérdida de material liofilizado.
- Agregar **exactamente 3 mL de agua destilada o de agua desionizada.**
- Cierre cuidadosamente el vial y disuelva el contenido por completo durante 30 minutos mezclando suavemente para evitar la formación de espuma.

DETERIORACIÓN DEL PRODUCTO

- El producto puede presentar un aspecto ligeramente turbio después de reconstitución, esto no afecta el rendimiento del producto. La presencia de partículas es un signo de deterioro.
- No utilice el producto si este presenta signos evidentes de contaminación o deterioro (p. ej, partículas después de reconstitución).
- Un frasco dañado puede tener un impacto en el rendimiento del producto. No utilice el producto si este tiene signos físicos de deterioro (p. ej, fugas).

ESTABILIDAD

Antes de la reconstitución :
- Conservar a 2-8 °C y protegidos de la luz.
- No utilice después de la fecha de caducidad indicada en la etiqueta del frasco.

Después de reconstitución :
- Estos productos deben ser bien cerrados de inmediato para evitar contaminación y evaporación.

- Estabilidad de los componentes:
<u>Entre 15 y 25 °C</u> : 8 horas
<u>Entre 2 y 8 °C</u> : 2 días
<u>Entre -25 y -15 °C</u> : 4 semanas (no congelar más de una vez)

Excepciones:
- Estabilidad de la bilirrubina total (proteger de la luz) :
<u>Entre 15 y 25 °C</u> : 6 horas
<u>Entre 2 y 8 °C</u> : 1 día
<u>Entre -25 y -15 °C</u> : 2 semanas (no congelar más de una vez)
- Estabilidad de la bilirrubina directa (proteger de la luz) :
<u>Entre 15 y 25 °C</u> : 3 horas
<u>Entre 2 y 8 °C</u> : 8 horas
<u>Entre -25 y -15 °C</u> : 2 semanas (no congelar más de una vez)

Nota : Conservar los frascos bien cerrados y protegidos de la luz.

PROCEDIMIENTO

Para utilizar ELICAL 2, siga el procedimiento descrito en el inserto del reactivo ELITech Clinical Systems utilizado.

LIMITACIONES

El uso de ELICAL 2 ha sido validado con los sistemas ELITech (equipos y reactivos enumerados en la hoja de valores).
El uso de cualquier otro sistema debe ser validado por el laboratorio.

VALORES

Las concentraciones son indicadas en la ficha de valores incluida en el kit.
Para usuarios de los equipos Selectra que permiten la importación de pruebas, calibradores y controles, use el código de barras correspondiente, disponible en la hoja de valores.

DECLARACIÓN DE INCIDENTES GRAVES

Por favor notifique al fabricante (por medio de su distribuidor) y autoridad competente del Estado miembro de la Unión Europea en donde el usuario o paciente radique, de cualquier incidente grave que se produzca con relación al dispositivo.
Para otras jurisdicciones, la declaración de incidentes graves debe realizarse
de acuerdo con los requisitos reglamentarios locales, estatales y federales.
Reportando incidentes graves usted contribuye a proporcionar más información sobre la seguridad del dispositivo médico de diagnóstico *in vitro*.

ASISTENCIA TÉCNICA

Contacte a su distribuidor local o con ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

Português - PT

UTILIZAÇÃO PREVISTA

Este dispositivo de diagnóstico *in vitro* é destinado a calibração dos testes quantitativos ELITech Clinical Systems listados na folha de valores.
Este dispositivo de diagnóstico *in vitro* é apenas para uso profissional.

COMPOSIÇÃO

- Produto liofilizado preparado a partir de soro humano enriquecido com aditivos químicos e biológicos.
- Azida de sódio < 0.1 % (p/p)
- As concentrações de cada analito a ser testado são específicas de cada lote.

MATERIAIS NECESSÁRIOS MAS NÃO FORNECIDOS

- ELITech Clinical Systems reagentes listados na folha de valores.
- Equipamento geral de laboratório.

RASTREABILIDADE

A rastreabilidade é indicada na folha de valores incluída no kit.

PRECAUÇÕES DE USO E AVISOS

- Cada unidade de sangue humano utilizada na fabricação desses produtos foi testada e se mostrou negativa / não reativa para a presença de HbsAg, HCV e HIV1 / 2. Os métodos utilizados foram aprovados e liberados pela FDA em conformidade com a Diretiva Européia 98/79 / EC, Anexo II, Lista A. No entanto, como o risco de infecção não pode ser totalmente excluído, esses produtos devem ser manuseados como potencialmente infecciosos. Em caso de exposição, siga as orientações das autoridades sanitárias competentes.
- Tome precauções ao manusear frascos de vidro quebrados, pois bordas afiadas podem ferir o usuário.
- Os produtos contém azida de sódio que pode reagir com o chumbo ou cobre das canalizações formando azidas metálicas explosivas. Ao manusear estes reagentes lave as mãos sempre com grandes quantidades de água para evitar a produção de azida.
- Respeitar as precauções de utilização e as boas práticas de laboratório.
- Utilizar material de laboratório limpo ou destinado a uma única utilização de modo a evitar qualquer contaminação.
- Consulte a ficha de dados de segurança (SDS) para obter um manuseio adequado.

TRATAMENTO DOS RESÍDUOS

O descarte de todo material residual deve estar de acordo com os requisitos regulamentares locais, estaduais e federais (consulte a Ficha de dados de segurança (SDS)).

PREPARAÇÃO

- Abrir cuidadosamente o frasco, evitando a perda de pó liofilizado.
- Acrescentar **exatamente 3 mL de água destilada ou deionizada**.
- Feche cuidadosamente o frasco para injetáveis e dissolva completamente o conteúdo dentro de 30 minutos, mexendo suave e ocasionalmente, evitando a formação de espuma.

DETERIORAÇÃO DO PRODUTO

- O produto pode apresentar uma aparência um pouco turva após a reconstituição. Isto não tem efeito sobre o desempenho do produto. A presença de partículas indica deterioração.
- Não use o produto se houver evidência visível de contaminação ou dano (por exemplo, partículas após a reconstituição).
- Não utilizar o calibrador caso haja danos na embalagem que possam causar algum efeito sobre o desempenho do produto (ex. vazamentos).

ESTABILIDADE

Antes da reconstituição:
- Conservado a 2-8 °C e ao abrigo da luz.
- Não utilizar após as datas de validade indicadas nos rótulos
dos frascos.

Após a reconstituição:
- Esses produtos devem ser tampados imediatamente e firmemente para evitar contaminação e evaporação.

- Estabilidade dos constituintes:
<u>Entre 15 e 25 °C</u> : 8 horas
<u>Entre 2 e 8 °C</u> : 2 dias
<u>Entre -25 e -15 °C</u> : 4 semanas (congelar apenas uma única vez)

Excepções:
- Estabilidade da bilirrubina total (a conservar ao abrigo da luz) :
<u>Entre 15 e 25 °C</u> : 6 horas
<u>Entre 2 e 8 °C</u> : 1 dia
<u>Entre -25 e -15 °C</u> : 2 semanas (congelar apenas uma única vez)
- Estabilidade da bilirrubina direta (a conservar ao abrigo da luz) :
<u>Entre 15 e 25 °C</u> : 3 horas
<u>Entre 2 e 8 °C</u> : 8 horas
<u>Entre -25 e -15 °C</u> : 2 semanas (congelar apenas uma única vez)

***Observação**: Conservar os frascos bem fechados e ao abrigo da luz.*

PROCEDIMENTO

Para usar ELICAL 2, siga o procedimento descrito nas instruções de uso do reagente ELITech Clinical Systems utilizado.

LIMITAÇÕES

O uso de ELICAL 2 foi validado com o sistema ELITech (analisador e reagentes listados na folha de valores).
O uso de qualquer outro sistema deve ser validado pelo laboratório.

VALORES

As concentrações são indicadas na folha de valores colocada no kit.
Para usuários de instrumentos Selectra que permitem a importação de dados para testes, calibradores e controles, se o código de barras correspondente, disponível na folha de valores.

DECLARAÇÃO DE INCIDENTE GRAVE

Notifique o fabricante (através do seu distribuidor) e a autoridade competente da União Européia em que o usuário e/ou o paciente está estabelecido, de qualquer incidente grave que tenha ocorrido em relação ao dispositivo.
Para outras jurisdições, a declaração de incidente grave deve estar de acordo com as normas locais, requisitos regulatórios estaduais e federais.
Ao relatar um incidente grave, você fornece informações que podem contribuir para o segurança de dispositivos médicos *in vitro*.

ASSISTÊNCIA TÉCNICA

Entre em contato com o seu distribuidor local ou com a ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

Ελληνικά - EL

ΠΡΟΒΛΕΠΟΜΕΝΗ ΧΡΗΣΗ

Τα εν λόγω *in vitro* διαγνωστικά προορίζονται για τον ποιοτικό προσδιορισμό της απόδοσης των ποσοτικών τεστ της ELITech Clinical Systems καταγεγραμμένα στο φύλλο τιμών.
Τα εν λόγω *in vitro* διαγνωστικά προορίζονται μόνο για επαγγελματική χρήση.

ΣΥΣΤΑΣΗ

- Τα λυοφιλοποιημένα προϊόντα που ετοιμάζονται για ανθρώπινο ορό είναι δεσμευμένα με χημικά και βιολογικά πρόσθετα.
- Αζίδια του νατρίου < 0.1 % (w/w)
- Οι ελεγχόμενες συγκεντρώσεις για κάθε αναλυτή είναι συγκεκριμένες σύμφωνα με την παρτίδα.

ΑΠΑΙΤΟΥΜΕΝΑ ΥΛΙΚΑ ΠΟΥ ΔΕΝ ΣΥΜΠΕΡΙΛΑΜΒΑΝΟΝΤΑΙ

- Αντιδραστήρια της ELITech Clinical Systems καταγεγραμμένα στο φύλλο τιμών.
- Γενικός Εργαστηριακός Εξοπλισμός.

ΙΧΝΗΛΑΣΙΜΟΤΗΤΑ

Η ιχνηλασιμότητα ορίζεται στο φύλλο τιμών που συμπεριλαμβάνεται στο κιτ.

ΠΡΟΦΥΛΑΞΕΙΣ ΧΡΗΣΗΣ ΚΑΙ ΠΡΟΕΙΔΟΠΟΙΗΣΕΙΣ

- Κάθε μονάδα ανθρώπινου αίματος που χρησιμοποιείται για την Παρασκευή αυτών των προϊόντων έχει ελεγχθεί και βρεθεί αρνητική/ μη-αντιδρούσα στην παρουσία HbsAg, HCV και HIV1/2. Οι μέθοδοι που χρησιμοποιούνται είναι εγκεκριμένες από τον FDA ή σύμφωνες με την Ευρωπαϊκή Οδηγία 98/79/EC, Παράρτημα II, Λίστα A. Μολονότι και εφόσον ο κίνδυνος μόλυνσης δεν μπορεί να αποκλειστεί εντελώς, τα εν λόγω προϊόντα πρέπει να χειρίζονται ως πιθανώς μολυσματικά. Σε περίπτωση έκθεσης, ακολουθείστε τις οδηγίες των αρμόδιων υγειονομικών αρχών.
- Πάρτε προφυλάξεις όταν χειρίζεστε σπασμένα γυάλινα φιαλίδια καθώς οι αιχμηρές γωνίες μπορεί να τραυματίσουν τον χρήστη.
- Τα συγκεκριμένα προϊόντα περιέχουν αζίδια του νατρίου που μπορεί να αντιδράσει με το χαλκό ή το μόλυβδο των σωληνώσεων δημιουργώντας πιθανά εκρηκτικά αζωτούχα μέταλλα. Όταν απορρίπτονται στην αποχέτευση τα αντιδραστήρια αυτά, να ξεπλένετε πάντοτε με άφθονο νερό για την αποφυγή συσσώρευσης αζιδίων.
- Λάβετε συνήθεις προφυλάξεις και εφαρμόστε καλή εργαστηριακή πρακτική.
- Χρησιμοποιήστε μόνο καθαρά ή μίας χρήσης εργαστηριακά σκεύη για την αποφυγή επιμολύνσεων.
- Συμβουλευτείτε το Δελτίο Δεδομένων Ασφαλείας (SDS) για σωστό χειρισμό.

ΔΙΑΧΕΙΡΗΣΗ ΑΠΟΒΛΗΤΩΝ

Απόρριψη όλων των αποβλήτων πρέπει να γίνεται σύμφωνα με τις τοπικές, εθνικές και ομοσπονδιακές ρυθμιστικές απαιτήσεις (παρακαλώ ανατρέξτε στο Δελτίο Δεδομένων Ασφαλείας (SDS)).

ΠΡΟΕΤΟΙΜΑΣΙΑ

- Χτυπήστε απαλά την φιάλη ώστε το υλικό ελέγχου να βρίσκεται στο κάτω μέρος της φιάλης.
- Ανοίξτε προσεκτικά το φιαλίδιο, αποφεύγοντας την απώλεια της λυοφιλιωμένης ουσίας.
- Προσθέστε **ακριβώς 3 mL απεσταγμένου/ απιονισμένου νερού**.
- Κλείστε το φιαλίδιο προσεκτικά και διαλύστε εντελώς το περιεχόμενο εντός 30 λεπτών με ελαφρύ ανακάτεμα αποφεύγοντας την δημιουργία αφρού.

ΑΛΛΟΙΩΣΗ ΤΟΥ ΠΡΟΪΟΝΤΟΣ

- Μετά την ανασύσταση : Ο βαθμονομητής μπορεί να παρουσιάζει μία ελαφρά θολή εμφάνιση. Αυτή δεν έχει καμία επίδραση στην απόδοση του προϊόντος. Η παρουσία μεριδίων μπορεί να υποδεικνύει καταστροφή.
- Μην χρησιμοποιείτε το προϊόν αν υπάρχει εμφανής ένδειξη μόλυνσης ή αλλοίωσης (πχ σωματίδια μετά την ανασύσταση).
- Αλλοίωση στο φιαλίδιο μπορεί να έχει επίδραση στην απόδοση του προϊόντος. Να μην χρησιμοποιείται το προϊόν αν υπάρχει εμφανής απόδειξη αλλοίωσης (πχ διαρροή)

ΣΤΑΘΕΡΟΤΗΤΑ

Πριν την ανασύσταση:
- Αποθήκευση στους 2-8ο C μακριά από το φως.
- Να μην χρησιμοποιείται πέραν των ημερομηνιών λήξης που
αναγράφονται στις ετικέτες των φιαλιδίων.

Μετά την ανασύσταση:
- Μη χρησιμοποιείτε μετά τις ημερομηνίες λήξης που αναφέρονται στις ετικέτες των φιαλιδίων.

- Σταθερότητα των συστατικών:
<u>Στους 15 έως 25ο C</u> : 8 ώρες
<u>Στους 2 έως 8ο C</u> : 2 ημέρες
<u>Στους -25 έως -15ο C</u> : 4 εβδομάδες (μία φορά κατάψυξη)

Εξαιρέσεις:
- Σταθερότητα ολικής χολερυθρίνης (όταν αποθηκεύεται μακριά από φως)
<u>Στους 15 έως 25ο C</u> : 6 ώρες
<u>Στους 2 έως 8ο C</u> : 1 ημέρα
<u>Στους -25 έως -15ο C</u> : 2 εβδομάδες (μία φορά κατάψυξη)
-Σταθερότητα άμεσης χολερυθρίνης (όταν αποθηκεύεται μακριά από φως)
<u>Στους 15 έως 25ο C</u> : 3 ώρες
<u>Στους 2 έως 8ο C</u> : 8 ώρες
<u>Στους -25 έως -15ο C</u> : 2 εβδομάδες (μία φορά κατάψυξη)

***Σημείωση**: Αποθηκεύστε τα φιαλίδια ερμητικά πωματισμένα και προστατευμένα από το φως όταν δε χρησιμοποιούνται.*

ΔΙΑΔΙΚΑΣΙΑ

Για την χρήση ELICAL 2, ακολουθείστε την περιγραφόμενη διαδικασία στις οδηγίες χρήσης του αντιδραστηρίου της ELITech Clinical Systems που χρησιμοποιείται.

ΠΕΡΙΟΡΙΣΜΟΙ

Την χρήση ELICAL 2 έχει επικυρωθεί με τα συστήματα της ELITech (Αναλυτές και αντιδραστήρια είναι καταγεγραμμένα στο φύλλο τιμών).
Η χρήση οποιουδήποτε άλλου συστήματος πρέπει να επικυρωθεί από το εργαστήριο.

ΤΙΜΕΣ

Οι συγκεντρώσεις υποδεικνύονται στο φύλλο τιμών μου συμπεριλαμβάνεται στο κιτ.
Για να επιτρέπεται η εισαγωγή δεδομένων τέστ, βαθμονομητών και ορών ελέγχου στους χρήστες μηχανημάτων Selectra, χρησιμοποιείστε τον ανάλογο γραμμικό κώδικα διαθέσιμο στο φύλλο τιμών.

ΔΗΛΩΣΗ ΣΟΒΑΡΟΥ ΑΤΥΧΗΜΑΤΟΣ

Παρακαλώ ενημερώστε τον κατασκευαστή (μέσω του διανομέα σας) και τις αρμόδιες αρχές του Κράτους Μέλους της ευρωπαϊκής ένωσης στον οποίο ο χρήστης ή/και ο ασθενής είναι εγκατεστημένος, για κάθε σοβαρό ατύχημα που μπορεί να συμβεί σε σχέση με το μηχάνημα. Για λοιπές δικαιοδοσίες, η δήλωση σοβαρού ατυχήματος πρέπει να συμφωνεί με τις τοπικές, εθνικές και ομοσπονδιακές ρυθμιστικές απαιτήσεις. Αναφέροντας ένα σοβαρό ατύχημα, παρέχετε πληροφορίες που μπορεί να συμβάλλουν στην ασφάλεια των *in vitro* ιατρικών μηχανημάτων.

ΤΕΧΝΙΚΗ ΒΟΗΘΕΙΑ

Επικοινωνήστε με τον τοπικό σας διανομέα ή την ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

☞SYMBOLES/ SYMBOLS/ SÍMBOLOS/ ΣΥΜΒΟΛΑ

- Les symboles utilisés sont décrits dans la norme ISO-15223-1 hormis ceux présentés ci-dessous.
- Symbols used are defined on ISO-15223-1 standard, except those presented below.
- Los símbolos utilizados son descritos en la norma ISO-15223-1 a la excepción de los presentados a continuación.
- Os símbolos utilizados são definidos na norma ISO-15223-1, exceto os apresentados abaixo.
- Τα χρησιμοποιούμενα σύμβολα ορίζονται στο πρότυπο ISO 15223-1, εκτός από αυτά που παρουσιάζονται παρακάτω.

CONT	Contenu/ Content/ Contiene/ Conteúdo/ περιεχόμενο
CAL	Calibrant/ Calibrator/ Calibrador/ Calibrador/ Βαθμονομητής
RCNS : X mL	Reconstituer avec x mL/ Reconstitute with x mL/ Reconstituir con x mL / Reconstituir com x mL/ Ανασύσταση με x mL
3 mL	Ajouter précisément 3 mL d'eau distillée ou désionisée/ Add exactly 3 mL of distilled or deionised water/ Agregar exactamente 3 mL de agua destilada o de agua desionizada Acrescentar exactamente 3 mL água destilada ou desionizada/ Προσθέστε ακριβώς 3 mL απεσταγμένου/απιονισμένου νερού
30 min 25°c 15°c	Conserver à température ambiante pendant 30 minutes avant utilisation/ Keep at room temperature for 30 minutes before use/ Conserve a temperatura ambiente durante 30 minutos antes de utiliza/ Mantenha em temperatura ambiente por 30 minutos antes de usar/ Να κρατηθεί σε θερμοκρασία δωματίου για 30 λεπτά πριν τη χρήση
X hours horas heures stunden x x°C	Les produits sont stables X heures à X°C / These products are stable X hours at X°C / Los productos son estables X horas a X°C/ Os produtos seja estável X horas a X°C/ Τα προϊόντα είναι σταθερά x ώρες στους x oC
X weeks semanas semaines wochen x x°C	Les produits sont stables x semaines à x°C/ These products are stable x weeks at x °C /Los productos son estables x semanas a x °C / Os produtos seja estável x semanas a x°C / Τα προϊόντα είναι σταθερά x εβδομάδες στους x oC
X days días jours tage x x°C	Les produits sont stables x jours à x°C/ These products are stable x days at x °C / Los productos son estables x días a x °C / Os produtos seja estável x dias a x°C / Τα προϊόντα είναι σταθερά x ημέρες στους x oC
	Ces produits doivent être immédiatement et correctement refermés afin d'éviter toute contamination ou évaporation / These products should be immediately and tightly capped to prevent contamination and evaporation / Estos productos deben ser bien cerrados de inmediato para evitar contaminación y evaporación / Esses produtos devem ser tampados imediatamente e firmemente para evitar contaminação e evaporação Στα εν λόγω προϊόντα πρέπει το πώμα να τοποθετείται αμέσως και σφικτά προς αποφυγή μόλυνσης και εξάτμισης.
☞	Modification par rapport à la version précédente/ Modification from previous version Modificación con respecto a la versión anterior/ Modificação relativamente à versão anterior/ Τροποποίηση από προηγούμενη έκδοση
CE	Conformité Européenne/ European Conformity/ Conformidad Europea/ Conformidade Europeia/ Ευρωπαϊκή Συμμόρφωση

ELITROL I
ELITROL II

ELITechGroup EMPOWERING IVD

CONT
ELITROL I ; CONT-0060 : 10 x 5 mL
ELITROL II ; CONT-0160 : 10 x 5 mL

CE

FTCE-CONT-5-v7 (05/2021)

Français - FR

USAGE PRÉVU
Ces dispositifs de diagnostic *in vitro* sont destinés au contrôle qualité des performances des tests quantitatifs ELITech listés dans la fiche de valeurs.
Ces dispositifs de diagnostic *in vitro* sont uniquement destinés aux professionnels.

COMPOSITION
- Produit sous forme lyophilisée préparé à partir de sérum humain contenant des additifs chimiques et biologiques.
- Les concentrations pour chaque analyte à doser sont spécifiques à chaque lot.

MATÉRIELS REQUIS MAIS NON FOURNIS
- Réactifs ELITech Clinical Systems listés dans la fiche de valeurs.
- Equipement général de laboratoire.

TRACABILITE
La traçabilité est indiquée dans la fiche technique du réactif ELITech Clinical Systems utilisé en combinaison avec le calibrant recommandé.

PRÉCAUTIONS D'EMPLOI ET MISES EN GARDE
- Chaque unité de sang humain utilisée pour la fabrication de ces produits a été testée et trouvée négative/non-réactive pour la présence d'HBsAg, HCV et HIV1/2. Les méthodes utilisées étaient approuvées par la FDA. Cependant le risque d'infection ne pouvant être exclu avec certitude par aucune méthode, ces produits doivent être manipulés comme étant potentiellement infectieux. En cas d'exposition, suivre les directives des autorités sanitaires compétentes.
- Prendre les précautions lors de la manipulation de flacons de verre brisés, car les bords tranchants peuvent blesser l'utilisateur.
- Respecter les précautions d'usage et les bonnes pratiques de laboratoire.
- Utiliser du matériel de laboratoire propre ou à usage unique afin d'éviter toute contamination.
- Consulter la fiche de données de sécurité (FDS) pour une manipulation appropriée.

TRAITEMENT DES DÉCHETS
L'élimination de tous les déchets doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales (veuillez-vous référer à la fiche de données de sécurité (FDS)).

PRÉPARATION
- Tapoter doucement le flacon pour que le matériel de contrôle soit en bas du flacon.
- Ouvrir avec précaution le flacon en évitant la perte de poudre lyophilisée.
- Ajouter **précisément 5 mL d'eau distillée ou désionisée**.
- Reboucher le flacon avec soin et dissoudre le contenu complètement dans les 30 minutes en remuant délicatement le flacon et en évitant la formation de mousse.

<u>Remarque importante</u> : *Pour réactiver la phosphatase alcaline, laissez reposer le flacon reconstitué à 15 - 25 °C pendant une heure.*

DÉTÉRIORATION DU PRODUIT
- Le produit peut présenter un aspect légèrement trouble après reconstitution. Cela n'a aucun effet sur les performances du produit. Toute présence de particules serait le signe d'une détérioration.
- Ne pas utiliser le produit s'il y a des signes évidents de détérioration biologique ou chimique (ex : particules après reconstitution).
- Un flacon endommagé peut avoir un impact sur les performances du produit. Ne pas utiliser le produit si les flacons présentent des signes physiques de détérioration (par exemple, fuite).

STABILITÉ
Avant reconstitution :
- Stocker à 2-8 °C et à l'abri de la lumière.
- Ne pas utiliser après la date d'expiration indiquée sur l'étiquette du flacon.
Après reconstitution :
- Ces produits doivent être immédiatement et correctement refermés afin d'éviter toute contamination ou évaporation.
- Stabilité des constituants :
<u>Entre 2 et 8 °C</u> : 5 jours
<u>Entre -25 et -15 °C</u> : 4 semaines (ne congeler qu'une seule fois)

Exceptions :
- Stabilité de la bilirubine totale (à conserver à l'abri de la lumière) :
<u>Entre 2 et 8 °C</u> : 24 heures
<u>Entre -25 et -15 °C</u> : 5 jours (ne congeler qu'une seule fois)

- Stabilité de la bilirubine directe (à conserver à l'abri de la lumière) :
<u>Entre 2 et 8 °C</u> : 8 heures
<u>Entre -25 et -15 °C</u> : 5 jours (ne congeler qu'une seule fois)

- Stabilité de la phosphatase alcaline :
<u>Entre 2 et 8 °C</u> : 24 heures
<u>Entre -25 et -15 °C</u> : 4 semaines (ne congeler qu'une seule fois)

<u>Note :</u>
- Conserver les flacons bien fermés et à l'abri de la lumière après reconstitution.
- Bien mélanger avant utilisation.
- La décongélation des échantillons à 37°C ainsi que leur agitation énergique (vortex) doivent être évitées car elles peuvent dénaturer la ferritine.

PROCÉDURE
Pour utiliser ELITROL I & II, suivre la procédure décrite dans la fiche technique du réactif ELITech Clinical Systems utilisé.

LIMITATIONS
L'utilisation de ELITROL I & II a été validée avec les systèmes ELITech (Automates et réactifs listés dans la fiche de valeurs).
L'utilisation sur un autre système doit être validée par le laboratoire.

VALEURS
Les concentrations sont indiquées dans la fiche de valeurs incluse dans le coffret.
Les valeurs obtenues par les laboratoires peuvent être différentes de celles annoncées. La technique, l'équipement et des erreurs expérimentales peuvent induire ces différences. Par conséquent, il est recommandé à chaque laboratoire de redéfinir ses propres normes.
Pour les utilisateurs d'automates Selectra permettant l'import de tests, de calibrants et de contrôles, utiliser le code barre correspondant, disponible sur la fiche de valeurs.

DECLARATION DES INCIDENTS GRAVES
Veuillez notifier au fabricant (par l'intermédiaire de votre distributeur) et à l'autorité compétente de l'Etat membre de l'union européenne dans lequel l'utilisateur et/ou le patient est établi, les cas d'incident grave survenu en lien avec le dispositif.
Pour les autres juridictions, la déclaration d'incident grave doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales.
En signalant les incidents graves, vous contribuez à fournir davantage d'informations sur la sécurité des dispositifs médicaux de diagnostic *in vitro*.

TECHNICAL ASSISTANCE
Contacter votre distributeur local ou ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

English - EN

INTENDED USE
These *in vitro* diagnostic devices are intended for the quality control of the performances of ELITech Clinical Systems quantitative tests listed in the value sheet.
These *in vitro* diagnostic devices are for professional use only.

COMPOSITION
- Lyophilized product prepared from human serum spiked with chemical and biological additives.
- Concentrations for each analyte to test are lot-specific.

MATERIALS REQUIRED BUT NOT PROVIDED
- ELITech Clinical Systems reagents listed in the value sheet.
- General Laboratory equipment.

TRACEABILITY
The traceability is indicated on the instructions for use of the ELITech Clinical Systems reagent used in combination with the recommended calibrator.

PRECAUTIONS FOR USE AND WARNINGS
- Each unit of human blood used in the manufacture of these products was tested and found to be negative/non-reactive for the presence of HbsAg, HCV and HIV1/2. The methods used were FDA approved. Nevertheless, since the risk of infection cannot be fully excluded these products must be handled as potentially infectious. In case of exposure, follow the guidelines of the competent health authorities.
- Take precautions when handling broken glass vials as sharp edges can injure the user.
- Take normal precautions and adhere to good laboratory practice.
- Use clean or single use laboratory equipment only to avoid contaminations.
- Consult Safety Data Sheet (SDS) for a proper handling.

WASTE MANAGEMENT
Disposal of all waste material should be in accordance with local, state and federal regulatory requirements (please refer to the Safety Data Sheet (SDS)).

PREPARATION
- Gently tap the vial so that the control material can be at the bottom of the vial.
- Carefully open the vial, avoiding the loss of lyophilizate.
- Add **exactly 5 mL of distilled or deionized water.**
- Carefully close the vial and dissolve the contents completely within 30 minutes by occasional gentle stirring avoiding the formation of foam.

<u>Important:</u> *To reactivate the alkaline phosphatase, allow the reconstituted control serum to stand for one hour at 15–25 °C.*

PRODUCT DETERIORATION
- The product may present a slightly hazy appearance after reconstitution. This has no effect on the performances of the product. All presence of particules would indicate deterioration.
- Do not use the product if there is visible evidence of contamination or damage (e.g. particle matter after reconstitution).
- Damage to the container may impact on product performance. Do not use the product if there is physical evidence of deterioration (e.g. leakages).

STABILITY
Prior to reconstitution :
- Store at 2-8 °C and protect from light. Do not freeze.
- Do not use after the expiry date stated on the vial label.
After reconstitution :
- These products should be immediately and tightly capped to prevent contamination and evaporation.
- Stability of the components:
<u>Between 2 and 8 °C</u> : 5 days
<u>Between -25 and -15 °C</u> : 4 weeks (when frozen once)

Exceptions:

- Stability of total bilirubin (when stored protected from light) :
<u>Between 2 and 8 °C</u> : 24 hours
<u>Between -25 and -15 °C</u> : 5 days (when frozen once)

- Stability of direct bilirubin (when stored protected from light) :
<u>Between 2 and 8 °C</u> : 8 hours
<u>Between -25 and -15 °C</u> : 5 days (when frozen once)

- Stability of alkaline phosphatase:
<u>Between 2 and 8 °C</u> : 24hours
<u>Between -25 and -15 °C</u> : 4 weeks (when frozen once)

<u>*Note:*</u>
- Store the vials tightly capped and protected from light after reconstitution.
- Mix content thoroughly prior to use.
- Thawing frozen specimen at 37°C, and vigorous mixing (vortex), should be avoided as this may denature ferritin.

PROCEDURE
To use ELITROL I & II, follow the procedure described in the instructions for use of the ELITech Clinical Systems reagent used.

LIMITATIONS
Using ELITROL I & II has been validated with the ELITech systems (Analyzers and reagents listed in the value sheet).
Using any other system should be validated by the laboratory.

VALUES
The concentrations are indicated in the value sheet enclosed in the kit.
Individual laboratories may obtain values different from those announced. Technique, equipment and experimental error may produce slightly different values. Each laboratory should determine their own mean values.
For users of Selectra instruments allowing data import for tests, calibrators and controls, use corresponding barcode, available on the value sheet.

DECLARATION OF SERIOUS INCIDENT
Please notify the manufacturer (through your distributor) and competent authority of the Member State of the european union in which the user and/or the patient is established, of any serious incident that has occurred in relation to the device. For other jurisdictions, the declaration of serious incident should be in accordance with local, state and federal regulatory requirements.
By reporting a serious incident, you provide information that can contribute to the safety of *in vitro* medical devices.

ASSISTANCE TECHNIQUE
Contact your local distributor or ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

Español - ES

USO PREVISTO
Estos dispositivos de diagnóstico *in vitro* están diseñados para el control de calidad del rendimiento de las pruebas cuantitativas ELITech Clinical Systems listadas en la hoja de valores.
Estos dispositivos de diagnóstico *in vitro* están destinados unicamente para los profesionales.

COMPOSICIÓN
- Producto liofilizado preparado a partir de suero humano enriquecido con aditivos químicos y biológicos.
- Las concentraciones de cada analito a analizar son específicas a cada lote.

MATERIALES REQUERIDOS PERO NO INCLUIDOS
- Reactivos ELITech Clinical Systems listados en la hoja de valores.
- Equipo de laboratorio de uso general.

TRAZABILIDAD
La trazabilidad se indica en el inserto del reactivo ELITech Clinical Systems utilizado en combinación con el calibrador recomendado.

PRECAUCIONES DE USO Y ADVERTENCIAS
- Cada unidad de sangre humana utilizada en la fabricación de estos productos fue analizada y resultó ser negativa / no reactiva ante la presencia de HbsAg, VHC y VIH1/2. Los métodos utilizados fueron aprobados de conformidad por la FDA. Sin embargo, dado que el riesgo de infección no puede excluirse por completo, estos productos deben manejarse como potencialmente infecciosos. En caso de exposición, siga las indicaciones de las autoridades sanitarias competentes.
- Tenga precauciones al manipular viales de vidrio roto, ya que los bordes afilados pueden dañar al usuario.
- Respetar las precauciones de uso y las buenas prácticas de laboratorio.
- Para evitar contaminaciones utilizar equipo nuevo o completamente limpio.
- Consulte la Hoja de Datos de Seguridad (SDS) para un manejo adecuado.

TRATAMIENTO DE LOS RESIDUOS
Todos los materiales de desecho deben eliminarse de acuerdo con los requisitos regulatorios locales, estatales y federales (diríjase a la hoja de seguridad (SDS)).

PREPARACIÓN
- Golpee suavemente el frasco para que el material de control quede en el fondo del frasco.
- Destapar cuidadosamente el frasco con el fin de evitar la pérdida de material liofilizado.
- Agregar exactamente 5 mL de agua destilada o de agua desionizada.
- Cierre cuidadosamente el vial y disuelva el contenido por completo durante 30 minutos mezclando suavemente para evitar la formación de espuma.

<u>*Importante:*</u> *Para reactivar la fosfatasa alcalina, deje el vial reconstituido descansar a 15 - 25 ° C durante una hora.*

DETERIORACIÓN DEL PRODUCTO
- El producto puede presentar un aspecto ligeramente turbio después de reconstitución, esto no afecta el rendimiento del producto. La presencia de partículas es un signo de deterioro.
- No utilice el producto si este presenta signos evidentes de contaminación o deterioro (p. ej, partículas después de reconstitución).
- Un frasco dañado puede tener un impacto en el rendimiento del producto. No utilice el producto si este tiene signos físicos de deterioro (p. ej, fugas).

ESTABILIDAD
Antes de reconstituir :
- Conservar a 2-8 °C y protegidos de la luz. No congelar.
- No utilice después de la fecha de caducidad indicada en la etiqueta de los frascos.
Después de reconstituir :
- Estos productos deben ser bien cerrados de inmediato para evitar contaminación y evaporación.
- Estabilidad de los componentes:
<u>Entre 2 y 8 °C</u> : 5 días
<u>Entre -25 y - 15 °C</u> : 4 semanas (no congelar más de una vez)

Excepciones:

- Estabilidad de la bilirrubina total (proteger de la luz) :
<u>Entre 2 y 8 °C</u> : 24 horas
<u>Entre -25 y -15 °C</u> : 5 días (no congelar más de una vez)

- Estabilidad de la bilirrubina directa (proteger de la luz) :
<u>Entre 2 y 8 °C</u> : 8 horas
<u>Entre -25 y -15 °C</u> : 5 días (no congelar más de una vez)

- Estabilidad de la fosfatasa alcalina:
<u>Entre 2 y 8 °C</u> : 24 horas
<u>Entre -25 y -15 °C</u> : 4 semanas (no congelar más de una vez)

<u>*Nota:*</u>
- Mantenga los frascos bien cerrados y protéjalos de la luz después de reconstituir.
- Mezclar bien antes de utilizar.
- La descongelación de las muestras a 37 ° C así como una agitación vigorosa (vórtice) deben evitarse ya que pueden desnaturalizar la ferritina.

PROCEDIMIENTO
Para utilizar ELITROL I & II, siga el procedimiento descrito en el inserto del reactivo ELITech Clinical Systems utilizado.

LIMITACIONES
El uso de ELITROL I & II ha sido validado con los sistemas ELITech (equipos y reactivos enumerados en la hoja de valores).
El uso de cualquier otro sistema debe ser validado por el laboratorio.

VALORES
Las concentrationes son indicadas en la ficha de valores incluida en el kit.
Los laboratorios pueden obtener valores differentes de los valores anunciados. Procedimento, equipo, errores experimentales pueden producir valores con pequeñas diferencias. Se recomienda que cada laboratorio determine su propia media para estos controles.
Para usuarios de los equipos Selectra que permiten la importación de pruebas, calibradores y controles, use el código de barras correspondiente, disponible en la hoja de valores.

DECLARACIÓN DE INCIDENTES GRAVES
Por favor notifique al fabricante (por medio de su distribuidor) y autoridad competente del Estado miembro de la Unión Europea en donde el usuario o paciente radique, de cualquier incidente grave que se produzca con relación al dispositivo.
Para otras jurisdicciones, la declaración de incidentes graves debe realizarse de acuerdo con los requisitos reglamentarios locales, estatales y federales. Reportando incidentes graves usted contribuye a proporcionar más información sobre la seguridad del dispositivo médico de diagnóstico *in vitro*.

ASISTENCIA TÉCNICA
Contacte a su distribuidor local o con ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

Português - PT

UTILIZAÇÃO PREVISTA
Estes dispositivos de diagnóstico *in vitro* são destinados ao controle de qualidade dos desempenhos dos testes quantitativos ELITech Clinical Systems listados na folha de valores.
Estes dispositivos de diagnóstico *in vitro* são apenas para uso profissional.

COMPOSIÇÃO
- Produto liofilizado preparado a partir de soro humano enriquecido com aditivos químicos e biológicos.
- As concentrações de cada analito a ser testado são específicas de cada lote.

MATERIAIS NECESSÁRIOS MAS NÃO FORNECIDOS
- ELITech Clinical Systems reagentes listados na folha de valores.
- Equipamento geral de laboratório.

RASTREABILIDADE
A rastreabilidade é indicada nas instruções de uso do reagente ELITech Clinical Systems utilizado em combinação com o calibrador recomendado.

PRECAUÇÕES DE USO E AVISOS
Cada unidade de sangue humano utilizada na fabricação desses produtos foi testada e se mostrou negativa / não reativa para a presença de HbsAg, HCV e HIV1 / 2. Os métodos utilizados foram aprovados e liberados pela FDA. No entanto, como o risco de infecção não pode ser totalmente excluído, esses produtos devem ser manuseados como potencialmente infecciosos. Em caso de exposição, siga as orientações das autoridades sanitárias competentes.
- Tome precauções ao manusear frascos de vidro quebrados, pois bordas afiadas podem ferir o usuário.
- Respeitar as precauções de utilização e as boas práticas de laboratório.
- Utilizar material de laboratório limpo ou destinado a uma única utilização de modo a evitar qualquer contaminação.
- Consulte a ficha de dados de segurança (SDS) para obter um manuseio adequado.

TRATAMENTO DOS RESÍDUOS
O descarte de todo material residual deve estar de acordo com os requisitos regulamentares locais, estaduais e federais (consulte a Ficha de dados de segurança (SDS)).

PREPARAÇÃO
- Bata levemente no frasco para que o material de controle possa estar no fundo do frasco.
- Abrir cuidadosamente o frasco, evitando a perda de pó liofilizado.
- Acrescentar **exatamente 5 mL de água destilada ou deionizada**.
- Feche cuidadosamente o frasco para injetáveis e dissolva completamente o conteúdo dentro de 30 minutos, mexendo suave e ocasionalmente, evitando a formação de espuma.

Observação importante: Para reativar a fosfatase alcalina, deixe o frasco reconstituído descansar a 15 - 25 °C por uma hora.

DETERIORAÇÃO DO PRODUTO
- O produto pode apresentar uma aparência um pouco turva após a reconstituição. Isto não tem efeito sobre o desempenho do produto. A presença de partículas indica deterioração.
- Não use o produto se houver evidência visível de contaminação ou dano (por exemplo, partículas após a reconstituição).
- Não utilizar o calibrador caso haja danos na embalagem que possam causar algum efeito sobre o desempenho do produto (ex. vazamentos).

ESTABILIDADE
Antes da reconstituição :
- Conservar a 2-8 °C e ao abrigo da luz.
- Não utilizar após as datas de validade indicadas nos rótulos dos frascos.
Após a reconstituição :
- Esses produtos devem ser tampados imediatamente e firmemente para evitar contaminação e evaporação.
- Estabilidade dos constituintes:
Entre 2 e 8 °C : 5 dias
Entre -25 e -15 °C : 4 semanas (congelar apenas uma única vez)

Excepções:

- Estabilidade da bilirrubina total (a conservar ao abrigo da luz) :
Entre 2 e 8 °C : 24 horas
Entre -25 e -15 °C : 5 dias (congelar apenas uma única vez)

- Estabilidade da bilirrubina direta (a conservar ao abrigo da luz) :
Entre 2 e 8 °C : 8 horas
Entre -25 e -15 °C : 5 dias (congelar apenas uma única vez)

- Estabilidade do fosfatase alcalina :
Entre 2 e 8 °C : 24 horas
Entre -25 e -15 °C : 4 semanas (congelar apenas uma única vez)

Observação:
- Armazene os frascos bem fechados e protegidos da luz após a reconstituição.
- Misture bem o conteúdo antes de usar.
- Descongelar a amostra a 37 ° C e a mistura vigorosa (vórtice) devem ser evitados, pois isso pode desnaturar a ferritina.

PROCEDIMENTO
Para usar ELITROL I & II, siga o procedimento descrito nas instruções de uso do reagente ELITech Clinical Systems utilizado.

LIMITAÇÕES
O uso de ELITROL I & II foi validado com o sistema ELITech (analisador e reagentes listados na folha de valores).
O uso de qualquer outro sistema deve ser validado pelo laboratório.

VALORES
As concentrações são indicadas na folha de valores colocada no kit.
Os valores obtidos pelos laboratórios podem ser diferentes dos anunciados. A técnica, o equipamento e erros experimentais podem induzir essas diferenças. Consequentemente aconselha-se que cada laboratório redefina as suas próprias normas.
Para usuários de instrumentos Selectra que permitem a importação de dados para testes, calibradores e controles, se o código de barras correspondente, disponível na folha de valores.

DECLARAÇÃO DE INCIDENTE GRAVE
Notifique o fabricante (através do seu distribuidor) e a autoridade competente da União Européia em que o usuário e/ou o paciente está estabelecido, de qualquer incidente grave que tenha ocorrido em relação ao dispositivo.
Para outras jurisdições, a declaração de incidente grave deve estar de acordo com as normas locais, requisitos regulatórios estaduais e federais. Ao relatar um incidente grave, você fornece informações que podem contribuir para o segurança de dispositivos médicos *in vitro*.

ASSISTÊNCIA TÉCNICA
Entre em contato com o seu distribuidor local ou com a ELITech Clinical Systems SAS. (CCsupport@elitechgroup.com).

Ελληνικά - EL

ΠΡΟΒΛΕΠΟΜΕΝΗ ΧΡΗΣΗ
Τα εν λόγω *in vitro* διαγνωστικά προορίζονται για τον ποιοτικό προσδιορισμό της απόδοσης των ποσοτικών τεστ της ELITech Clinical Systems καταγεγραμμένα στο φύλλο τιμών.
Τα εν λόγω *in vitro* διαγνωστικά προορίζονται μόνο για επαγγελματική χρήση.

ΣΥΣΤΑΣΗ
- Τα λυοφιλοποιημένα προϊόντα που ετοιμάζονται για ανθρώπινο ορό είναι δεσμευμένα με χημικά και βιολογικά πρόσθετα.
- Οι ελεγχόμενες συγκεντρώσεις για κάθε αναλυτή είναι συγκεκριμένες σύμφωνα με την παρτίδα.

ΑΠΑΙΤΟΥΜΕΝΑ ΥΛΙΚΑ ΠΟΥ ΔΕΝ ΣΥΜΠΕΡΙΛΑΜΒΑΝΟΝΤΑΙ
- Αντιδραστήρια της ELITech Clinical Systems καταγεγραμμένα στο φύλλο τιμών.
- Γενικός Εργαστηριακός Εξοπλισμός.

ΙΧΝΗΛΑΣΙΜΟΤΗΤΑ
Η ιχνηλασιμότητα ορίζεται στις οδηγίες χρήσης του αντιδραστηρίου της ELITech Clinical Systems που χρησιμοποιείται σε συνδυασμό με τον προτεινόμενο βαθμονομητή.

ΠΡΟΦΥΛΑΞΕΙΣ ΧΡΗΣΗΣ ΚΑΙ ΠΡΟΕΙΔΟΠΟΙΗΣΕΙΣ
- Κάθε μονάδα ανρθρώπινου αίματος που χρησιμοποιείται για την Παρασκευή αυτών των προϊόντων έχει ελεγχθεί και βρεθεί αρνητική/ μη-αντιδρούσα στην παρουσία HbsAg, HCV και HIV1/2. Οι μέθοδοι που χρησιμοποιούνται είναι εγκεκριμένες από τον FDA. Μολονότι και εφόσον ο κίνδυνος μόλυνσης δεν μπορεί να αποκλειστεί εντελώς, τα εν λόγω προϊόντα πρέπει να χειρίζονται ως πιθανώς μολυσματικά. Σε περίπτωση έκθεσης, ακολουθείστε τις οδηγίες των αρμόδιων υγειονομικών αρχών.
- Πάρτε προφυλάξεις όταν χειρίζεστε σπασμένα γυάλινα φιαλίδια καθώς οι αιχμηρές γωνίες μπορεί να τραυματίσουν τον χρήστη.
- Λάβετε συνήθεις προφυλάξεις και εφαρμόστε καλή εργαστηριακή πρακτική.
- Χρησιμοποιήστε μόνο καθαρά ή μίας χρήσης εργαστηριακά σκεύη για την αποφυγή επιμολύνσεων.
- Συμβουλευτείτε το Δελτίο Δεδομένων Ασφαλείας (SDS) για σωστό χειρισμό.

ΔΙΑΧΕΙΡΗΣΗ ΑΠΟΒΛΗΤΩΝ
Απόρριψη όλων των αποβλήτων πρέπει να γίνεται σύμφωνα με τις τοπικές, εθνικές και ομοσπονδιακές ρυθμιστικές απαιτήσεις (παρακαλώ ανατρέξτε στο Δελτίο Δεδομένων Ασφαλείας (SDS)).

ΠΡΟΕΤΟΙΜΑΣΙΑ
- Χτυπήστε απαλά την φιάλη ώστε το υλικό ελέγχου να βρίσκεται στο κάτω μέρος της φιάλης.
- Ανοίξτε προσεκτικά το φιαλίδιο, αποφεύγοντας την απώλεια της λυοφιλιωμένης ουσίας.
- Προσθέστε **ακριβώς 5 mL απεσταγμένου/ απιονισμένου νερού**.
- Κλείστε το φιαλίδιο προσεκτικά και διαλύστε εντελώς το περιεχόμενο εντός 30 λεπτών με ελαφρύ ανακάτεμα αποφεύγοντας την δημιουργία αφρού.

Σημαντικό: Για ενεργοποίηση της αλκαλικής φωσφατάσης, αφήστε τον ανασυσταμένο ορό ελέγχου να παραμείνει για μία ώρα στους 15-25o C.

ΑΛΛΟΙΩΣΗ ΤΟΥ ΠΡΟΪΟΝΤΟΣ
- Μετά την ανασύσταση : Το προϊόν ελέγχου μπορεί να παρουσιάζει μία ελαφρά θολή εμφάνιση. Αυτή δεν έχει καμία επίδραση στην απόδοση του προϊόντος. Η παρουσία μεριδίων μπορεί να υποδεικνύει καταστροφή.
- Μην χρησιμοποιείτε το προϊόν αν υπάρχει εμφανής ένδειξη μόλυνσης ή αλλοίωσης (πχ σωματίδια μετά την ανασύσταση).
- Αλλοίωση στο φιαλίδιο μπορεί να έχει επίδραση στην απόδοση του προϊόντος. Να μην χρησιμοποιείται το προϊόν αν υπάρχει εμφανής απόδειξη αλλοίωσης (πχ διαρροή).

ΣΤΑΘΕΡΟΤΗΤΑ
Πριν την ανασύσταση :
- Αποθηκεύστε στους 2-8 °C και προστατέψτε από το φως.
- Μη χρησιμοποιείτε μετά τις ημερομηνίες λήξης που αναφέρονται στις ετικέτες των φιαλιδίων.
Κατόπιν ανασύστασης :
- Στα εν λόγω προϊόντα πρέπει το πώμα να τοποθετείται αμέσως και σφικτά προς αποφυγή μόλυνσης και εξάτμισης.
- Σταθερότητα των συστατικών:
Στους 2 έως 8ο C : 5 ημέρες
Στους -25 έως -15ο C : 4 εβδομάδες (μία φορά κατάψυξη)

Εξαιρέσεις:

- Σταθερότητα ολικής χολερυθρίνης (όταν αποθηκεύεται μακριά από φως)
Στους 2 έως 8ο C : 24 ώρες
Στους -25 έως -15ο C : 5 ημέρες (μία φορά κατάψυξη)
- Σταθερότητα άμεσης χολερυθρίνης (όταν αποθηκεύεται μακριά από φως)
Στους 2 έως 8ο C : 8 ώρες
Στους -25 έως -15ο C : 5 ημέρες (μία φορά κατάψυξη)

- Σταθερότητα της αλκαλικής φωσφατάσης
Στους 2 έως 8ο C : 24 ώρες
Στους -25 έως -15ο C : 4 εβδομάδες (μία φορά κατάψυξη)

Σημείωση:
- Αποθηκεύστε το φιαλίδιο σφικτά κλειστό και μακριά από το φως μετά την ανασύσταση.
- Αναμίξτε το περιεχόμενο διεξοδικά πριν τη χρήση του.
- Η απόψυξη κατεψυγμένου δείγματος στους 37°C και η έντονη ανάμειξη του (με vortex) πρέπει να αποφεύγετε καθώς μπορεί να αλλοιώσει τη φερριτίνη.

ΔΙΑΔΙΚΑΣΙΑ
Για την χρήση ELITROL I & II, ακολουθείστε την περιγραφόμενη διαδικασία στις οδηγίες χρήσης του αντιδραστηρίου της ELITech Clinical Systems που χρησιμοποιείται.

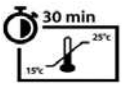
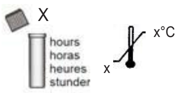
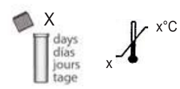
ΠΕΡΙΟΡΙΣΜΟΙ
Την χρήση ELITROL I & II έχει επικυρωθεί με τα συστήματα της ELITech (Αναλυτές και αντιδραστήρια είναι καταγεγραμμένα στο φύλλο τιμών).
Η χρήση οποιουδήποτε άλλου συστήματος πρέπει να επικυρωθεί από το εργαστήριο.

ΤΙΜΕΣ
Οι συγκεντρώσεις υποδεικνύονται στο φύλλο τιμών που συμπεριλαμβάνεται στο κιτ.
Μεμονωμένα εργαστήρια μπορεί να λάβουν τιμές διαφορετικές από τις ανακοινώσιμες. Η τεχνική, ο εξοπλισμός και το πειραματικό σφάλμα μπορεί να δώσουν ελαφρώς διαφορετικές τιμές. Κάθε εργαστήριο πρέπει να ορίζει τις δικές του μέσες τιμές.
Για να επιτρέπεται η εισαγωγή δεδομένων τέστ, βαθμονομητών και ορών ελέγχου στους χρήστες μηχανημάτων Selectra, χρησιμοποιείστε τον ανάλογο γραμμικό κώδικα διαθέσιμο στο φύλλο τιμών.

ΔΗΛΩΣΗ ΣΟΒΑΡΟΥ ΑΤΥΧΗΜΑΤΟΣ
Παρακαλώ ενημερώστε τον κατασκευαστή (μέσω του διανομέα σας) και τις αρμόδιες αρχές του Κράτους Μέλους της ευρωπαϊκής ένωσης στον οποίο ο χρήστης ή/και ο ασθενής είναι εγκατεστημένος, για κάθε σοβαρό ατύχημα που μπορεί να συμβεί σε σχέση με το μηχάνημα. Για λοιπές δικαιοδοσίες, η δήλωση σοβαρού ατυχήματος πρέπει να συμφωνεί με τις τοπικές, εθνικές και ομοσπονδιακές ρυθμιστικές απαιτήσεις. Αναφέροντας ένα σοβαρό ατύχημα, παρέχετε πληροφορίες που μπορεί να συμβάλλουν στην ασφάλεια των *in vitro* ιατρικών μηχανημάτων.

ΤΕΧΝΙΚΗ ΒΟΗΘΕΙΑ
Επικοινωνήστε με τον τοπικό σας διανομέα ή την ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

☞SYMBOLES/ SYMBOLS/ SÍMBOLOS/ ΣΥΜΒΟΛΑ
- Les symboles utilisés sont décrits dans la norme ISO-15223-1 hormis ceux présentés ci-dessous.
- Symbols used are defined on ISO-15223-1 standard, except those presented below.
- Los símbolos utilizados son descritos en la norma ISO-15223-1 a la excepción de los presentados a continuación.
- Os símbolos utilizados são definidos na norma ISO-15223-1, exceto os apresentados abaixo.
- Τα χρησιμοποιούμενα σύμβολα ορίζονται στο πρότυπο ISO 15223-1, εκτός από αυτά που παρουσιάζονται παρακάτω

CONT	Contenu/ Content/ Contiene/ Conteúdo/ περιεχόμενο
CONTROL	Contrôle /Control /Control / Controlo /Ορός Ελέγχου
RCNS : X mL	Reconstituer avec x mL/ Reconstitute with x mL/ Reconstituir con x mL / Reconstituir com x mL/ Ανασύσταση με x mL
	Ajouter précisément 5 mL d'eau distillée ou désionisée/ Add exactly 5 mL of distilled or deionised water/ Agregar exactamente 5 mL de agua destilada o de agua desionizada/ Acrescentar exactamente 5 mL água destilada ou desionizada/ Προσθέστε ακριβώς 5 mL απεσταγμένου/ απιονισμένου νερού
	Conserver à température ambiante pendant 30 minutes avant utilisation/ Keep at room temperature for 30 minutes before use/ Conserve a temperatura ambiente durante 30 minutos antes de utiliza/ Mantenha em temperatura ambiente por 30 minutos antes de usar/ Να κρατηθεί σε θερμοκρασία δωματίου για 30 λεπτά πριν τη χρήση
	Les produits sont stables X heures à X°C / These products are stable X hours at X°C / Los productos son estables X horas a X°C/ Os produtos seja estável X horas a X°C/ Τα προϊόντα είναι σταθερά x ώρες στους x oC
	Les produits sont stables x semaines à x°C/ These products are stable x weeks at x °C /Los productos son estables x semanas a x °C / Os produtos seja estável x semanas a x°C / Τα προϊόντα είναι σταθερά x εβδομάδες στους x oC
	Les produits sont stables x jours à x°C/ These products are stable x days at x °C /Los productos son estables x días a x °C / Os produtos seja estável x dias a x°C / Τα προϊόντα είναι σταθερά x ημέρες στους x oC
	Ces produits doivent être immédiatement et correctement refermés afin d'éviter toute contamination ou évaporation / These products should be immediately and tightly capped to prevent contamination and evaporation / Estos productos deben ser bien cerrados de inmediato para evitar contaminación y evaporación / Esses produtos devem ser tampados imediatamente e firmemente para evitar contaminação e evaporação Στα εν λόγω προϊόντα πρέπει το πώμα να τοποθετείται αμέσως και σφικτά προς αποφυγή μόλυνσης και εξάτμισης.
☞	Modification par rapport à la version précédente/ Modification from previous version/ Modificación con respecto a la versión anterior/ Modificação relativamente à versão anterior/ Τροποποίηση από προηγούμενη έκδοση
CE	Conformité Européenne/ European Conformity/ Conformidad Europea/ Conformidade Europeia/ Ευρωπαϊκή Συμμόρφωση

ALBUMIN

☞Referinţe:
ALBU-0250
ALBU-0600
ALBU-0700

Compoziţia trusei:
R *12 x 20 mL*
R *2 x 125 mL +* ***Std*** *1 x 2 mL*
R *4 x 250 mL +* ***Std*** *1 x 2 mL*

FTRO-ALBU-v18 (09/2020)_PIT-ALBU-4-v18

☞SCOPUL UTILIZĂRII

ELITech Clinical Systems ALBUMIN este un reactiv de diagnostic *in vitro* destinat determinării cantitative a albuminei din probele serul uman și plasmă.

☞SEMNIFICAŢIE CLINICĂ [1-3]

Albumina este sintetizată în special de ficat şi reprezintă aproximativ 50% din proteinele plasmatice. Funcţia principală a albuminei este menţinerea presiunii oncotice şi transportul unui număr mare de compuşi. Măsurarea albuminei serice sau plasmatice este indicată în special pentru a ajuta la diagnosticarea şi monitorizarea bolilor cu pierdere de proteine sau sinteză scăzută (sindromul nefrotic, pierderea gastrointestinală, insuficienţa hepatică), inflamaţia acută şi cronică, şi malnutriţia severă.

☞METODĂ[4]

Verde de bromocresol (BCG). Punct final

PRINCIPIU [4]

Determinarea colorimetrică a albuminei utilizând verdele de bromocresol la pH 4,20.

$$\text{Albumină + BCG} \xrightarrow{pH=4,20} \text{Complex albumină - BCG}$$

☞COMPOZIŢIA REACTIVULUI

Reactiv: R

Tampon succinat, pH 4,20		
Verde de bromocresol	0.2	mmol/L
Surfactant		
Standard: Std. (Ref.: ALBU-0600/0700)		
Albumină bovină	3.5	g/dL
	35	g/L
Azidă de sodiu	< 0,1	%

☞MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Echipamente generale de laborator.
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

☞AVERTISMENTE ŞI PRECAUŢII

- Acest dispozitiv de diagnostic *in vitro* (Reactiv şi Standardul) este destinat numai pentru uz profesional.
- Standardul conţine azidă de sodiu care poate reacţiona cu plumbul sau instalaţiile din cupru pentru a forma potenţiale azide metalice explozive. În momentul eliminării acestui standard, spălaţi întotdeauna cu apă din abundenţă pentru a preveni acumularea de azide.
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Standardul trebuie să fie imediat inchis cu capacul pentru a preveni contaminarea şi evaporarea.
- Pentru mai multe informaţii, Fişa de date privind siguranţa (SDS) este disponibilă la cerere pentru utilizatorul profesional.

☞STABILITATEA

A se depozita la 2-25ºC şi a se proteja împotriva luminii. A nu se îngheţa.

A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultaţi § DATE PRIVIND PERFORMANŢA).

PREGĂTIRE

Reactivii şi Standardul sunt gata pentru utilizare.

☞ DETERIORAREA PRODUSELOR

- Soluţia de reactivi trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiolă perforată).

☞PROBE

Specimen[2]

- Ser.
- Plasmă (heparină de litiu)
- A nu se utiliza alte specimene.

Avertismente şi precauţii

Conform bunei practici de laborator, puncţia venoasă trebuie efectuată înainte de administrarea de medicamente.

Depozitare [1]

- Analizaţi serul proaspăt sau stocaţi-le la 2-8ºC mai puţin de 72 de ore.
- Stocate la -20ºC, probele sunt stabile 6 luni. Pentru o depozitare mai îndelungată, probele sunt îngheţate la -70ºC.

☞VALORI DE REFERINŢĂ [1]

Ser, plasmă:

Pacienţii în repaus

< 60 ani:	3.5 – 5.2 g/dL	(35 – 52 g/L)
60-90 ani:	3.2 – 4.6 g/dL	(32 – 46 g/L)
>90 ani:	2.9 – 4.5 g/dL	29 – 45 g/L)

În cazul adulţilor din ambulatoriu, valorile pot fi mai mari cu 0,3 - 0,5 g/dL (3 - 5 g/L).

Notă: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

ALBUMIN

☞Referinţe:	Compoziţia trusei:
ALBU-0250	***R*** *12 x 20 mL*
ALBU-0600	***R*** *2 x 125 mL +* ***Std*** *1 x 2 mL*
ALBU-0700	***R*** *4 x 250 mL +* ***Std*** *1 x 2 mL*

CE

FTRO-ALBU-v18 (09/2020)_PIT-ALBU-4-v18

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems, aplicaţiile sunt disponibile la cerere.
Lungime de undă 620 nm
Temperatură: 37ºC
Citiţi pe reactivul martor.

	MARTOR	CALIBRARE	TEST
Reactiv R	360 µL	360 µL	360 µL
Apă distilată	3 µL	-	-
Calibrator/ Standard	-	3 µL	-
Probă	-	-	3 µL

Amestecaţi şi citiţi absorbanţele (A) după o incubaţie de 4 minute şi 30 de secunde.

- Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert.

☞CALCUL

$$\frac{\text{A Sample}}{\text{A Standard/ Calibrator}} \times n \qquad n = \text{calibrator/standard concentration}$$

Factor de conversie: g/dL x 10 = g/L

☞CALIBRARE

Pentru referinţa ALBU-0600/0700: Pentru calibrare, trebuie utilizat fie calibratorul multiparametric ELICAL 2 fie Standardul Albumin 3.5 g/dL.
Pentru referinţa ALBU-0250: Pentru calibrare, utilizaţi calibratorul multiparametric ELICAL 2.

Valorile concentraţiei Standardului Albumin 3.5 g/dL şi calibratorului multiparametric ELICAL 2 sunt trasabile conform materialului de referinţă ERM-DA 470k.

Frecvenţa de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

☞CONTROLUL CALITĂŢII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum ELITROL I şi ELITROL II. Aceste controale trebuie efectuate şi validate înainte ca probele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform reglementărilor locale.

☞MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele de reglementare locale, statale şi federale.

☞DATE DE PERFORMANŢĂ la 37ºC privind Analizoarele Selectra ProM ale ELITech Clinical Systems

- **Interval de măsurare**
  Determinat conform protocolului CLSI EP6-A[5], intervalul de măsurare este între 1.6 şi 6.0 g/dL (de la 16 la 60 g/L) .

- **Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)**
Determinată conform protocolului CLSI EP17-A[6].
LoD= 0.003 g/dL (0,03 g/L).
LoQ= 0.50 g/dL (5.0 g/L).

- **Precizie**
Determinată conform protocolului CLSI EP5-A2[7].

		Medie		În interiorul ciclului	Total
	n	**g/dL**	**g/L**	**CV (%)**	
Nivelul 1	80	2.54	25.4	0.9	2.3
Nivelul 2	80	3.53	35.3	0.5	2.1
Nivelul 2	80	4.98	49.8	0.8	2.1

- Corelaţie
A fost efectuat un studiu comparativ între un analizor ELITech Clinical Systems ProM şi un sistem similar disponibil în comerţ (metoda BCG) pe eşantioane de ser uman 100 determinată conform protocolului CLSI EP9-A2[8].
Concentraţiile eșantioanelor au fost între 1.43 şi 5.89 g/dL (14.3 – 58.9 g/L).
Rezultatele sunt după cum urmează:
Coeficient de corelaţie: (r)=0.997
Regresie liniară: y = 0.961x + 0.12 g/dL (1.2 g/L)

- Limitări şi interferenţe
- Nu raportaţi rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2[9]. Recuperarea este în intervalul ±10% din valoarea iniţială a activităţii Albumina de 3.5 şi 5.00 g/dL.
Bilirubină neconjugată: Nicio interferenţă semnificativă până la 30,0 mg/dL (513 µmol/L).
Bilirubină conjugată: Nicio interferenţă semnificativă până la 29,5 mg/dL (504 µmol/L).
Hemoglobină: Nicio interferenţă semnificativă până la 500 mg/dL.
Trigliceride: Nicio interferenţă semnificativă până la 3000 mg/dL (33.90 mmol/L).
Acid ascorbic: Nicio interferenţă semnificativă până la 20.0 mg/dL.
Acetaminofen : Nicio interferenţă semnificativă până la 30 mg/dL.
Acid acetilsalicilic: Nicio interferenţă semnificativă până la 200 mg/dL.
Gamma globulină : Nicio interferenţă semnificativă până la 1500 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [10]

- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [11-12]

- Rezultatele acestui studiu trebuie interpretate doar în corelaţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- **Stabilitatea la bord/Frecvenţa calibrării**

Stabilitatea la bord: 28 zile
Frecvenţa calibrării: 28 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit şi după o operaţie de întreţinere.

☞BIBLIOGRAFIE

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☞SIMBOLURI

Simbolurile folosite sunt definite conform standardului ISO-15223-1 cu exceptia celor prezentate mai jos.

CONT	Conţinut
R	Reactiv
Std	Standard
CE	Conformitate europeană
☞	Modificare faţă de versiunea precedentă

Notă
Doar pentru ref. **ALBU-0250**, utilizate cu software-ul Selectra TouchPro.

☞

Albumin. 0
101 PIT-ALBU

ALT/GPT 4+1 SL

Referinţe:		Compoziţia trusei:
ALSL-0250	*8 x 25 mL*	***R1** 8 x 20 mL + **R2** 8 x 5 mL*
ALSL-0455	*4 x 55 mL*	***R1** 4 x 44 mL + **R2** 4 x 11 mL*
ALSL-0410	*2 x 62,5 mL*	***R1** 2 x 50 mL + **R2** 1 x 26 mL*
ALSL-0430	*4 x 62,5 mL*	***R1** 4 x 50 mL + **R2** 2 x 26 mL*
ALSL-0510	*5 x 125 mL*	***R1** 5 x100 mL + **R2** 1 x 127 mL*

FTRO-ALSL4+1-v18(12/2018)_PIT-ALSL4+1-4-v18

SCOPUL UTILIZĂRII

ALT/GPT 4+1 SL ELITech Clinical Systems este conceput pentru determinarea cantitativă de diagnosticare *in vitro* a alaninaminotransferazei (ALT) în serul uman şi plasmă.

SEMNIFICAŢIE CLINICĂ [1-3,6]

Alaninaminotransferaza (ALT), cunoscută şi ca glutamat piruvat transferaza (GPT), este o transaminază. ALT catalizează transferul grupului amino al L-alaninei la α-ketoglutarat pentru a rezulta L-glutamatul. Cele mai mari nivele se găsesc în ficat şi rinichi, şi cele mai mici cantităţi în inimă şi muşchiul scheletic. Concentraţia ALT este crescută când celulele hepatice sunt deteriorate (necroză celulară hepatică sau leziune de orice cauză). Într-adevăr, hepatita virală şi toxică induce o creştere marcată a activităţii ALT în ser. Aportul de alcool, delirium tremens, şi administrarea diverselor medicamente induc creşterea uşoară sau moderată a ALT. Concentraţia ALT în ser este, de asemenea, crescută uşor în diverse afecţiuni precum: distrofia musculară, boala hemolitică, infarctul miocardic…

ALT este mai specifică ficatului decât AST (aspartataminotransferaza). Măsurarea atât a AST, cât şi a ALT are o anumită valoare în distingerea hepatitei de alte leziuni parenchimale.

Nivelul ALT din ser poate fi scăzut în cazul deficienţei de vitamina B6.

METODĂ [4]

Metoda IFCC fără piridoxal fosfat (P-5'-P). cinetică. UV.

PRINCIPIU [4]

Determinarea cinetică a activităţii alaninaminotransferazei (ALT).

$$\text{L-Alanină} + \alpha\text{-ketoglutarat} \xrightarrow{ALT} \text{Piruvat} + \text{L-glutamat}$$

$$\text{Piruvat} + \text{NADH+H+} \xrightarrow{LDH} \text{L-lactat+NAD+}$$

LDH=lactat dehidrogenază

COMPOZIŢIA REACTIVULUI

Reactiv 1: R1

Tampon Tris, pH 7,5 (30°C)	125 mmol/L
L-alanină	680 mmol/L
LDH	≥ 2000 U/L
Azidă de sodiu	< 0,1 %

Reactiv 2: R2

Ketoglutarat	97 mmol/L
NADH	1,1 mmol/L
Azidă de sodiu	< 0,1 %

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550, ELICAL 2
- CONT-0060, ELITROL I
- CONT-0160, ELITROL II
- Echipamente generale de laborator.
- Soluţie salină obişnuită (NaCl 9 g/L).
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ŞI PRECAUŢII

- Acest reactiv este conceput doar pentru utilizarea în scopul diagnosticării *in vitro*.
- Aceşti reactivi conţin azidă de sodiu care poate reacţiona cu plumbul sau instalaţiile sanitare din cupru şi poate forma azide metalice explozibile. În cazul aruncării acestor reactivi, spălaţi întotdeauna cu cantităţi mari de apă pentru a preveni formarea de azide.
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Nu interschimbaţi fiolele de reactiv din truse diferite.
- Pentru mai multe informaţii, consultați Fişa de date privind siguranţa (SDS).

STABILITATEA REACTIVILOR

A se depozita la 2-8°C şi a se proteja împotriva luminii. A nu se îngheţa.

A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA REACTIVILOR

- Soluţia de reactivi trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.

AMBALAJ DETERIORAT

Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, recipient perforat).

PROBE [1,5]

Specimen

- Ser şi plasmă heparinizată de litiu, libere de hemoliză.
- A nu se utiliza alte specimene.

Avertisment şi precauţii

Conform bunei practici de laborator, prelevarea trebuie efectuată înainte de administrarea de medicamente.

Depozitare
Eşantioanele sunt stabile timp de 3 zile la temperatura camerei şi 7 zile la 2-8ºC. Stabilitatea ALT este menţinută mai bine la -70ºC.

VALORI DE REFERINŢĂ [1,4]

Bărbaţi: < 45 U/L
Femei: < 34 U/L

__Notă__: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

PROCEDURĂ

__Pentru Analizoarele Selectra ale ELITech Clinical Systems.__
Aplicaţiile sunt disponibile la cerere
Lungime de undă 340 nm
Temperatură 37ºC
Citiţi pe reactivul martor.

Reactiv R1	240 µL
Proba	15 µL

Amestecaţi şi aşteptaţi 4 minute şi 43 de secunde incubaţia.

Reactiv R2	60 µL

Amestecaţi şi aşteptaţi o incubaţie de 50 de secunde, măsuraţi modificarea absorbanţei pe minut (ΔA/min.) timp de 159 de secunde.

- Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert.

- Valorile mari ale ALT pot induce rezultate scăzute în mod fals datorită golirii substratului (consumul total de NADH înainte de citirea rezultatului). Pentru Analizoarele Selectra pro Series ELITech Clinical Systems, aplicaţia conţine o alarmă specifică pentru a avertiza utilizatorii.

CALCUL

__(ΔA) Proba__ x n n=concentraţie calibrator
(ΔA) Calibrator

__Factor de conversie__: U/L x 0,0167 = µkat/L

CALIBRARE

Pentru calibrare, trebuie utilizat calibratorul multiparametric ELICAL 2. Valoarea sa este trasabilă conform metodei de referinţă IFCC [5].

__Frecvenţa de calibrare__: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

CONTROLUL CALITĂŢII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I (control normal) şi ELITROL II (control patologic). Aceste controale trebuie efectuate şi validate înainte ca probele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare, şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele locale şi legale.

DATE DE PERFORMANŢĂ la 37°C privind Analizoarele Selectra ProM ale ELITech Clinical Systems

- **Interval de măsurare**

Determinat conform protocolului CLSI EP6-A[7], intervalul de măsurare este între 10,0 şi 450,0 U/L (de la 0,17 la 7,50 µkat/L). Probele care depăşesc 450,0 U/L trebuie să fie diluate 1:10 cu soluţie de NaCl 9 g/L (salină normală) şi re-analizate. Utilizarea acestei proceduri extinde intervalul de măsurare de la 250,0 la 4500,0 U/L (de la 7,50 la 75,00 µkat/L).

Pentru utilizatorii Selectra TouchPro, funcţia „reluare diluare” efectuează diluţia automată a eşantionului. Rezultatele iau în considerare diluţia.

- **Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)**

Determinată conform protocolului CLSI EP17-A[8].
LoD= 2,9 U/L (0,05 µkat/L).
LoQ= 5,0 U/L (0,08 µkat/L).

Precizie
Determinată conform protocolului CLSI EP5-A2[9].

		Medie		**În interiorul ciclului**	**Total**
	n	**U/L**	**µkat/L**	**CV (%)**	
Nivel scăzut	80	34,2	0,57	1,1	4,4
Nivel mediu	80	71,2	1,19	1,2	2,9
Nivel înalt	80	367,0	6,12	0,5	1,8

- Corelaţie
A fost efectuat un studiu comparativ între Analizorul Selectra ProM ELITech Clinical Systems şi un alt echipament al unui sistem aprobat de FDA (metoda IFCC) pe 100 de eşantioane de ser uman conform protocolului CLSI EP9-A2[10].
Valorile acoperă domeniul de măsurare.
Parametrii regresiei liniare sunt după cum urmează:
Coeficient de corelaţie: (r)= 0,996
Regresie liniară: y= 1,017x + 0,6 U/L (0,01 µkat/L

- Limitări şi interferenţe

- Eşantioanele hemolizate nu trebuie să fie utilizate deoarece hemoliza semnificativă poate creşte concentraţia ALT din cauza nivelelor ridicate de ALT în eritrocite.
- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2 [11] al CLSL. Recuperarea este în intervalul ±10% din valoarea iniţială a lipazei de 35,0 şi 350,0 U/L.

Bilirubină neconjugată: Nicio interferenţă semnificativă până la 30,0 mg/dL (513 µmol/L).
Bilirubină conjugată: Nicio interferenţă semnificativă până la 29,5 mg/dL (504 µmol/L).
Trigliceride: Nicio interferenţă semnificativă până la 2300 mg/dL (25,99 mmol/L).
Piruvat: Nicio interferenţă semnificativă până la 3,0 mg/dL.
Acid ascorbic: Nicio interferenţă semnificativă până la 20 mg/dL.
Acid acetilsalicilic: Nicio interferenţă semnificativă până la 200,0 mg/dL.
Acetaminofen: Nicio interferenţă semnificativă până la 30 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [12]
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young şi Glick. [13-14]
- Rezultatele acestui studiu trebuie interpretate doar în corelaţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- **Stabilitatea la bord/Frecvenţa calibrării**

Stabilitatea la bord: 28 de zile
Frecvenţa calibrării: 28 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit, şi după o operaţie de întreţinere.

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SIMBOLURI

IVD	Dispozitiv medical de diagnosticare in vitro.
	Consultaţi instrucţiunea de utilizare.
	Producător
	Limită de temperatură
LOT	Număr de lot
	Data expirării
REF	Număr catalog
CONT	Conţinut
R1	Reactiv 1
R2	Reactiv 2
CE	Conformitate europeană

ALT/GPT 4+1 SL

Referinţe:		**Compoziţia trusei:**
ALSL-0250	*8 x 25 mL*	***R1** 8 x 20 mL + **R2** 8 x 5 mL*
ALSL-0455	*4 x 55 mL*	***R1** 4 x 44 mL + **R2** 4 x 11 mL*
ALSL-0410	*2 x 62,5 mL*	***R1** 2 x 50 mL + **R2** 1 x 26 mL*
ALSL-0430	*4 x 62,5 mL*	***R1** 4 x 50 mL + **R2** 2 x 26 mL*
ALSL-0510	*5 x 125 mL*	***R1** 5 x100 mL + **R2** 1 x 127 mL*

FTRO-ALSL4+1-v18(12/2018)_PIT-ALSL4+1-4-v18

Notă

Doar pentru ref. **ALSL-0250/ALSL-0455**, utilizată cu software-ul Selectra TouchPro.

ALT (GPT) 1
140 PIT-ALSL

☞:Modificare faţă de versiunea precedentă.

AMYLASE SL

Referinţe:		Compoziţia trusei:
AMSL-0230	*6 x 20 mL*	***R** 6 x 20 mL*
AMSL-0390	*1 x 50 mL*	***R** 1 x 50 mL*
AMSL-0400	*6 x 50 mL*	***R** 6 x 50 mL*

FTRO-AMSL-v18 (12/2018)_PIT-AMSL-4-v18

SCOPUL UTILIZĂRII

AMYLASE SL ELITech Clinical Systems este conceput pentru determinarea cantitativă a amilazei în serul uman şi plasmă pentru diagnosticare *in vitro*.

SEMNIFICAŢIE CLINICĂ [1-2]

α-amilaza este o enzimă de origine pancreatică sau salivară care hidrolizează legăturile 1,4-α-glucozidice, ajutând astfel la digestia amidonului. Analiza amilazei serice este utilizată în special în diagnosticarea bolilor pancreatice (pancreatită acută sau cronică şi complicaţiile acestora, carcinoame). În timpul pancreatitei acute, se observă o creştere tranzitorie a amilazei serice, un vârf corespunzând unei creşteri de 4-6 ori fiind obţinut în 12-72 de ore de la începere, activitatea revenind la normal după 3-5 zile. Cu toate acestea, o creştere a amilazei serice este de asemenea observată în alte patologii intra-abdominale, insuficienţă renală, cancere ovariene, leziuni ale glandelor salivare, alcoolism acut, insuficienţă renală sau macroamilazemie (prezenţa unui complex amilază-IgG nefiltrată de glomerul).

METODĂ [3]

Substrat: CNP-G_3 (2-cloro-4-nitrofenil-α-maltotriozidă)
Enzimatică, cinetică

PRINCIPIU [3]

Substratul CNP-G_3 este hidrolizat prin acţiunea catalitică a α-amilazei pentru a produce CNP (2-cloro-4-nitrofenol).

$$5\ \text{CNP-G}_3 \xrightarrow{\alpha\text{-amilază}} 3\text{CNP} + 2\text{CNP-G}_2 + 3\ \text{maltotrioză} + 2\ \text{glucoză}$$

CNP-G_2= 2-cloro-4-nitrofenil-α-maltozidă

Rata de creştere a absorbanţei este măsurată la 405 nm şi este direct proporţională cu activitatea α-amilazei în probă,

COMPOZIŢIA REACTIVULUI

Reactiv: R

Tampon MES, pH 6,15		50	mmol/L
Clorură de sodiu		70	mmol/L
Clorură de calciu		6	mmol/L
Tiocianat de potasiu		900	mmol/L
CNP-G3		2,27	mmol/L
Azidă de sodiu	<	0,1	%

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550 ELICAL 2 — 4 x 3 mL
- CONT-0060 ELITROL I — 10 x 5 mL
- CONT-0160 ELITROL II — 10 x 5 mL
- Echipamente generale de laborator.
- Soluţie salină obişnuită (NaCl 9 g/L).
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ŞI PRECAUŢII

- Această trusă de reactiv este concepută doar pentru utilizarea profesională în scopul diagnosticării *in vitro*.
- În contact cu acizi, degajă un gaz toxic.
- Reactivul conţine azidă de sodiu, care poate reacţiona cu plumbul sau instalaţiile sanitare din cupru şi poate forma azide metalice explozibile. În cazul aruncării acestor reactivi, spălaţi întotdeauna cu cantităţi mari de apă pentru a preveni formarea de azide.
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Saliva şi transpiraţia conţine amilază. Astfel, se recomandă purtarea mănuşilor şi a unei măşti pentru a evita contaminarea reactivului.
- Fişa cu date de securitate disponibilă la cerere.

STABILITATEA REACTIVILOR

A se depozita la 2-8ºC şi a se proteja împotriva luminii. A nu se îngheţa.

A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultaţi § DATE PRIVIND PERFORMANŢA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA REACTIVILOR

- Soluţia de reactivi trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.

AMBALAJ DETERIORAT

Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiole perforate).

PROBE [4]

Specimen

- Ser
- Plasmă heparinizată cu litiu
- A nu se utiliza alte specimene.

Avertisment şi precauţii

Conform bunei practici de laborator, prelevarea trebuie efectuată înainte de administrarea de medicamente.

Depozitare şi stabilitate

Probele sunt stabile timp de 1 săptămână la temperatura camerei, 1 săptămână la 2-8ºC, şi 1 an la -20ºC.

VALORI DE REFERINŢĂ [5]

Ser, plasmă (37ºC): 31-107 U/L

Notă: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems.

Aplicaţiile sunt disponibile la cerere

Lungime de undă 405 nm

Temperatură 37°C

Citiţi pe reactivul martor.

Reactiv R	300 µL
Probă	3 µL

Amestecaţi şi după o incubaţie de 50 de secunde, măsuraţi modificarea absorbanţei pe minut (ΔA/min.) timp de 159 de secunde.

Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert.

CALCUL

$\frac{(\Delta A)\ \text{Probă}}{(\Delta A)\ \text{Calibrator}} \times n$ n=concentraţie calibrator

Factor de conversie: U/L x 0,0167 = µkat/L

CALIBRARE [5]

Pentru calibrare, trebuie utilizat calibratorul multiparametric ELICAL 2. Valoarea sa este trasabilă conform metodei IFCC.

Frecvenţa de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

CONTROLUL CALITĂŢII

Pentru a asigura precizia analizelor, vor fi utilizate serurile de control precum ELITROL I (control normal) şi ELITROL II (control patologic). Aceste controale trebuie efectuate şi validate înainte ca probele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare şi trebuie adaptată procedurilor de Controlul Calităţii fiecărui laborator şi cerinţelor reglementarilor in vigoare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele locale şi legale.

DATE DE PERFORMANŢĂ la 37°C privind Analizoarele Selectra ProM ale ELITech Clinical Systems

- Interval de măsurare

Determinat conform protocolului CLSI EP6-A[6], intervalul de măsurare este între 20 şi 1500 U/L (de la 0,33 la 25,00 µkat/L). Probele care depăşesc 1500 U/L trebuie să fie diluate 1:10 cu soluţie de NaCl 9 g/L (salină normală) şi re-analizate. Utilizarea acestei proceduri extinde intervalul de măsurare de la 1500 la 15000 U/L (de la 25,00 la 250,00 µkat/L).

Pentru utilizatorii Selectra TouchPro, funcţia „diluare" efectuează diluţia automată a probei. Rezultatele iau în considerare diluţia.

- **Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)**

Determinată conform protocolului CLSI EP17-A[7].

LoD = 6 U/L (0,10 µkat/L).

LoQ = 13 U/L (0,22 µkat/L).

- **Precizie**

Determinată conform protocolului CLSI EP5-A2[8].

		Medie		**În interiorul ciclului**	**Total**
	n	**U/L**	**µkat/L**	**CV (%)**	
Nivel scăzut	80	82	1,37	1,3	2,7
Nivel mediu	80	204	3,40	0,9	2,2
Nivel înalt	80	992	16,53	1,5	2,6

- Corelaţie

A fost efectuat un studiu comparativ între Analizorul Selectra ProM ELITech Clinical Systems şi un alt echipament al unui sistem aprobat de FDA (metoda IFCC) pe 100 de probe de ser uman conform protocolului CLSI EP9-A2[9].

Valorile au fost între 21 şi 1439 U/L (între 0,35 şi 23,98 µkat/L).

Parametrii regresiei liniare sunt după cum urmează:

Coeficient de corelaţie: (r)=0,999

Regresie liniară: y=0,976x – 1 U/L (0,02 µkat/L)

- Limitări şi interferenţe

- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2 [10] al CLSL. Recuperarea este în intervalul ±10% din valoarea iniţială a amilasa de 80 U/L şi 1000 U/L.

Trigliceride: Nicio interferenţă semnificativă până la 3000 mg/dL (33,9 mmol/L).
Bilirubină neconjugată: Nicio interferenţă semnificativă până la 30,0 mg/dL (513 µmol/L).
Bilirubină conjugată: Nicio interferenţă semnificativă până la 29,5 mg/dL (504 µmol/L).
Hemoglobină: Nicio interferenţă semnificativă până la 500 mg/dL.
Acid ascorbic: Nicio interferenţă semnificativă până la 20,0 mg/dL.
Acid acetilsalicilic: Nicio interferenţă semnificativă până la 200 mg/dL.
Acetaminofen: Nicio interferenţă semnificativă până la 30 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [11]
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [12-13]

- Rezultatele acestui studiu trebuie interpretate doar în corelaţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

ELITechGroup
EMPOWERING IVD

AMYLASE SL

Referinţe:		**Compoziţia trusei:**
AMSL-0230	*6 x 20 mL*	***R** 6 x 20 mL*
AMSL-0390	*1 x 50 mL*	***R** 1 x 50 mL*
AMSL-0400	*6 x 50 mL*	***R** 6 x 50 mL*

FTRO-AMSL-v18 (12/2018)_PIT-AMSL-4-v18

CE

Stabilitatea la bord/Frecvenţa calibrării
Stabilitatea la bord: 28 de zile
Frecvenţa calibrării: 28 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit şi după o operaţie de întreţinere.

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12. Young, D.S., Effects of preanalytical variables on clinical laboratory tests, 2nd Ed., AACC Press, (1997).
13. Young, D.S., Effects of drugs on clinical laboratory tests, 4th Ed., AACC Press, (1995).

SIMBOLURI

IVD	Dispozitiv medical de diagnosticare *in vitro*.
	Consultaţi instrucţiunea de utilizare.
	Producător
	Limită de temperatură
LOT	Număr de lot
	Data expirării
REF	Număr catalog
CONT	Conţinut
R	Reactiv
CE	Conformitate europeană

Notă
- Doar pentru ref. AMSL-0230, utilizată cu software-ul Selectra TouchPro.

Amylase IFCC 0
165 PIT-AMSL

:Modificare faţă de versiunea precedentă.

AST/GOT 4+1 SL

Referinţe:		**Compoziţia trusei:**
ASSL-0250	*8 x 25 mL*	**R1** *8 x 20 mL* + **R2** *8 x 5 mL*
ASSL-0455	*4 x 55 mL*	**R1** *4 x 44 mL* + **R2** *4 x 11 mL*
ASSL-0410	*2 x 62,5 mL*	**R1** *2 x 50 mL* + **R2** *1 x 26 mL*
ASSL-0430	*4 x 62,5 mL*	**R1** *4 x 50 mL* + **R2** *2 x 26 mL*
ASSL-0510	*5 x 125 mL*	**R1** *5 x 100 mL* + **R2** *1 x 127 mL*

FTRO-ASSL4+1-v19(12/2018)_PIT-ASSL4+1-4-v19

SCOPUL UTILIZĂRII

AST/GOT 4+1 SL ELITech Clinical Systems este conceput pentru determinarea cantitativă a aspartat aminotransferazei (AST) în serul uman şi plasmă pentru diagnosticare *in vitro* .

SEMNIFICAŢIE CLINICĂ [1-4]

Aspartat aminotransferaza (AST), cunoscută şi ca glutamat oxalat transaminază (GOT), este o transaminază. AST catalizează transferul grupului amino al L-aspartatului la α-ketoglutarat pentru a rezulta L-glutamatul. AST este distribuită în mare măsură în organism, însă cele mai mari nivele se găsesc în inimă, ficat, muşchii scheletici şi rinichi.

Deteriorarea celulelor acestor ţesuturi induce creşterea AST în ser. În cazul formelor fulminante de hepatită, în special hepatita virală, nivelul enzimei este marcat ridicat. În cazului infarctului miocardic, activitatea AST creşte şi atinge un vârf după 18-24 ore. Activitatea scade din nou după 4-5 zile, cu condiţia să nu aibă loc un infarct.

Următoarele stări patologice sunt exemple ale afecţiunilor care duc, de asemenea, la o creştere a activităţii enzimatice: necroza celulelor ficatului sau leziunea de orice cauză (de exemplu aportul de alcool, delirium tremens, şi administrarea diverselor medicamente induc creşterea moderată a AST), hepatita alcoolică, distrofia musculară şi gangrena, mononucleoza infecţioasă, pancreatita acută, afecţiunile cardiace precum miocardita sau pericardita, emboliile pulmonare…

Nivelul AST în ser poate fi redus în cazul deficienţei de vitamina B6.

METODĂ [5]

Metoda IFCC fără piridoxal fosfat (P-5'-P).

Cinetică. UV.

PRINCIPIU [5]

Determinarea cinetică a activităţii aspartat aminotransferazei (AST).

$$\text{L-aspartat} + \alpha\text{-ketoglutarat} \xrightarrow{AST} \text{Oxaloacetat} + \text{L-glutamat}$$

$$\text{Oxaloacetat} + \text{NADH} + H^+ \xrightarrow{MDH} \text{L-malat} + NAD^+$$

MDH=malat dehidrogenază

COMPOZIŢIA

Reactiv 1: R1

Tampon Tris, pH 7,80 (30ºC)	100 mmol/L
L-aspartat	330 mmol/L
LDH	$\geq$ 2000 U/L
MDH	$\geq$ 1000 U/L
Azidă de sodiu	< 0,1%

Reactiv 2: R2

α-Ketoglutarat	78 mmol/L
NADH	1,1 mmol/L
Azidă de sodiu	< 0,1%

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550, ELICAL 2
- CONT-0060, ELITROL I
- CONT-0160, ELITROL II
- Soluţie salină obişnuită (NaCl 9 g/L).
- Echipamente generale de laborator.
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ŞI PRECAUŢII

- Acest reactiv este conceput doar pentru utilizarea în scopul diagnosticării *in vitro*.
- Aceşti reactivi conţin azidă de sodiu care poate reacţiona cu plumbul sau instalaţiile sanitare din cupru şi poate forma azide metalice explozibile. În cazul aruncării acestor reactivi, spălaţi întotdeauna cu cantităţi mari de apă pentru a preveni formarea de azide.
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Nu interschimbaţi fiolele de reactiv din truse diferite.
- Pentru mai multe informaţii, Fişa de date privind siguranţa (SDS) este disponibilă la cerere pentru utilizatorul profesional.

STABILITATEA

A se depozita la 2-8ºC şi a se proteja împotriva luminii. A nu se îngheţa.

A nu se utiliza după datele de expirare indicate pe etichetele recipientelor.

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultaţi § DATE PRIVIND PERFORMANŢA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

- Soluţia de reactivi trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, recipient perforat).

PROBE [2,6]

Specimen

- Ser şi plasmă heparinizată de litiu, libere de hemoliză.
- A nu se utiliza aste specimene.

Avertisment şi precauţii

Conform bunei practici de laborator, puncţia venoasă trebuie efectuată înainte de administrarea de medicamente.

ELITechGroup
EMPOWERING IVD

AST/GOT 4+1 SL

Referinţe:		**Compoziţia trusei:**
ASSL-0250	*8 x 25 mL*	**R1** *8 x 20 mL* + **R2** *8 x 5 mL*
ASSL-0455	*4 x 55 mL*	**R1** *4 x 44 mL* + **R2** *4 x 11 mL*
ASSL-0410	*2 x 62,5 mL*	**R1** *2 x 50 mL* + **R2** *1 x 26 mL*
ASSL-0430	*4 x 62,5 mL*	**R1** *4 x 50 mL* + **R2** *2 x 26 mL*
ASSL-0510	*5 x 125 mL*	**R1** *5 x 100 mL* + **R2** *1 x 127 mL*

CE

Depozitare şi stabilitate
Eşantioanele sunt stabile timp de 24 de ore la temperatura camerei, 7 zile la 2-8ºC, şi 3 luni la -20ºC.

VALORI DE REFERINŢĂ [2,3]

Ser, plasmă (37ºC): <40 U/L
Valorile de referinţă pentru infanţi sunt mai mari decât pentru adulţi.

Notă: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems.
Aplicaţiile sunt disponibile la cerere
Lungime de undă 340 nm
Temperatură 37ºC
Citiţi pe reactivul martor.

Reactiv R1	240 µL
Proba	15 µL

Amestecaţi şi aşteptaţi o incubaţie de 4 minute şi 43 de secunde, apoi adăugaţi:

Reactiv R2	60 µL

Amestecaţi şi aşteptaţi o incubaţie de 50 de secunde, măsuraţi modificarea absorbanţei per minut (ΔA/min) timp de 159 de secunde.

- Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert.
- Valorile mari ale AST pot induce rezultate scăzute în mod fals datorită golirii substratului (consumul total de NADH înainte de citirea rezultatului). Pentru Analizoarele Selectra pro Series ELITech Clinical Systems, aplicaţia conţine o alarmă specifică pentru a avertiza utilizatorii.

CALCUL

$$\frac{(\Delta A)\ \text{Proba}}{(\Delta A)\ \text{Calibrator}} \times n \qquad n=\text{concentraţie calibrator}$$

Factor de conversie: U/L x 0.0167 = µkat/L

CALIBRARE

Pentru calibrare, trebuie utilizat calibratorul multiparametric ELICAL 2. Valoarea sa este trasabilă conform metodei de referinţă IFCC [5].
Frecvenţa de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

CONTROLUL CALITĂŢII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I şi ELITROL II. Aceste controale trebuie efectuate şi validate înainte ca probele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare, şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite.
Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele de reglementare locale, statale şi federale.

DATE DE PERFORMANŢĂ la 37ºC privind Analizoarele Selectra ProM ale ELITech Clinical Systems

- **Interval de măsurare**

Determinat conform protocolului CLSI EP6-A[7], intervalul de măsurare este între 10,0 şi 450,0 U/L (de la 0,17 la 7,50 µkat/L). Probele care depăşesc 450,0 U/L trebuie să fie diluate 1:10 cu soluţie de NaCl 9 g/L (salină normală) şi re-analizate. Utilizarea acestei proceduri extinde intervalul de măsurare de la 450,0 la 4500,0 U/L (de la 7,50 la 75,00 µkat/L).

Pentru utilizatorii Selectra TouchPro, funcţia „dilute" efectuează diluţia automată a eşantionului. Rezultatele iau în considerare diluţia.

- **Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)**

Determinată conform protocolului CLSI EP17-A[8].
LoD= 2,5 U/L (0,04 µkat/L).
LoQ= 5,0 U/L (0,08 µkat/L).

- **Precizie**

Determinată conform protocolului CLSI EP5-A2[9].

		Medie		**În interiorul ciclului**	**Total**
	n	**U/L**	**µkat/L**	**CV (%)**	
Nivel scăzut	80	34,1	0,57	1,7	3,4
Nivel mediu	80	67,9	1,13	0,8	1,9
Nivel înalt	80	353,6	5,89	0,4	2,0

- Corelaţie
A fost efectuat un studiu comparativ între Analizorul Selectra ProM ELITech Clinical Systems şi un alt echipament al unui sistem aprobat de FDA (metoda IFCC fără piridoxal fosfat) pe 114 de eşantioane de ser uman conform protocolului CLSI EP9-A2[10].
Valorile acoperă domeniul de măsurare.
Parametrii regresiei liniare sunt după cum urmează:
Coeficient de corelaţie: (r)=0,999
Regresie liniară: y= 0,927 x -0,3 U/L (0,01 µkat/L).

- Limitări şi interferenţe
- Eşantioanele hemolizate nu trebuie să fie utilizate deoarece hemoliza semnificativă poate creşte concentraţia AST din cauza nivelelor ridicate de AST în eritrocite.
- Nu raportaţi rezultatele în afara intervalului utilizabil.

AST/GOT 4+1 SL

Referinţe:		Compoziţia trusei:
ASSL-0250	*8 x 25 mL*	**R1** *8 x 20 mL* + **R2** *8 x 5 mL*
ASSL-0455	*4 x 55 mL*	**R1** *4 x 44 mL* + **R2** *4 x 11 mL*
ASSL-0410	*2 x 62,5 mL*	**R1** *2 x 50 mL* + **R2** *1 x 26 mL*
ASSL-0430	*4 x 62,5 mL*	**R1** *4 x 50 mL* + **R2** *2 x 26 mL*
ASSL-0510	*5 x 125 mL*	**R1** *5 x 100 mL* + **R2** *1 x 127 mL*

CE

- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2 [11] al CLSL şi recomandările SFBC[12]. Recuperarea este în intervalul ±10% din valoarea iniţială a activităţii AST de 35,0 U/L şi 350,0 U/L.

Bilirubină neconjugată: Nicio interferenţă semnificativă până la 30 mg/dL (513 µmol/L).
Bilirubină conjugată: Nicio interferenţă semnificativă până la 29,5 mg/dL (504 µmol/L).
Trigliceride: Nicio interferenţă semnificativă până la 2400 mg/dL (27,12 mmol/L) echivalent trigliceride.
Piruvat: Nicio interferenţă semnificativă până la 3 mg/dl.
Acid ascorbic: Nicio interferenţă semnificativă până la 20 mg/dL.
Acid acetilsalicilic: Nicio interferenţă semnificativă până la 200 mg/dL.
Acetaminofen: Nicio interferenţă semnificativă până la 30 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [13]
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [14-15]
- Rezultatele acestui studiu trebuie interpretate doar în conjuncţie cu aste rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- **Stabilitatea la bord/Frecvenţa calibrării**

Stabilitatea la bord: 28 de zile
Frecvenţa calibrării: 28 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit, şi după o operaţie de întreţinere.

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8.Protocols for Determination of Limits of Detection and Limits of Quantification; Approved Guideline. CLSI (NCCLS) document EP17-A (2004), **24** (34).
9.Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition. CLSI (NCCLS) document EP5-A2 (2004), **24** (25).
10.Method Comparison and Bias estimation Using Patient Samples; Approved Guideline—Second Edition. CLSI (NCCLS) document EP9-A2 (2002), **22** (19).
11.Interference Testing in Clinical Chemistry ; Approved Guideline—Second Edition. CLSI (NCCLS) document EP7-A2 (2005), **25** (27).
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14.Young, D. S., Effects of preanalytical variables on clinical laboratory tests, 2nd Ed., AACC Press, (1997).
15.Young, D. S., Effects of drugs on clinical labora-tory tests, 4th Ed., AACC Press, (1995).

SIMBOLURI

Simbolurile folosite sunt definite conform standardului ISO-15223-1 cu excepţia celor prezentate mai jos.

CONT	Conţinut
R1	Reactiv 1
R2	Reactiv 2
CE	Conformitate europeană

Notă:
Doar pentru ref. **ASSL-0250/ASSL-0455**, utilizată cu software-ul Selectra TouchPro.

ASAT (GOT) 1
180 PIT-ASSL

☞:Modificare faţă de versiunea precedentă.

BILIRUBIN TOTAL & DIRECT 4+1

Referinţe:

BIDI-0250 Directă 4+1 8 x 25 mL
BITO-0250 Totală 4+1 8 x 25 mL
BIDI-0600 Directă 4+1 2 x 125 mL
BITO-0600 Totală 4+1 2 x 125 mL
BITD-0600 T&D 4+1 2 x 125 mL

Compoziţia trusei:

R1 Directă *8 x 20 mL* + ***R2*** *8 x 5 mL*
R1 Totală *8 x 20 mL* + ***R2*** *8 x 5 mL*
R1 Directă *2 x 100 mL* + ***R2*** *1 x 50 mL*
R1 Totală *2 x 100 mL* + ***R2*** *1 x 50 mL*
R1 Totală *1 x 100 mL* + ***R1 Directă*** *1 x 100 mL* + ***R2*** *1 x 50 mL*

FTRO-BITD-v12 (12/2018)_PIT_BITD-4-v12

CE

SCOPUL UTILIZĂRII

Pentru Bilirubină Totală: BILIRUBIN TOTAL 4+1 ELITech Clinical Systems este conceput pentru determinarea cantitativă a bilirubinei totale în serul uman şi plasmă în cazul adulţilor şi copiilor cu vârsta de peste 10 zile pentru diagnosticare *in vitro*.

Pentru Bilirubină Directă: BILIRUBIN DIRECT 4+1 ELITech Clinical Systems este conceput pentru determinarea cantitativă a bilirubinei directe în serul uman şi plasmă pentru diagnosticare *in vitro*.

SEMNIFICAŢIE CLINICĂ [1-2]

Aproximativ 80-85% din bilirubina este produsă din fractiunea hem a hemoglobinei eliberate de eritrocitele care îmbătrânesc in celulele reticuloendoteliale. Bilirubina, legată de albumină, este transportată în ficat, unde este conjugată rapid cu glucuronida pentru a-i mări solubilitatea. Apoi, aceasta este excretată în canaliculii biliari şi hidrolizată în tractul gastrointestinal.

Concentraţia serului de bilirubină neconjugată creşte în cazul supra-producerii de bilirubină (anemie hemolitică acută şi cronică) şi în cazul afecţiunilor metabolismului bilirubinei şi defectelor de transport (aport afectat de celulele hepatice: sindromul Gilbert; defectele în reacţia de conjugare: sindromul Crigler-Najjar). Excreţia redusă (deteriorare hepatocelulară: hepatită, ciroză…; sindromul Dubin-Jonhson şi Rotor) şi obstrucţia fluxului biliar (cel mai adesea produsă de calculii biliari sau de tumori) induc o creştere importantă a bilirubinei conjugate şi într-o măsură minoră o creştere a bilirubinei neconjugate (hiperbilirubinemia conjugată).

METODĂ[2]

Malloy-Evelyn modificată. Punct final.

PRINCIPIU [1-2]

Acidul sulfanilic reacţionează cu nitritul de sodiu pentru a forma acidul sulfanilic diazotat. În prezenţa acceleratorului (cetrimida), bilirubina conjugată şi neconjugată reacţionează cu acidul sulfanilic diazotat pentru a forma azobilirubina (Bilirubina totală 4+1). În absenţa acceleratorului, doar bilirubina conjugată reacţionează (Bilirubină directă 4+1). Creşterea absorbanţei la 546 nm este proporţională cu concentraţia bilirubinei.

Acidul sulfanilic + $NaNO_2$ $\longrightarrow$ Acid sulfanilic diazotat

Bilirubină + Acid sulfanilic diazotat $\longrightarrow$ Azobilirubină

COMPOZIŢIA REACTIVULUI

BILIRUBINĂ TOTALĂ 4+1

Reactiv 1: R1

Acid sulfanilic	29	mmol/L
Cetrimidă	29	mmol/L

BILIRUBINĂ DIRECTĂ 4+1

Reactiv 1: R1

Acid sulfanilic	29	mmol/L

BILIRUBINĂ TOTALĂ & DIRECTĂ 4+1

Reactiv 2: R2

Nitrit de sodiu	11	mmol/L

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Soluţie salină obişnuită (NaCl 9 g/L)
- Echipamente generale de laborator.
- Analizor de biochimie echipat cu filtrele necesare. (Consultati § PROCEDURA).
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ŞI PRECAUŢII

- Aceşti reactivi sunt doar pentru utilizarea profesională, în scopul diagnosticării *in vitro*.
- Reactivii R1 conţine acid sulfanilic. Poate provoca o reacţie alergică.
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Nu interschimbaţi fiolele de reactiv din truse diferite.
- Fişa cu date de securitate disponibilă la cerere.

STABILITATEA

A se depozita la 2-8ºC şi a se proteja împotriva luminii. A nu se îngheţa.

A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultaţi § DATE PRIVIND PERFORMANŢA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

- Reactivul R1 din Bilirubină totală 4+1 poate fi uşor tulbure. Acesta conţine un detergent care poate duce la formarea de spumă în unităţile de spălare ale unor echipamente. Aceste două caracteristici nu au consecinţe asupra performanţelor produsului.
- Reactivii R1 din Bilirubină directă 4+1 şi reactivul R2 din Bilirubină totală şi directă 4+1 trebuie să fie limpezi. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiolă perforată).

PROBE [3]

Specimen

- Ser sau plasmă heparinizată cu litiu.
- A nu se utiliza alte specimene.

Avertisment şi precauţii

- *Pentru bilirubina directă*: Nu utilizaţi probe hemolizate.
- Conform bunei practici de laborator, prelevarea trebuie efectuată înainte de administrarea de medicamente.
- Trebuie acordată o atenţie specială umplerii tuburilor heparinizate conform instrucţiunilor producătorului. O umplere insuficientă poate duce la rezultate eronate.
- Protejaţi probele împotriva luminii înainte şi în timpul analizei.

Depozitare şi stabilitate

Dacă plasma şi serul sunt protejate împotriva luminii, probele sunt stabile 1 zi (Bilirubină totală) sau 2 zile (Bilirubina directă) la temperatura camerei, 7 zile la 2-8ºC şi 6 luni la -20ºC.

VALORI DE REFERINŢĂ [4]

Ser, plasmă:

Bilirubină totală:

Adulţi şi copii peste 10 zile:

0,2-1,2 mg/dL (3,4-21 µmol/L)

Bilirubină directă:

<0,2 mg/dL (3,4 µmol/L)

Notă: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems, aplicaţiile sunt disponibile la cerere.

A) Bilirubină totală

Lungime de undă 546-700 nm

Temperatură: 37ºC

Citiţi pe reactivul martor.

	CALIBRARE	TEST
Reactiv R1	240 µL	240 µL
Calibrator	15 µL	-
Probă	-	15 µL

Amestecaţi şi citiţi absorbanţa (∆A1) după o incubaţie de 4 minute 40 (proba martor), apoi adăugaţi:

Reactiv R2	60 µL

Amestecaţi şi citiţi absorbanţa (∆A2) după o incubaţie de 6 minute 30.

Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestei inserţii.

Pentru utilizatorii Selectra ProXS, este nevoie de un filtru suplimentar de 700nm.

B) Bilirubină directă

Lungime de undă 546 nm

Temperatură: 37ºC

Citiţi pe reactivul martor.

	CALIBRARE	TEST	
Reactiv R1	240 µL	240 µL	
Calibrator	30 µL	-	
Probă	-	30 µL	

Amestecaţi şi citiţi absorbanţa (A1) după o incubaţie de 4 minute 40 (proba martor), apoi adăugaţi:

Reactiv R2	60 µL

Amestecaţi şi citiţi absorbanţa (A2) după o incubaţie de 50 de secunde.

Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert.

În aplicaţie, compensarea trebuie setată la: -0,05 mg/dL (-0,9 µmol/L).

CALCUL

A) Bilirubină totală

$$\frac{(\Delta A2-\Delta A1)\ \text{Probă}}{(\Delta A2-\Delta A1)\ \text{Calibrator}} \times \text{concentraţie calibrator}$$

B) Bilirubină directă

$$\frac{(A2-A1)\ \text{Probă}}{(A2-A1)\ \text{Calibrator}} \times \text{concentraţie calibrator}$$

Factor de conversie: mg/dL x 17,1= µmol/L

CALIBRARE

Pentru calibrare, trebuie utilizat calibratorul multiparametric ELICAL 2. Valoarea sa este definită în raport cu materialul de referinţă SRM 916a (al Institutului Naţional de Standarde şi Tehnologie).

Frecvenţa de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

CONTROLUL CALITĂŢII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum ELITROL I (control normal) şi ELITROL II (control patologic). Aceste controale trebuie efectuate şi validate înainte ca probele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele locale, statale şi federale.

DATE DE PERFORMANŢĂ la 37ºC privind Analizoarele Selectra ProM ale ELITech Clinical Systems

A) Bilirubină totală

- Interval de măsurare

Determinat conform protocolului CLSI EP6-A[5], intervalul de măsurare este între 0,25 mg/dL şi 25,00 mg/dL (de la 4,3 la 427,6 µmol/L). Probele care depăşesc 25,00 mg/dL trebuie diluate 1:5 cu soluţie de NaCl 9 g/l (soluţie salină normală) şi re-testate. Utilizarea acestei proceduri extinde intervalul de măsurare între 25,00 şi 60,00 mg/dL (de la 427,6 la 1026,3 µmol/L).

Pentru utilizatorii Selectra TouchPro, funcţia „diluare" efectuează diluarea probelor automat. Rezultatele iau în considerare diluţia.

- Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)
Determinată conform protocolului CLSI EP17-A[6].

LoD=0,04 mg/dL (0,7 µmol/L)
LoQ=0,15 mg/dL (2,6 µmol/L)

- Precizie
Determinată conform protocolului CLSI EP5-A2[7].

		Medie		**În interiorul ciclului**	**Total**
	n	**mg/dL**	**µmol/L**	**CV (%)**	
Nivelul 1	80	1,15	19,7	1,8	5,0
Nivelul 2	80	4,08	69,8	0,4	3,1
Nivelul 3	80	14,61	249,9	0,5	2,9

- Corelaţie
A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems şi un alt echipament al sistemului aprobat de FDA (metoda DCA) pe 100 de probe de ser uman conform protocolului CLSI EP9-A2[8].
Concentraţiile probelor au fost între 0,32 şi 23,02 mg/dL (5,5 şi 393,7 µmol/L).
Parametrii regresiilor liniare sunt după cum urmează:
Coeficient de corelaţie: (r)=0,999
Regresie liniară: y= 0,948 x -0,11 mg/dL (1,9 µmol/L)

- Limitări şi interferenţe
- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2 [9]. Recuperarea este în intervalul ±15% din valoarea iniţială a concentraţiei bilirubinei totale de 1,00 mg/dL şi 15,00 mg/dL.

Trigliceride: Nicio interferenţă semnificativă până la 2100 mg/dL (23,73 mmol/L).
Hemoglobină: Nicio interferenţă semnificativă până la 500 mg/dL.
Acetaminofen: Nicio interferenţă semnificativă până la 30 mg/dL.
Acid ascorbic: Nicio interferenţă semnificativă până la 4 mg/dL.
Acid acetilsalicilic: Nicio interferenţă semnificativă până la 200 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [10]
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [11-12]
- Rezultatele acestui studiu trebuie interpretate doar în corelaţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- Stabilitatea la bord/Frecvenţa calibrării
Stabilitatea la bord: 28 de zile
Frecvenţa calibrării: 28 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit şi după o operaţie de întreţinere.

B) Bilirubină directă

- Interval de măsurare
Determinat conform protocolului CLSI EP6-A[5], intervalul de măsurare este între 0,08 mg/dL şi 10,55 mg/dL (de la 1,4 la 180,4 µmol/L). Probele care depăşesc 10,55 mg/dL trebuie diluate cu soluţie de NaCl 9 1:5 (soluţie salină normală) şi re-testate. Utilizarea acestei proceduri extinde intervalul de măsurare între 10,55 şi 50,00 mg/dl (de la 180,4 la 855,2 µmol/L).

Pentru utilizatorii Selectra TouchPro, funcţia „diluare" efectuează diluarea probelor automat. Rezultatele iau în considerare diluţia.

- Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)
Determinată conform protocolului CLSI EP17-A[6].

LoD=0,01 mg/dL (0,2 µmol/L)
LoQ=0,08 mg/dL (1,4 µmol/L)

- Precizie
Determinată conform protocolului CLSI EP5-A2[7].

		Medie		**În interiorul ciclului**	**Total**
	n	**mg/dL**	**µmol/L**	**CV (%)**	
Nivelul 1	80	0,36	6,2	3,8	5,2
Nivelul 2	80	1,51	25,8	1,9	5,3
Nivelul 3	80	3,99	68,2	0,9	4,7

- Corelaţie
A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems şi un alt echipament al sistemului aprobat de FDA (metoda DCA) pe 100 de probe de ser uman conform protocolului CLSI EP9-A2[8].
Concentraţiile probelor au fost între 0,09 şi 10,52 mg/dL (1,5 şi 179,9 µmol/L).
Parametrii regresiilor liniare sunt după cum urmează:
Coeficient de corelaţie: (r)=0,998
Regresie liniară: y=0,926 x -0,03 mg/dL (0,5 µmol/L)

- Limitări şi interferenţe
- Concentraţia acidului ascorbic mai mare de 0,5 mg/dL poate duce la rezultate fals pozitive ale bilirubinei directe.
- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2 [9]. Recuperarea este în intervalul ±15% din valoarea iniţială a concentraţiei bilirubinei directe de 0,40 mg/dL şi 4,00 mg/dL.

Trigliceride: Nicio interferenţă semnificativă până la 2000 mg/dL (22,60 mmol/L).
Hemoglobină: Nicio interferenţă semnificativă până la 125 mg/dL.
Acetaminofen: Nicio interferenţă semnificativă până la 30 mg/dL.

Acid ascorbic: Nicio interferenţă semnificativă până la 0,5 mg/dL.
Acid acetilsalicilic: Nicio interferenţă semnificativă până la 200 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [10]
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [11-12]
- Rezultatele acestui studiu trebuie interpretate doar în conjuncţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- Stabilitatea la bord/Frecvenţa calibrării

Stabilitatea la bord: 28 de zile
Frecvenţa calibrării: 28 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit şi după o operaţie de întreţinere.

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SIMBOLURI

Simbolurile folosite sunt definite conform standardului ISO-15223-1 cu exceptia celor prezentate mai jos.

CONT	Conţinut
R1	Reactiv 1
R2	Reactiv 2
CE	Conformitate europeană

:Modificare faţă de versiunea precedentă.

BILIRUBINĂ DIRECTĂ 4+1:

NOTĂ IMPORTANTĂ

- Doar pentru ref. **BIDI-0250**, utilizată cu software-ul Selectra TouchPro.
- **Vezi §PROCEDURĂ:** Este necesară introducerea manuală

Bilirubin Direct New 0
205 PIT-BITD

BILIRUBINĂ TOTALĂ 4+1:

- Doar pentru ref. **BITO-0250**, utilizată cu software-ul Selectra TouchPro.

Bilirubin Total New 0
225 PIT-BITD

CALCIUM ARSENAZO

☞Referinţe:	Compoziţia trusei:
CALA-0600	***R*** *2 x 125 mL +* ***Std*** *1 x 5 mL*
CALA-0250	***R*** *12 x 20 mL*

FTRO-CALA-v18 (09/2020)_PIT-CALA-4-v18

☞SCOPUL UTILIZĂRII

ELITech Clinical Systems CALCIUM ARSENAZO este un reactiv de diagnostic *in vitro* destinat determinării cantitative a calciului total din probele serul uman, plasmă şi urină.

SEMNIFICAŢIE CLINICĂ [1-3]

În sânge, aproximativ 45% din calciul plasmatic este liber, 45% este legat de proteine, asociat în principal cu albumina şi 10% formează complexe. Calcemia măsoară calciul total, însă doar calciul liber este activ din punct de vedere biologic. Calciul are un rol fiziologic activ în mineralizarea oaselor, excitabilitatea neuromusculară, contracţia musculară şi coagularea sângelui. Nivelurile de proteine serice sau albuminia trebuie avute în vedere pentru interpretarea corespunzătoare a nivelurilor de calciu seric total. Hipocalcemia poate rezulta din insuficienţa renală cronică cu hipoproteinemia şi hiperfosfatemia, sau hipoparatiroidismul, sau deficienţa de vitamina D (osteomalachia, rahitismul...). Cele mai frecvente cazuri de hipercalcemie sunt asociate cu hiperparatiroidismul sau supradoza de vitamina D...

Calciuria are o valoare practică mică în diverse diagnostice, cu excepţia tubulopatiilor renale.

METODĂ

Testul direct colorimetric complexometric (Arsenazo III).

Punct final.

PRINCIPIU [4]

La un pH usor acid, ionii Ca2+ formeaza cu Arsenazo III (acid 2,7-(bis(2-arsonofenilazo))-1,8-dihidroxinaftalen-3,6-disulfonic) un complex a carui absorbanta este direct proportionala cu concentratia totala de calciu.

COMPOZIŢIA REACTIVULUI

Reactiv: R

Tampon MES, pH 6,50	100 mmol/L
Arsenazo III	200 µmol/L
Standard: Std. (Ref.: CALA-0600)	
Calciu	10 mg/dL
	2.5 mmol/L

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Echipamente generale de laborator.
- Analizor de biochimie echipat cu filtrele necesare. (Consultati § PROCEDURA).
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ŞI PRECAUŢII

- Acest dispozitiv de diagnostic *in vitro* (Reactiv şi Standardul) este destinat numai pentru uz profesional.
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Standardul trebuie să fie imediat inchis cu capacul pentru a preveni contaminarea şi evaporarea.
- Pentru mai multe informaţii, Fişa de date privind siguranţa (SDS) este disponibilă la cerere pentru utilizatorul profesional.

STABILITATEA

A se depozita la 2-8ºC şi a se proteja împotriva luminii. A nu se îngheţa.

A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultaţi § DATE PRIVIND PERFORMANŢA).

PREGĂTIRE

Reactivii şi Standardul sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

- Reactivul şi soluţia standard trabuie să fie limpezi. Turbiditatea ar indica deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiolă perforată).

PROBE [1,2,5]

Specimen

- Ser
- Plasmă heparinizată cu litiu.
- Urină colectată peste 24 de ore.
- A nu se utiliza alte specimene.

Avertismente şi precauţii

- Conform bunei practici de laborator, prelevarea trebuie efectuată înainte de administrarea de medicamente.
- Serul trebuie separat de celule cât mai repede posibil.
- După colectare, specimenele de urină trebuie să fie acidifiate cu acid clorhidric 6N la un pH < 2, pentru a preveni precipitarea sării de calciu.

Depozitare

- Calciul total este stabil în ser şi plasmă la temperatura camerei până la 7 zile, la 2-8ºC timp de 3 săptămâni şi în stare îngheţată (-20ºC) până la 8 luni.
- Urina poate fi conservată la temperatura camerei timp de 2 zile, la 2-8ºC timp de 4 zile şi în stare îngheţată (-20ºC) până la 3 săptămâni.

VALORI DE REFERINŢĂ [1,6]

Ser, plasmă:	8,6-10,3 mg/dL
	2,15-2,57 mmol/L
Urină:	100-300 mg/24 ore
	2,50-7,50 mmol/24 ore
	6,7-20,0 mg/dL*
	1,67-5,00 mmol/L*

Calcemia este întotdeauna interpretată în funcţie de ratele proteinei plasmatice.

*pentru un volum urinar de 1,5 L pe 24 de ore.

<u>**Notă**</u>: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

CALCIUM ARSENAZO

☞Referinţe:	Compoziţia trusei:
CALA-0600	***R*** *2 x 125 mL +* ***Std*** *1 x 5 mL*
CALA-0250	***R*** *12 x 20 mL*

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems,
aplicaţiile sunt disponibile la cerere.
Lungime de undă 660-700 nm
Temperatură: 37ºC
Citiţi pe reactivul martor.

	CALIBRARE	CALIBRARE	TEST
Reactiv R	300 µL	300 µL	300 µL
Apă distilată	6 µL	-	-
Standard/ Calibrator	-	6 µL	-
Proba	-	-	6 µL

Amestecaţi, aşteptaţi 4 minute şi 30 de secunde şi apoi citiţi absorbanţa (A).

Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert.

Pentru utilizatorii Selectra ProXS, este nevoie de un filtru suplimentar de 700 nm.

CALCUL

$$\frac{\Delta A \text{ Proba}}{\Delta A \text{ Standard/Calibrator}} \times n \qquad n = \text{concentraţie calibrator/standard}$$

Factor de conversie: mg/dL x 0,25= mmol/L

☞CALIBRARE

Pentru referinţa CALA-0600: Pentru calibrare, trebuie utilizat fie calibratorul multiparametric ELICAL 2 fie Standardul de calciu de 10 mg/dL.
Pentru referinţa CALA-0250: Pentru calibrare, utilizaţi calibratorul multiparametric ELICAL 2.

Valorile concentraţiei Standardului de calciu de 10 mg/dL şi calibratorului multiparametric ELICAL 2 sunt trasabile conform Materialului Standard de Referinţă 956d (al Institutului Naţional de Standarde şi Tehnologie).

Frecvenţa de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

CONTROLUL CALITĂŢII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum ELITROL I şi ELITROL II . Aceste controale trebuie efectuate şi validate înainte ca probele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele de reglementare locale, statale şi federale.

DATE DE PERFORMANŢĂ la 37ºC privind Analizoarele Selectra ProM ale ELITech Clinical Systems

- Interval de măsurare
Determinat conform protocolului CLSI EP6-A[7].

a) Ser/Plasmă
Intervalul de măsurare este între 5,00 şi 15,00 mg/dL (de la 1,25 la 3,74 mmol/L).

☞b) Urină
Intervalul de măsurare este între 1,50 şi 18,00 mg/dL (0,37 - 4,49 mmol/L). care depăşesc 18,00 mg/dL trebuie să fie diluate 1:5 cu soluţie NaCl 9g/L (salină obişnuită) şi re-evaluate. Utilizarea acestei proceduri extinde intervalul de măsurare până la 90,00 mg/dL (22,46 mmol/L.)

Pentru utilizatorii Selectra TouchPro, funcţia „diluare” efectuează diluarea probelor automat. Rezultatele iau în considerare diluţia.

- Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)
Determinată conform protocolului CLSI EP17-A[8].
LoD=0,04 mg/dL (0,01 mmol/L)
LoQ=5,00 mg/dL (1,25 mmol/L)

a) Urină
LoD=0,15 mg/dL (0,04 mmol/L)
LoQ=1,50 mg/dL (0,37 mmol/L)

- Precizie
Determinată conform protocolului CLSI EP5-A2[9].

a) Ser/Plasmă

		Medie		În interiorul ciclului	Total
	n	**mg/dL**	**mmol/L**	**CV (%)**	
Nivelul 1	80	8,28	2,07	1,1	1,7
Nivelul 2	80	10,32	2,57	0,5	1,4
Nivelul 3	80	12,96	3,23	0,5	1,0

b) Urină

		Medie		În interiorul ciclului	Total
	n	**mg/dL**	**mmol/L**	**CV (%)**	
Nivelul 1	80	4,53	1,13	1,3	1,8
Nivelul 2	80	10,89	2,72	0,5	1,2
Nivelul 3	80	17,51	4,37	0,3	0,8

☞- Corelaţie
a) Ser/Plasmă
A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems şi un alt echipament al sistemului aprobat de FDA (metoda colorimetrică) pe 106 probe de ser uman conform protocolului CLSI EP9-A2[10].
Valorile au fost între 5,33 şi 15,53 mg/dL (1,33 şi 3,87 mmol/L).
Parametrii regresiilor liniare sunt după cum urmează:
Coeficient de corelaţie: (r)=0,993
Regresie liniară: y=0,996x +0,43 mg/dL (0,11 mmol/L)

CALCIUM ARSENAZO

☞Referinţe:	Compoziţia trusei:
CALA-0600	***R*** *2 x 125 mL* + ***Std*** *1 x 5 mL*
CALA-0250	***R*** *12 x 20 mL*

b) Urină

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems şi un alt echipament al sistemului aprobat de FDA (metoda colorimetrică) pe 52 probe de urină conform protocolului CLSI EP9-A2[10].

Valorile au fost între 1,57 şi 17,99 mg/dL (0,39 şi 4,49 mmol/L).

Parametrii regresiilor liniare sunt după cum urmează:

Coeficient de corelaţie: (r)=0,995

Regresie liniară: y=0,983x +0,21 mg/dL (0,05 mmol/L)

- Limitări şi interferenţe

- Nu raportaţi rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2 [11].

a) Ser/Plasmă

Recuperarea este în intervalul ±10% din valoarea iniţială a concentraţiei calciului de 8,00 mg/dL şi 12,00 mg/dL.

Bilirubină neconjugată: Nicio interferenţă semnificativă până la 30,0 mg/dL (513 µmol/L).

Bilirubină conjugată: Nicio interferenţă semnificativă până la 29,5 mg/dL (504 µmol/L).

Hemoglobină: Nicio interferenţă semnificativă până la 500 mg/dL.

Trigliceride: Nicio interferenţă semnificativă până la 1726 mg/dL (19,50 mmol/L).

Magneziu: Nicio interferenţă semnificativă până la 12,0 mg/dL.

Acid ascorbic: Nicio interferenţă semnificativă până la 20,00 mg/dL.

Acid acetilsalicilic: Nicio interferenţă semnificativă până la 200 mg/dL.

Acetaminofen: Nicio interferenţă semnificativă până la 30 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [12]

- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [13-14]

- Rezultatele acestui studiu trebuie interpretate doar în corelaţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

b) Urină

Recuperarea este în intervalul ±10% din valoarea iniţială a concentraţiei calciului de 4,00 mg/dL şi 16,00 mg/dL.

Bilirubină conjugată: Nicio interferenţă semnificativă până la 29,5 mg/dL (504 µmol/L).

Hemoglobină: Nicio interferenţă semnificativă până la 500 mg/dL.

Acid ascorbic: Nicio interferenţă semnificativă până la 20,00 mg/dL.

Uree: Nicio interferenţă semnificativă până la 5000 mg/dL.
(832 mmol/L) .

Acid uric: Nicio interferenţă semnificativă până la 100 mg/dL
(5,9 mmol/L).

Magneziu: Nicio interferenţă semnificativă până la 1,0 mg/dL
(4,1 mmol/L).

pH: Nicio interferenţă semnificativă pentru pH în intervalul 2,5 – 6,0.

- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [13-14]

- Rezultatele acestui studiu trebuie interpretate doar în corelaţie cu alte rezultate ale testelor de diagnosticare, constatări clinice şi istoricul medical al pacientului.

- Stabilitatea la bord/Frecvenţa calibrării

Stabilitatea la bord: 28 de zile

Frecvenţa calibrării: 28 zile

Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit şi după o operaţie de întreţinere.

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SIMBOLURI

Simbolurile folosite sunt definite conform standardului ISO-15223-1 cu exceptia celor prezentate mai jos.

CONT	Conţinut
R	Reactiv
Std	Standard
CE	Conformitate europeană
☞	Modificare faţă de versiunea precedentă

<u>**Notă:**</u>
Doar pentru ref. **CALA-0250**, utilizată cu software-ul Selectra TouchPro.

Calcium New 0
245 PIT-CALA

CK NAC SL

Referinţe:		**Compoziţia trusei:**
CKSL-0230	*4 x 25 mL*	***R1** 4 x 20 mL+**R2** 4 x 5 mL*
CKSL-0410	*2 x 62,5 mL*	***R1** 2 x 50 mL+**R2** 1 x 26 mL*
CKSL-0430	*4 x 62,5 mL*	***R1** 4 x 50 mL+**R2** 2 x 26 mL*

FTRO-CKSL-v21 (12/2018)_PIT-CKSL-4-v21

SCOPUL UTILIZĂRII

CK NAC SL ELITech Clinical Systems este conceput pentru determinarea cantitativă a creatinkinazei în serul uman şi plasmă pentru diagnosticare *in vitro*.

SEMNIFICAŢIE CLINICĂ [1-4]

Creatinkinaza (CK) există în 3 forme citoplasmatice: CK-MM (în muşchiul striat şi cardiac), CK-MB (doar in muşchiul cardiac), şi CK-BB (în special în creier). Determinarea CK este utilizată pentru diagnosticarea şi urmărirea bolilor musculare (în special distrofiile musculare) şi ale leziunilor muşchiului cardiac. În infarctul miocardic, ratele CK totale cresc rapid până este atins un vârf la 10-24 de ore de la debutul infarctului. Nivelurile revin la normal în 3-4 zile.
Anumite medicamente antipsihotice (olanzapina şi quetiapina) şi în unele cazuri hipotiroidismul, declansează de asemenea creşterea activităţii CK.

METODĂ [5]

Metoda IFCC - cinetică. UV.

PRINCIPIU [5]

$$\text{Creatina fosfat+ADP} \xrightarrow{\text{Creatinkinaza}} \text{Creatină + ATP}$$

$$\text{ATP + D-Glucoza} \xrightarrow{\text{Hexokinaza}} \text{D-Glucoza-6-Fosfat + ADP}$$

$$\text{G-6-P + NADP}^{+} \xrightarrow{\text{G-6-PDH}} \text{D-Gluconat-6-Fosfat +NADPH + H}^{+}$$

G-6-P: D-Glucoza-6-Fosfat
G-6-PDH: Glucoza-6-Fosfat Dehidrogenaza.

Creşterea concentraţiei NADPH este direct proporţională cu activitatea CK enzimatice.

COMPOZIŢIA REACTIVULUI

Reactiv 1: R1	
Tampon imidazol, pH 6,10	125 mmol/L
D-Glucoză	25 mmol/L
N-Acetil-L-Cisteină	25 mmol/L
Acetat de magneziu	12,5 mmol/L
NADP	2,4 mmol/L
EDTA	2,0 mmol/L
Hexokinază	≥ 6800 U/L
Azidă de sodiu	< 0,1 %
Reactiv 2: R2	
Tampon imidazol, pH 8,9	125 mmol/L
Creatină fosfat	250 mmol/L
ADP	15,2 mmol/L
AMP	23 mmol/L
Deadenozină pentafosfat	103 µmol/L
G-6-PDH	≥ 8800 U/L
Azidă de sodiu	< 0,1 %

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Echipamente generale de laborator.
- Soluţie salină obişnuită (NaCl 9 g/L).
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ŞI PRECAUŢII

- Această trusă de reactivi este doar pentru utilizarea profesională, în scopul diagnosticării *in vitro*.
- Reactivii R1 şi R2 sunt clasificaţi ca fiind periculoşi (Imidazol).

PERICOL: Poate dăuna fătului. Procuraţi instrucțiuni speciale înainte de utilizare. Purtaţi mănuşi de protecţie/îmbrăcăminte de protecţie/echipament de protecţie a ochilor/echipament de protecţie a feţei.
ÎN CAZ DE expunere sau de posibilă expunere: consultaţi medicul

- Reactivii conţin azidă de sodiu care poate reacţiona cu plumbul sau instalaţiile din cupru pentru a forma potenţiale azide metalice explozive. În momentul eliminării acestor reactivi, spălaţi întotdeauna cu apă din abundenţă pentru a preveni acumularea de azide.
- Pentru mai multe informaţii, consultaţi Fişa de date privind siguranţa (SDS).
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Nu interschimbaţi reactivii din truse diferite.

STABILITATEA

A se depozita la 2-8°C şi a se proteja împotriva luminii. A nu se îngheţa.
A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.
<u>Stabilitatea la bord:</u>
Stabilitatea la bord este specifică pentru fiecare analizor.
(Consultaţi § DATE PRIVIND PERFORMANŢA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

- Soluţia de reactiv trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiolă perforată).

PROBE [1,5]

Specimen

- Ser liber din hemoliză (specimen recomandat de IFCC).
- Plasmă heparinizată liberă din hemoliză.
- A nu se utiliza alte specimene.

Avertismente şi precauţii

Conform bunei practici de laborator, prelevarea trebuie efectuată înainte de administrarea de medicamente.

Depozitare şi stabilitate

Probele trebuie analizate imediat sau depozitate protejate împotriva aerului şi luminii timp de 8 ore la temperatura camerei, 2 zile la 2-8°C, sau 1 lună la -20°C.

VALORI DE REFERINŢĂ [5]

Bărbaţi < 171 U/L
Femei < 145 U/L

<u>Notă</u>: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

PROCEDURĂ

<u>*Pentru Analizoarele Selectra ale ELITech Clinical Systems,*</u>
aplicaţiile sunt disponibile la cerere.
Lungime de undă 340 nm
Temperatură: 37°C
Citiţi pe reactivul martor.

Reactiv 1	240 µL
Proba	12 µL

Amestecaţi şi aşteptaţi 4 minute şi 43 de secunde, apoi adăugaţi:

Reactiv 2	60 µL

Amestecaţi şi după o incubaţie de 130 de secunde, măsuraţi modificarea absorbanţei pe minut (ΔA/min.) timp de 106 secunde.
Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert.

CALCUL

$$\frac{\Delta A\ \text{Proba}}{\Delta A\ \text{Calibrator}} \times n \qquad n=\text{concentraţie calibrator}$$

<u>Factor de conversie</u>: U/L x 0,0167= µkat/L

CALIBRARE

Pentru calibrare, trebuie utilizat calibratorul multiparametric Elical 2. Valoarea sa este definită conform metodei IFCC[5].

<u>Frecvenţa de calibrare</u>: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

CONTROLUL CALITĂŢII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum ELITROL I (control normal) şi ELITROL II (control patologic). Aceste controale trebuie efectuate şi validate înainte ca probele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare, şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele de reglementare locale, statale şi federale.

DATE DE PERFORMANŢĂ la 37°C privind Analizoarele Selectra ProM ale ELITech Clinical Systems

- Interval de măsurare

Determinat conform protocolului CLSI EP6-A[6], intervalul de măsurare este între 10 şi 1714 U/L (de la 0,17 la 28,57 µkat/L). Probele care depăşesc 1714 U/L trebuie diluate 1:10 cu soluţie de NaCl 9 g/L (soluţie salină normală) şi re-testate. Utilizarea acestei proceduri extinde intervalul de măsurare între 1714 şi 17140 U/L (de la 28,57 la 285,67 µkat/L).

Pentru utilizatorii Selectra TouchPro, funcţia „diluare” efectuează diluarea probelor automat. Rezultatele iau în considerare diluţia.

- Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)

Determinată conform protocolului CLSI EP17-A[7].

LoD=1 U/L (0,02 µkat/L)
LoQ=5 U/L (0,08 µkat/L)

- Precizie

Determinată conform protocolului CLSI EP5-A2[8].

		Medie		**În interiorul ciclului**	**Total**
	n	**mg/dL**	**µkat/L**	**CV (%)**	
Nivel redus	80	147	2,45	0,7	1,7
Nivel mediu	80	406	6,77	1,1	2,4
Nivel înalt	80	1154	19,23	1,1	3,9

- Corelaţie

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems şi un alt echipament al sistemului aprobat de FDA (metoda IFCC) pe 100 de probe de ser uman conform protocolului CLSI EP9-A2[9].
Concentraţiile probelor au fost între 11 şi 1712 U/L (0,18 şi 28,53 µkat/L).
Parametrii regresiilor liniare sunt după cum urmează:
Coeficient de corelaţie: (r)=0,998
Regresie liniară: y=1,012 x +2 U/L (0,03 µkat/L)

- Limitări şi interferenţe

- Probele hemolizate nu trebuie utilizate deoarece hemoliza semnificativă poate duce la concentraţie fals crescută a CK din cauza eliberării adenilat kinazei.
- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2 [10]. Recuperarea este în intervalul ±10% din valoarea iniţială a activităţii CK de 150 şi 1200 U/L.

<u>Trigliceride:</u> Nicio interferenţă semnificativă până la 3000 mg/dL (33,9 mmol/L).

Bilirubină neconjugată: Nicio interferenţă semnificativă până la 30,0 mg/dL (513 µmol/L).
Bilirubină conjugată: Nicio interferenţă semnificativă până la 29,5 mg/dL (504 µmol/L).
Acid ascorbic: Nicio interferenţă semnificativă până la 20,0 mg/dL.
Acid acetilsalicilic: Nicio interferenţă semnificativă până la 200 mg/dL.
Acetaminofen: Nicio interferenţă semnificativă până la 30 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [11]
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [12-13]
- Rezultatele acestui studiu trebuie interpretate doar în conjuncţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- Stabilitatea la bord/Frecvenţa calibrării
Stabilitatea la bord: 28 de zile
Frecvenţa calibrării: 28 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit şi după o operaţie de întreţinere.

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13. Young, D.S., Effects of drugs on clinical laboratory tests, 4th Ed., AACC Press, (1995).

SIMBOLURI

Simbolurile folosite sunt definite conform standardului ISO-15223-1 cu exceptia celor prezentate mai jos.

CONT	Conţinut
R1	Reactiv 1
R2	Reactiv 2
CE	Conformitate europeană

Doar pentru ref. **CKSL-0230**, utilizată cu software-ul Selectra TouchPro.

CK Total 0
390 PIT-CKSL

☞:Modificare faţă de versiunea precedentă.

CK-MB SL

Referinţe:		Compoziţia trusei:
CMSL-0230	4 x 25 mL	**R1** 4 x 20 mL+ **R2** 1 x 20 mL
CMSL-0410	2 x 62,5 mL	**R1** 2 x 50 mL+ **R2** 1 x 26 mL
CMSL-0430	4 x 62,5 mL	**R1** 4 x 50 mL+ **R2** 2 x 26 mL

FTRO-CMSL-v23(12/2018)_PIT-CMSL-4-v23

SCOPUL UTILIZĂRII

CK-MB SL ELITech Clinical Systems este conceput pentru determinarea cantitativă de diagnosticare *in vitro* a formei CK-MB a creatinkinazei (CK) în serul uman.

SEMNIFICAŢIE CLINICĂ (1-2)

Creatinkinaza există în 3 forme citoplasmatice: CK-MB (doar în muşchiul cardiac), CK-MM (în muşchiul striat şi cardiac) şi CK-BB (în special în creier).
Determinarea CK în ser este utilizată pentru diagnosticarea şi urmărirea leziunilor musculare cardiace. În infarctul miocardic, ratele CK totale şi CK-MB cresc rapid până este atins un vârf la 10-24 de ore de la debutul infarctului. Nivelele revin la normal în 3-4 zile. Nivelele CK-MB mai mari decât cele normale pot fi, de asemenea, observate după deteriorările musculare.

METODĂ(3-4)

Imuno-inhibarea, Metoda IFCC.
Cinetică. UV.

PRINCIPIU (3-4)

Reactivul CK-MB SL conţine un anticorp care inhibă în mod specific subunităţile CK-M (şi anume 100% din CK-MM şi 50% din izoenzimele CK-MB). Activitatea rămasă, corespunzând activităţii fracţiei CK-B, este măsurată conform metodei de referinţă IFCC pentru măsurarea activităţii CK. Activitatea CK-MB este apoi obţinută prin înmulţirea cu 2 a activităţii rămase.

COMPOZIŢIA REACTIVULUI

Reactiv 1: R1

Tampon imidazol, pH 6,10	125 mmol/L
D-Glucoză	25 mmol/L
N-Acetil-L-Cisteină	25 mmol/L
Acetat de magneziu	12,5 mmol/L
NADP	2,4 mmol/L
EDTA	2,0 mmol/L
Hexokinază	≥ 6800 U/L
Azidă de sodiu	< 0,1 %

Concentraţia anticorpului anti-CK-M conţinut de reactivul 1 este suficient pentru a inhiba 2000 U/L din CK-M la 37ºC.

Reactiv 2: R2

Tampon imidazol, pH 8,9	125 mmol/L
Creatină fosfat	250 mmol/L
ADP	15,2 mmol/L
AMP	23 mmol/L
Deadenozină pentafosfat	103 µmol/L
G-6-PDH	≥ 8800 U/L
Azidă de sodiu	< 0,1 %

MATERIALE NECESARE DAR NEFURNIZATE

- CKMB-0900, CK-MB CONTROL 4 x 3 mL
- Echipamente generale de laborator.
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ŞI PRECAUŢII

- Această trusă de reactivi este doar pentru utilizarea profesională, în scopul diagnosticării *in vitro*.
- Reactivii R1 şi R2 sunt clasificaţi ca fiind periculoşi (Imidazol).

PERICOL: Poate dăuna fătului. Procuraţi instrucţiuni speciale înainte de utilizare. Purtaţi mănuşi de protecţie/îmbrăcăminte de protecţie/echipament de protecţie a ochilor/echipament de protecţie a feţei. ÎN CAZ DE expunere sau de posibilă expunere: consultaţi medicul.
- Reactivii conţin azidă de sodiu care poate reacţiona cu plumbul sau instalaţiile din cupru pentru a forma potenţiale azide metalice explozive. În momentul eliminării acestor reactivi, spălaţi întotdeauna cu apă din abundenţă pentru a preveni acumularea de azide.
- Pentru mai multe informaţii, consultaţi Fişa de date privind siguranţa (SDS).
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Nu interschimbaţi reactivii din truse diferite.

STABILITATEA REACTIVILOR

A se depozita la 2-8ºC şi a se proteja împotriva luminii. A nu se îngheţa.
A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.

PREGĂTIREA ŞI STABILITATEA REACTIVULUI DE LUCRU

- **Pregătire**

Amestecaţi într-o fiolă goală (fiola goală furnizată cu ref. CMSL-0230) 4 volume de reactiv R1 cu 1 volum de reactiv R2.

- **Stabilitate**

1 zi la 20-25ºC
2 săptămâni la 2-8ºC

Stabilitatea la bord:
Stabilitatea la bord este specifică pentru fiecare analizor. (Consultaţi §DATE PRIVIND PERFORMANŢA).

DETERIORAREA REACTIVILOR

- Soluţia de reactiv trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.

AMBALAJ DETERIORAT

Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiolă perforată).

PROBE [6]

Specimen

- Ser liber din hemoliză.
- A nu se utiliza alte specimene.

Avertismente şi precauţii

Conform bunei practici de laborator, puncţia venoasă trebuie să fie efectuată înainte de administrarea de medicamente.

Depozitare şi stabilitate

Eşantioanele trebuie analizate imediat sau depozitate protejate împotriva aerului şi luminii 2 zile la 2-8°C, sau 1 lună la -20°C.

VALORI DE REFERINŢĂ [3-5]

Ser (37°C): 0-25 U/L

Activitatea CK-MB trebuie să fie comparată cu activitatea CK totale

(CK-MB/CK totală) x 100 <6%

Următorii 3 factori sunt indicatori ai deteriorării muşchiului cardiac:

CK totală

Bărbaţi > 171 U/L

Femei > 145 U/L

CK-MB:> 25 U/L

Raport: (CK-MB/CK totală) x 100: 6 – 25%

<u>**Notă**</u>: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

PROCEDURĂ

Acest reactiv poate fi utilizat pentru o procedură cu un singur reactiv.

Pentru Analizoarele Selectra ale ELITech Clinical Systems, aplicaţiile sunt disponibile la cerere.

ungime de undă 340 nm

Temperatură: 37°C

Citiţi pe reactivul martor.

Reactiv de lucru	250 µL
Proba	10 µL

Amestecaţi şi după o incubaţie de 130 de secunde, măsuraţi modificarea absorbanţei pe minut (ΔA/min.) timp de 159 secunde.

Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert.

CALCUL

a) **Activitatea CK totale:**
Determinarea cu reactivul CK NAC SL.

b) **Activitatea CK-MB:**

La 340 nm, cu o cuvetă cu calea luminii de 1 cm:

Activitate (U/L)= ΔA/min. x 8 254

c) **Procent activitate CK-MB în eşantion:**

$$\% \text{ CK-MB} = \frac{\text{CK-MB}}{\text{CK totală}} \times 100$$

<u>Factor de conversie</u>: U/L x 0,0167= µkat/L

CONTROLUL CALITĂŢII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum CK-MB CONTROL. Acest ser de control este pregătit din enzimă umană nemodificată.

Controlul calităţii trebuie efectuat şi validat înainte ca eşantioanele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare, şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele de reglementare locale, statale şi federale.

DATE DE PERFORMANŢĂ la 37°C privind Analizoarele Selectra E ale ELITech Clinical Systems

- **Interval de măsurare**

Reactivul este liniar între 15 şi 600 U/L.

- **Limita de detecţie** [7]

Determinată conform protocolului SFBC, limita de detecţie este egală cu 6 U/L.

- **Precizie**

Reproductibilitate în interiorul ciclului	**n**	**Medie U/L**	**CV (%)**
Nivel normal	20	11	16,3
Nivel patologic	20	152	1,0

Reproductibilitate între cicluri	**n**	**Medie U/L**	**CV (%)**
Nivel normal	20	14	14,1
Nivel patologic	20	145	1,6

- **Corelaţie**

A fost efectuat un studiu comparativ privind acest reactiv între Analizorul Selectra E ELITech Clinical Systems şi Cobas Mira pe 60 de eşantioane de ser uman. Valorile acoperă intervalul linearităţii.

Concentraţiile eşantioanelor au fost între 11 şi 1712 U/L (0,18 şi 28,53 µkat/L).

Parametrii regresiilor liniare sunt după cum urmează:

Coeficient de corelaţie: (r)=0,9980

Regresie liniară: y=1,0007 x +1,3 U/L

- Limitări şi interferenţe [2,7,8]

- Serurile hemolizate nu trebuie utilizate deoarece hemoliza semnificativă poate creşte concentraţia CK din cauza eliberării adenilat kinazei.
- metoda va măsura şi orice izoenzimă CK-BB prezentă doar în ser sau complexată cu imunoglobuline (macro-CK).

Activitatea izoenzimei este de obicei neglijabilă, însă dacă este prezentă o cantitate semnificativă a activităţii CK-BB, activitatea CK-MB va fi supraestimată.

- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Conform recomandărilor SFBC, au fost efectuate unele studii pentru a stabili nivelul interferenţei din diferiţi compuşi:

Bilirubină neconjugată: Polarizare negativă începând cu 9 mg/dL (153,9 µmol/L) pe serurile umane normale.
Polarizare negativă începând cu 15 mg/dL (256,6 µmol/L) pe serurile umane patologice.
Bilirubină conjugată: Polarizare negativă începând cu 2 mg/dL (34,2 µmol/L) pe serurile umane normale.
Polarizare negativă începând cu 6 mg/dL (102,6 µmol/L) pe serurile umane patologice.
Turbiditate: Nicio interferenţă semnificativă până la 600 mg/dL (6,78 mmol/L) echivalent trigliceride.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [9]
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [10-11]
- Rezultatele acestui studiu trebuie interpretate doar în conjuncţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- **Stabilitatea la bord**

Stabilitatea la bord: 7 zile

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SIMBOLURI

IVD	Dispozitiv medical de diagnosticare in vitro.
	Consultaţi instrucţiunea de utilizare.
	Producător
	Limită de temperatură
LOT	Număr de lot
	Data expirării
REF	Număr catalog
CONT	Conţinut
R1	Reactiv 1
R2	Reactiv 2
CE	Conformitate europeană

Notă :
Doar pentru ref. **CMSL-0230**, utilizată cu software-ul Selectra TouchPro.

CK-MB 0
400 PIT-CMSL

☞:Modificare faţă de versiunea precedentă

IRON FERENE

Referinţe:
FEFE-0230
FEFE-0600

Compoziţia trusei:
***R1** 4 x 14,6 mL + **R2** 4 x 3,9 mL*
***R1** 2 x 100 mL + **R2** 1 x 50 mL + **Std** 1 x 5 mL*

FTRO-FEFE-v6 (12/2018)_FTCE-FEFE-4-v6

SCOPUL UTILIZĂRII

IRON FERENE ELITech Clinical Systems este conceput pentru deteriorfrea cantitativ a fierului total în serul uman pentru diagnosticare *in vitro* .

SEMNIFICAŢIE CLINICĂ [1-2]

În organism, 65-70 % din fier intră în compoziţia hemoglobinei, 25% este stocat în celule sub forma unui complex fier-feritină şi 3% este transportat prin transferină. Nivelele de fier seric cresc în hemocromatoză sau leziunile hepatice. Nivelele scăzute de fier seric pot fi asociate cu necesităţile crescute, o deficienţă dietară sau afecţiuni gastrointestinale (diaree cronică, sângerare intestinală sau malabsorbţie). Nivelele de fier seric sunt întotdeauna interpretate împreună cu datele privind saturaţia transferinei.

METODĂ

Colorimetrică – Ferene
Punct final.

PRINCIPIU [1-2]

Fierul este eliberat din transferină în pH-ul acid ca ion feric Fe^{3+}. Acesta este apoi redus de acidul ascorbic în ion feros Fe^{2+} şi formează eventual un complex colorat cu Ferene. Absorbanţa la 578 nm de complex Fier - Ferene este proporţională cu concentraţia fierului din eşantion.

$$\text{Transferină} - (Fe^{3+})_2 \xrightarrow{\text{pH acid, Acid ascorbic}} 2\,Fe^{2+} + \text{Transferină}$$

$$Fe^{2+} + 3\ \text{Ferene} \longrightarrow \text{Albastru de Ferene (complex de fier)}$$

COMPOZIŢIA REACTIVULUI

Reactiv: R1		
Tiouree	120	mmol/L
Tampon de acetat (pH 4.5)	1	mol/L
Reactiv: R2		
Ferene	3	mmol/L
Acid ascorbic	240	mmol/L
Tiouree	120	mmol/L
Standard: Std		
Fier	100	µg/dL
	17,9	µmmol/L

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Echipamente generale de laborator.
- Analizor de biochimie echipat cu filtrele necesare. (Consultati § PROCEDURA).
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ŞI PRECAUŢII

- Acest reactiv este conceput doar pentru utilizarea profesională, în scopul diagnosticării *in vitro*.
- Reactivul R1 este clasificat ca periculos (C9-11-izoalcooli, C10-rich etoxilat; dodecan-1-ol etoxilat).

PERICOL: Provoacă iritarea pielii. Provoacă leziuni oculare grave. Purtaţi mănuşi de protecţie/îmbrăcăminte de protecţie/echipament de protecţie a ochilor/echipament de protecţie a feţei. ÎN CAZ DE CONTACT CU OCHII:
Clătiți cu atenție cu apă timp de mai multe minute. Scoateți lentilele de contact, dacă este cazul și dacă acest lucru se poate face cu ușurință. Continuați să clătiți. Sunați imediat la un CENTRU DE INFORMARE TOXICOLOGICĂ/un medic. ÎN CAZ DE CONTACT CU PIELEA: spălați cu multă apă și săpun. În caz de iritare a pielii: consultaţi medicul. Scoateți îmbrăcămintea contaminată și spalați-o înainte de reutilizare.

- Pentru mai multe informaţii, consultați Fişa de date privind siguranţa (SDS).
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Standardul trebuie să fie imediat inchis cu capacul pentru a preveni contaminarea şi evaporarea.
- Nu interschimbaţi fiolele de reactiv din truse diferite.

STABILITATEA

A se depozita la 2-8ºC şi a se proteja împotriva luminii. A nu se îngheţa.
A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.
<u>Stabilitatea la bord</u>:
Stabilitatea la bord este specifică pentru fiecare analizor.
(Consultaţi § DATE PRIVIND PERFORMANŢA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

- Soluţia de reactivi trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiole perforate).

PROBE [1,3]

Specimen

- Fără ser din hemoliză
- A nu se utiliza alte specimene.

Avertisment şi precauţii
Conform bunei practici de laborator, prelevarea trebuie efectuată înainte de administrarea de medicamente.

Depozitare
Serurile sunt stabile timp de 7 zile la temperatura camerei, sau la 2-8ºC sau 1 an la -20ºC.

VALORI DE REFERINŢĂ (4)

Ser

Nou-născuţi	100-250 µg/dL	17,9-44,8 µmol/L
Infanţi	40-100 µg/dL	7,2-17,9 µmol/L
Copii	50-120 µg/dL	9,0-21,5 µmol/L
Femei	50-170 µg/dL	9,0-30,4 µmol/L
Bărbaţi	65-175 µg/dL	11,6-31,3 µmol/L

Intervalul nivelelor de fier seric în cazul persoanelor sănătoase clinic poate fi influenţat de un număr de factori bine-cunoscuţi precum dieta, sexul, vârsta, ciclul menstrual, sarcina sau fluctuaţiile circadiene.

Notă: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems.
Aplicaţiile sunt disponibile la cerere
Lungime de undă 578-700 nm
Temperatură: 37ºC
Citiţi pe reactivul martor.

	CALIBRARE	TEST
Reactiv R1	240 µL	240 µL
Calibrator/Standard	30 µL	-
Proba	-	30 µL

Amestecaţi şi citiţi absorbanţa (A1) după o incubaţie de 4 minute 40.

Reactiv R2	60 µL	60 µL

Amestecaţi şi citiţi absorbanţa (A2) după o incubaţie de 6 minute 30.

Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert.

Pentru utilizatorii Selectra ProXS, este nevoie de un filtru suplimentar de 700nm.

CALCUL

$$\frac{(A2\text{-}A1)\ \text{Proba}}{(A2\text{-}A1)\ \text{Calibrator /Standard}} \times n \qquad n = \text{concentraţie calibrator/standard}$$

Factor de conversie: µg/dL x 0,179 = µmol/L

CALIBRARE

Pentru referinţa FEFE-0600: Pentru calibrare, trebuie utilizat fie calibratorul multiparametric ELICAL 2 fie Standardul de fler de 100 µg/dL.
Pentru referinţa FEFE-0230: Pentru calibrare, utilizaţi calibratorul multiparametric ELICAL 2.

Valorile concentraţiei Standardului de fier de 10 µg/dL şi calibratorului multiparametric ELICAL 2 sunt trasabile conform Materialului Standard de Referinţă SRM937 (al Institutului Naţional de Standarde şi Tehnologie).

Pentru calibrare, trebuie utilizat calibratorul multiparametric ELICAL 2. Valoarea sa este definită în raport cu materialul de referinţă NIST SRM937 (al Institutului Naţional de Standarde şi Tehnologie).

Frecvenţa de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

CONTROLUL CALITĂŢII
Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I (control normal) şi ELITROL II (control patologic). Aceste controale trebuie efectuate şi validate înainte ca probele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare, şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele locale şi legale.

DATE DE PERFORMANŢĂ la 37ºC privind Analizoarele Selectra ProM ale ELITech Clinical Systems

- **Interval de măsurare**

Determinat conform protocolului CLSI EP6-A(5), intervalul de măsurare este între 20 şi 1000 µg/dL (de la 3,6 la 179,1 µmol/L).

- **Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)**

Determinată conform protocolului CLSI EP17-A(6).
LoD=6 µg/dL (1,1 µmol/L)
LoQ=20 µg/dL (3,6 µmol/L)

- **Precizie**

Determinată conform protocolului CLSI EP5-A2[7].

		Medie		În interiorul ciclului	Total
	n	µg/dL	µmol/L	CV (%)	
Nivel scăzut	80	43	7,7	2,0	5,5
Nivel mediu	80	137	24,5	0,4	3,2
Nivel înalt	80	248	44,4	0,7	3,1

- **Corelaţie**

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems şi un alt echipament al sistemului aprobat de FDA (metoda colorimetrică Ferene) pe 99 de eşantioane de ser uman conform protocolului CLSI EP9-A2[8].
Concentraţiile eşantioanelor au fost între 22 şi 1048 µg/dL (3.9 şi 187.7 µmol/L).
Parametrii regresiilor liniare sunt după cum urmează:
Coeficient de corelaţie: (r)=1.000
Regresie liniară: y=1,041 x -2 µg/dL
(0,4 µmol/L)

- Limitări şi interferenţe

- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2 [9]. Recuperarea este în intervalul ±10% din valoarea iniţială a concentraţiei fierului de 40 µg/dL şi 250 µg/dL.

Bilirubină neconjugată: Nicio interferenţă semnificativă până la 30 mg/dL (513 µmol/L).
Bilirubină conjugată: Nicio interferenţă semnificativă până la 29.5 mg/dL (504 µmol/L).
Trigliceride: Nicio interferenţă semnificativă până la 3000 mg/dL (33.90 mmol/L).
Acid ascorbic: Nicio interferenţă semnificativă până la 20 mg/dL .
Cupru: Nicio interferenţă semnificativă până la 500 µg/dL (78,7 µmol/L).
Acid acetilsalicilic: Nicio interferenţă semnificativă până la 200 mg/dL.
Acetaminofen: Nicio interferenţă semnificativă până la 30.0 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [10]
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [11-12]
- Rezultatele acestui studiu trebuie interpretate doar în conjuncţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- Stabilitatea la bord/Frecvenţa calibrării

Aceste date sunt definite pentru un volum de umplere de 14 ml intr-un flacon de 25 ml pentru reactivul R1 si respectiv de 4 ml intr-un flacon de 10 ml pentru reactivul R2 (Ref: FEFE-0230).
În cazul unui format diferit al flaconului și / sau a unui volum diferit de umplere, este responsabilitatea fiecărui laborator de a revalida stabilitatea la bord și frecvența de calibrare.
Stabilitatea la bord: 28 de zile
Frecvenţa calibrării: 14 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit, şi după o operaţie de întreţinere.

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SIMBOLURI

Simbolurile folosite sunt definite conform standardului ISO-15223-1 cu exceptia celor prezentate mai jos.

CONT	Conţinut
R1	Reactiv 1
R2	Reactiv 2
Std	Standard
CE	Conformitate europeană

Notă:
Doar pentru ref. **FEFE-0230** , utilizată cu software-ul Selectra TouchPro.

Iron Ferene 0
510 FTCE-FEFE

:Modificare faţă de versiunea precedentă.

ALP (DEA) SL

Referinţe:		Compoziţia trusei:
PASL-0230	*4 x 25 mL*	***R1** 4 x 20 mL* + ***R2** 4 x 5 mL*
PASL-0400	*2 x 62,5 mL*	***R1** 2 x 50 mL* + ***R2** 1 x 26 mL*
PASL-0420	*4 x 62,5 mL*	***R1** 4 x 50 mL* + ***R2** 2 x 26 mL*

FTRO-PASL-v21(12/2018)_PIT-PASL-4-v21

SCOPUL UTILIZĂRII

ALP (DEA) SL ELITech Clinical Systems este conceput pentru determinarea cantitativă a fosfatazei alcaline în serul uman pentru de diagnosticare *in vitro.*

SEMNIFICAŢIE CLINICĂ [1-2]

Fosfataza alcalină (ALP) corespunde unui grup de fosfataze care prezintă activitatea maximă la pH alcalin. ALP este larg distribuită în ficat, osteoblaste, epiteliul intestinal, rinichi şi placentă.
Rata ALP creşte fiziologic pentru copii şi adolescenţi în perioadele creşterii active, precum şi pentru femeile în al treilea trimestru de sarcină.
Creşterile marcate ale ratei ALP sunt observate în cazul obstrucţiei extra-hepatice (calculi biliari, tumori…) şi bolile osoase precum boala Paget şi cancerul osteogenic osos.
Activitatea PAL poate creşte, de asemenea, moderat în cazul obstrucţiei intra-hepatice, hepatitei, cirozei, sau în cazul rahitismului, osteomalaciei, hiperparatiroidismului, vindecarea fracturilor osoase.

METODĂ[3-4]

Bazată pe metoda DGKC şi SCE.
Enzimatică. Cinetică.

PRINCIPIU [3-4]

În prezenţa $Mg2^+$ şi dietanolaminei ca acceptor al fosfatului, *p*-nitrofenilfosfatul este transformat de fosfatazele alcaline în fosfat şi p-nitrofenol (compus galben).

$$p\text{-nitrofenilfosfat} + H_2O \xrightarrow{\textit{Fosfataza alcalină}} \text{Fosfat anorganic} + p\text{-nitrofenol}$$

COMPOZIŢIA REACTIVULUI

Reactiv1: R1	
Dietanolamină, pH 10,2	1,4 mol/L
Clorură de magneziu	0,625 mmol/L
Azidă de sodiu	< 0,1%
Reactiv 2: R2	
p-nitrofenilfosfat	50 mmol/L
Azidă de sodiu	< 0,1 %

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550, ELICAL 2
- CONT-0060, ELITROL I
- CONT-0160, ELITROL II
- Echipamente generale de laborator.
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ŞI PRECAUŢII

- Acest reactiv este conceput doar pentru utilizarea profesională, în scopul diagnosticării *in vitro*.
- Reactivul R1 este clasificat ca periculos (2,2'-iminodietanol).


PERICOL: Poate provoca leziuni ale organelor în caz de expunere prelungită sau repetată. Provoacă leziuni oculare grave. Provoacă iritarea pielii. Nu inspirați ceața/vaporii/ spray-ul. Purtaţi mănuşi de protecţie/îmbrăcăminte de protecţie/echipament de protecţie a ochilor/echipament de protecţie a feţei.
ÎN CAZ DE CONTACT CU OCHII: Clătiți cu atenție cu apă timp de mai multe minute. Scoateți lentilele de contact, dacă este cazul și dacă acest lucru se poate face cu ușurință. Continuați să clătiți. Sunați imediat la un CENTRU DE INFORMARE TOXICOLOGICĂ/un medic. ÎN CAZ DE CONTACT CU PIELEA: spălați cu multă apă. În caz de iritare a pielii: consultaţi medicul.

- Reactivii conţin azidă de sodiu care poate reacţiona cu plumbul sau instalaţiile din cupru pentru a forma potenţiale azide metalice explozive. În momentul eliminării acestor reactivi, spălaţi întotdeauna cu apă din abundenţă pentru a preveni acumularea de azide.
- Pentru mai multe informaţii, consultaţi Fişa de date privind siguranţa (SDS).
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Nu interschimbaţi fiolele de reactiv din truse diferite.

STABILITATEA

A se depozita la 2-8ºC şi a se proteja împotriva luminii. A nu se îngheţa.
A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.
Stabilitatea la bord:
Stabilitatea la bord este specifică pentru fiecare analizor.
(Consultaţi § DATE PRIVIND PERFORMANŢA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

- Soluţia de reactivi trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiolă perforată).

PROBE [1,2,5]

Specimen

- Fără ser de hemoliză
- A nu se utiliza alte specimene.

Avertismente şi precauţii

- Conform bunei practici de laborator, puncţia venoasă trebuie efectuată înainte de administrarea de medicamente.
- Este mai bine să analizaţi specimenul proaspăt (nu mai târziu de 4 ore după prelevare) şi să le păstraţi la temperatura camerei.

Depozitare şi stabilitate

- Activitatea ALP poate creşte în cazul în care specimenul refrigerat (2-8ºC) sau îngheţat (-20ºC) este pus la temperatura camerei.
- Dacă specimenele sunt îngheţate în scopul depozitării prelungite, mutaţi-le la temperatura camerei cu 18 - 24 de ore înainte de analiză, pentru a activa complet enzima.
- Eșantioanele sunt stabile 1 săptămână la temperatura camerei, 1 săptămână la 2-8ºC şi 2 luni la -20ºC.

VALORI DE REFERINŢĂ [6]

Ser (37°C):

Bărbaţi <270 U/L
Femei <240 U/L

Valorile de referinţă pentru copii şi adolescenţi în timpul creşterii oaselor sunt mai mari decât pentru adulţi.

Notă: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems,
aplicaţiile sunt disponibile la cerere.
Lungime de undă 405 nm
Temperatură: 37°C
Citiţi pe reactivul martor.

Reactiv R1	200 µL
Proba	5 µL

Amestecaţi, aşteptaţi 4 minute şi 43 de secunde şi adăugaţi:

Reactiv R2	50 µL

Amestecaţi şi aşteptaţi o incubaţie de 50 de secunde, măsuraţi variaţia absorbanţei pe minut (ΔA/min.) timp de 133 secunde.
Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert. .

CALCUL

$\frac{\Delta A \text{ Proba}}{\Delta A \text{ Calibrator}} \times n$ n=concentraţie calibrator

Factor de conversie: U/L x 0,0167 = µkat/L

CALIBRARE

Pentru calibrare, trebuie utilizat calibratorul multiparametric ELICAL 2. Valoarea sa este trasabilă conform măsurătorii manuale.

Frecvenţa de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

CONTROLUL CALITĂŢII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I şi ELITROL II . Aceste controale trebuie efectuate şi validate înainte ca eşantioanele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare, şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform liniilor directoare locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele de reglementare locale, statale şi federale.

DATE DE PERFORMANŢĂ la 37°C privind Analizoarele Selectra XL ale ELITech Clinical Systems

- **Interval de măsurare**

Reactivul este liniar de la 20 la 900 U/L.

- **Limita de detecţie** [7]

Determinată conform protocolului SFBC, limita de detecţie este egală cu 6 U/L.

- **Precizie**

Reproductibilitate în interiorul ciclului	n	Medie U/L	CV (%)
Nivel 1	20	42	2,9
Nivel 2	20	146	0,8
Nivel 3	20	739	0,6

Reproductibilitate între cicluri	n	Medie U/L	CV (%)
Nivel 1	20	38	5,5
Nivel 2	20	147	1,1
Nivel 3	20	760	1,3

- Corelaţie

A fost efectuat un studiu comparativ pe analizorul Selectra XL ELITech Clinical Systems între procedura cu un reactiv şi procedura cu doi reactivi pe 30 de eşantioane de ser.
Valorile au fost între 17 şi 886 U/L.
Parametrii regresiei liniare sunt după cum urmează:
Coeficient de corelaţie: (r)=0,9999
Regresie liniară: y=1,9800 x + 3,19 U/L

- Limitări şi interferenţe [7-8]

- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Conform recomandărilor SFBC, au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi:

Bilirubină neconjugată: Nicio interferenţă semnificativă până la 36 mg/dL (615,8 µmol/L).
Bilirubină conjugată: Nicio interferenţă semnificativă până la 25 mg/dL (427,6 µmol/L).
Hemoglobină: Nicio interferenţă semnificativă până la 500 mg/dL (5 g/L).
Turbiditate: Nicio interferenţă semnificativă până la 600 mg/dL (6,78 mmol/L) echivalent trigliceride.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [9]
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [10-11]
- Rezultatele acestui studiu trebuie interpretate doar în conjuncţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- **Stabilitatea la bord/Frecvenţa calibrării**

Stabilitatea la bord: 14 zile
Frecvenţa calibrării: 7 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit, şi după o operaţie de întreţinere.

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10. Young, D.S., Effects of preanalytical variables on clinical laboratory tests, 2nd Ed., AACC Press, (1997).
11. Young, D.S., Effects of drugs on clinical laboratory tests, , 4th Ed., AACC Press, (1995).

SIMBOLURI

Simbolurile folosite sunt definite conform standardului ISO-15223-1 cu exceptia celor prezentate mai jos.

CONT	Conţinut
R1	Reactiv 1
R2	Reactiv 2
CE	Conformitate europeană

Notă:

Doar pentru ref. **PASL-0230,** utilizată cu software-ul Selectra TouchPro.

Alkaline Phosphatase 0
120 PIT-PASL

☞:Modificare faţă de versiunea precedentă.

TRIGLYCERIDES MONO SL NEW

TRIGLYCERIDES SL

Referinţe:	Compoziţia trusei:
TGML-0425	***R*** *6 x 50 mL*
TGML-0515	***R*** *6 x 100 mL*
TGML-0700	***R*** *4 x 250 mL*
TGML-0427	***R*** *6 x 50 mL +* ***Std*** *1 x 5 mL*
TGML-0497	***R*** *1 x 100 mL +* ***Std*** *1 x 5 mL*
TGML-0517	***R*** *6 x 100 mL +* ***Std*** *1 x 5 mL*
TGML-0707	***R*** *4 x 250 mL +* ***Std*** *1 x 5 mL*

Referinţe:	Compoziţia trusei:
TGML-0250	***R*** *12 x 20 mL*
TGML-0455	***R*** *6 x 45 mL*

FTRO-TGML-v24 (10/2020)_PIT-TGML-4-v24

☞SCOPUL UTILIZĂRII

ELITech Clinical Systems TRIGLYCERIDES SL şi TRIGLYCERIDES MONO SL NEW sunt reactiv de diagnostic *in vitro* destinat determinării cantitative a trigliceridelor din probele serul uman și plasmă.

SEMNIFICAŢIE CLINICĂ [1-2]

Trigliceridele constituie 95% din grăsimile depozitate în ţesuturi şi rolul lor principal este de a furniza energia pentru celulă. Acestea sunt sintetizate atât în intestin, din grăsimile dietetice şi în ficat din carbohidraţii dietetici, şi sunt apoi transportate în sânge prin chilomicroni şi VLDL.
Nivelele înalte de trigliceride serice sunt asociate cu riscurile importante de ateroscleroză. Acestea pot fi cauzate de bolile precum diferitele afecţiuni ale metabolismului lipidic (hiperlipoproteinemia, deficienţa activităţii lipazei, deficienţa apolipoproteinei C-II), însă şi de diabet, afecţiuni renale sau endocrine.

METODĂ[3]

Enzimatică - colorimetrică. Punct final.

PRINCIPIU [3]

Determinarea enzimatică a trigliceridelor conform următoarelor reacţii:

$$\text{Trigliceride} + H_2O \xrightarrow{\textit{Lipoproteină lipază}} \text{Glicerol+ Acizi graşi}$$

$$\text{Glicerol+ ATP} \xrightarrow{\textit{Glicerol kinază}} \text{Glicerol-3-fosfat+ADP}$$

$$\text{Glicerol-3-fosfat}+O_2 \xrightarrow{\textit{GPO}} \text{DHA-P}+H_2O_2$$

$$H_2O_2\text{+4-AAP-}p\text{-Clorofenol} \xrightarrow{\textit{Peroxidază}} \text{Quinoneimină}$$

GPO=Gliceorl-3-fosfat oxidază
DHA-P= Dihidroxiaceton-fosfat
4-AAP=Amino-4-antipirină

☞COMPOZIŢIA

Reactiv: R

Tampon Good, pH 7,00			
p-Clorofenol		2,7	mmol/L
ATP		3,15	mmol/L
4-Aminoantipirină		0,31	mmol/L
Lipoproteină lipază	≥	2000	U/L
Glicerol kinază	≥	500	U/L
Glicerol-3-fosfat oxidază	≥	4000	U/L
Peroxidază	≥	500	U/L
Azidă de sodiu	<	0,1	%

De asemenea, conţine săruri de magneziu, FAD şi surfactanţi pentru performanţă optimă.

Standard: Std. (Ref.: TGML-0427/0497/0517/0707)

Glicerol (echivalent trigliceride)		200	mg/dL
		2,26	mmol/L
Azidă de sodiu	<	0,1	%

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Soluţie salină obişnuită (NaCl 9 g/L)
- Echipamente generale de laborator.
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

☞AVERTISMENTE ŞI PRECAUŢII

- Acest dispozitiv de diagnostic *in vitro* (Reactiv şi Standardul) este destinat numai pentru uz profesional.
- Reactivul R şi Standardul conţine azidă de sodiu care poate reacţiona cu plumbul sau instalaţiile din cupru pentru a forma potenţiale azide metalice explozive. În momentul eliminării acestor reactivi, spălaţi întotdeauna cu apă din abundenţă pentru a preveni acumularea de azide.
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Standardul trebuie să fie imediat inchis cu capacul pentru a preveni contaminarea şi evaporarea.
- Pentru mai multe informaţii, Fişa de date privind siguranţa (SDS) este disponibilă la cerere pentru utilizatorul profesional.

STABILITATEA

A se depozita la 2-8ºC şi a se proteja împotriva luminii. A nu se îngheţa.
A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.
<u>Stabilitatea la bord</u>:
Stabilitatea la bord este specifică pentru fiecare analizor.
(Consultaţi § DATE PRIVIND PERFORMANŢA).

☞PREGĂTIRE

Reactivii şi Standardul sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

- Soluţia de reactiv trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiolă perforată).

PROBE [4]

Specimen

- Ser sau plasmă heparinizată de litiu de la pacienţii care ţin post (≥12 ore).
- Nu utilizaţi eşantioane icterice sau hemolizate.
- A nu se utiliza alte specimene.

Referinţe:	Compoziţia trusei:	Referinţe:	Compoziţia trusei:
TGML-0425	***R*** *6 x 50 mL*	*TGML-0250*	***R*** *12 x 20 mL*
TGML-0515	***R*** *6 x 100 mL*	*TGML-0455*	***R*** *6 x 45 mL*
TGML-0700	***R*** *4 x 250 mL*		
TGML-0427	***R*** *6 x 50 mL +* ***Std*** *1 x 5 mL*		
TGML-0497	***R*** *1 x 100 mL +* ***Std*** *1 x 5 mL*		
TGML-0517	***R*** *6 x 100 mL +* ***Std*** *1 x 5 mL*		
TGML-0707	***R*** *4 x 250 mL +* ***Std*** *1 x 5 mL*		

FTRO-TGML-v24 (10/2020)_PIT-TGML-4-v24

Avertismente şi precauţii

- Conform bunei practici de laborator, prelevarea trebuie efectuată înainte de administrarea de medicamente. Prelevarea poate duce la rezultate false dacă este efectuată în timpul sau imediat după administrarea anumitor medicamente.
- Colectaţi mostrele în tuburi şi tampoane fără glicerol.
- Separaţi de celule în termen de 2 ore.

Depozitare şi stabilitate

- Eşantioanele sunt stabile între 5 şi 7 zile, dacă sunt depozitate la 2-8°C, 3 luni de la -15°C până la -20°C şi mai mulţi ani la -70°C. Evitaţi îngheţarea şi dezgheţarea repetate.

VALORI DE REFERINŢĂ [2]

NCEP (Programul Naţional American de Educaţie privind Colesterolul) a stabilit următoarea clasificare pentru nivelele de colesterol total, în funcţie de riscul dezvoltării cardiopatiei coronariene:

Clasificarea riscurilor:

	Nivel (mg/dl)	Nivel (mmol/L)
Normal	< 150	1,69
Limită superioară	150-199	1,69-2,25
Mare	200-499	2,26-5,64
Foarte mare	≥ 500	5,65

Notă: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

☞PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems, aplicaţiile sunt disponibile la cerere.

Lungime de undă 505 nm

Temperatură: 37°C

Citiţi pe reactivul martor.

	CALIBRARE	CALIBRARE	TEST
Reactiv R	300 µL	300 µL	300 µL
Apă distilată	3 µL	-	-
Calibrator	-	3 µL	-
Proba	-	-	3 µL

Amestecaţi şi citiţi absorbanţele (A) după o incubaţie de 11 minute şi 30 secunde.

- Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestei inserţii.

- **Reactivii Triglycerides SL şi Triglyceride Mono SL New pot fi contaminaţi de reactivul Cholesterol HDL SL 2G.**

Pentru a evita contaminarea pe Selectra ProM şi ProXL, programaţi incompatibilităţile după cum urmează:

Software	Meniu	Parametru
TouchPro	Probe incompatibilities	Link / Cholecterol HDL SL 2G – Acide Solution
Altele	Needle incompatibility	Cholesterol HDL SL 2G <<HCl

Pentru alte instrumente Selectra Pro, repetaţi orice rezultate absurde după programarea unei spălări a acelor.

- **Reactivul LIPASE SL este puternic contaminat cu reactivul Triglycerides SL.**

Pentru a evita contaminarea cuvetei pe instrumentele Selectra Pro, programaţi următoarele incompatibilităţi:

Software	Meniu	Parametru
TouchPro	Test Incompatibilities	Link / Triglycerides SL – Acid Solution
Altele	Cuvette Incompatibility	Triglycerides SL <<HCl

Pentru a evita contaminarea acelor pe instrumentele Selectra Pro, nu programaţi Lipase SL şi Triglycerides SL în acelaşi ciclu. Asiguraţi-vă că instrumentul revine la statusul „stand-by" înainte de începerea unui ciclu care conţine Lipase SL.

☞CALCUL

$$\frac{\text{A Proba}}{\text{A Calibrator/Standard}} \times n$$

n = concentraţie calibrator/standard

Factor de conversie: mg/dL x 0,0113= mmol/L
mg/dL x 0,01= g/L

☞CALIBRARE

Pentru referinţa TGML-0427/0497/0517/0707: Pentru calibrare, trebuie utilizat fie calibratorul multiparametric ELICAL 2 fie Standardul Triglycerides 200 mg/dL.

Pentru referinţa TGML-0250/0455/0425/0515/0700: Pentru calibrare, utilizaţi calibratorul multiparametric ELICAL 2.

Valorile concentraţiei Standardului Triglycerides 200 mg/dL şi calibratorului multiparametric ELICAL 2 sunt trasabile în raport metoda de referinţă ID-GC-MS (Diluţia izotopică – Spectrometria de masă cromatografie de gaz - spectrometrie de masă).

Frecvenţa de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

CONTROLUL CALITĂŢII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum ELITROL I şi ELITROL II. Aceste controale trebuie efectuate şi validate înainte ca eşantioanele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare, şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform liniilor directoare locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele de reglementare locale, statale şi federale.

Referinţe:	Compoziţia trusei:	Referinţe:	Compoziţia trusei:
TGML-0425	***R*** *6 x 50 mL*	*TGML-0250*	***R*** *12 x 20 mL*
TGML-0515	***R*** *6 x 100 mL*	*TGML-0455*	***R*** *6 x 45 mL*
TGML-0700	***R*** *4 x 250 mL*		
TGML-0427	***R*** *6 x 50 mL +* ***Std*** *1 x 5 mL*		
TGML-0497	***R*** *1 x 100 mL +* ***Std*** *1 x 5 mL*		
TGML-0517	***R*** *6 x 100 mL +* ***Std*** *1 x 5 mL*		
TGML-0707	***R*** *4 x 250 mL +* ***Std*** *1 x 5 mL*		

CE

FTRO-TGML-v24 (10/2020)_PIT-TGML-4-v24

DATE DE PERFORMANŢĂ la 37ºC privind Analizoarele Selectra ProM ale ELITech Clinical Systems

- **☞Interval de măsurare**

Determinat conform protocolului CLSI EP6-A[5], Intervalul de măsurare este între 30 şi 1000 mg/dL (0,34 – 11,30 mmol/L). Probele cu concentraţii mai mari trebuie să fie diluate 1:5 cu soluţie NaCl 9g/L (salină obişnuită) şi re-evaluate. Utilizarea acestei proceduri extinde intervalul de măsurare până la 5 000 mg/dL (56,50 mmol/L.)

Pentru utilizatorii Selectra TouchPro, funcţia „dilute” efectuează diluarea eșantioanelor automat. Rezultatele iau în considerare diluţia.

- **Precizie**

Determinată conform protocolului CLSI EP5-A2[6].

		Medie		În interiorul ciclului	Total
	n	**mg/dL**	**mmol/L**	**CV (%)**	
Nivel redus	80	44	0,50	2,0	3,8
Nivel mediu	80	131	1,48	0,9	2,3
Nivel înalt	80	267	3,02	1,2	2,4

- **Corelaţie**

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems şi un alt echipament al sistemului aprobat de FDA (metoda enzimatică şi colorimetrică) pe 99 eşantioane de ser uman conform protocolului CLSI EP9-A2[7].
Valorile au fost între 30 şi 957 mg/dL (0,34 şi 10,81 mmol/L).
Parametrii regresiilor liniare sunt după cum urmează:
Coeficient de corelaţie: (r)=0,999
Regresie liniară: y=1,019 x +1 mg/dL (0,10 mmol/L)

- Limitări şi interferenţe

- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2[8]. Recuperarea este în intervalul ±10% din valoarea iniţială a concentraţiei trigliceridelor de 133 mg/dL şi 266 mg/dL.

Bilirubină neconjugată: Nicio interferenţă semnificativă până la 15 mg/dL (257 µmol/L).
Bilirubină conjugată: Nicio interferenţă semnificativă până la 5,9 mg/dL (101 µmol/L)
Hemoglobină: Nicio interferenţă semnificativă până la 125 mg/dL.
Acid uric: Nicio interferenţă semnificativă până la 24,2 mg/dL (1440 µmol/L).
Acid ascorbic: Nicio interferenţă semnificativă până la 2,0 mg/dL. Concentraţiile peste nivelele terapeutice vor interfera şi cauza rezultate eronate.
Metil-dopa: Nicio interferenţă semnificativă până la 1,0 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [9]
- Rezultatele pot fi fals reduse de nivele semnificative ale eşantionului de NAC (N-Acetil-Cisteină), NAPQI (metabolit de acetaminofen (paracetamol) sau metamizol).
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [10-11]
- Rezultatele acestui studiu trebuie interpretate doar în corelaţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- **Stabilitatea la bord/Frecvenţa calibrării**

Stabilitatea la bord: 28 zile
Frecvenţa calibrării: 14 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit, şi după o operaţie de întreţinere.

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Referinţe:	**Compoziţia trusei:**	**Referinţe:**	**Compoziţia trusei:**
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TGML-0497	***R*** *1 x 100 mL +* ***Std*** *1 x 5 mL*		
TGML-0517	***R*** *6 x 100 mL +* ***Std*** *1 x 5 mL*		
TGML-0707	***R*** *4 x 250 mL +* ***Std*** *1 x 5 mL*		

CE

FTRO-TGML-v24 (10/2020)_PIT-TGML-4-v24

☞SIMBOLURI

Simbolurile folosite sunt definite conform standardului ISO-15223-1 cu exceptia celor prezentate mai jos.

CONT	Conţinut
R	Reactiv
Std	Standard
CE	Conformitate europeană
☞	Modificare faţă de versiunea precedentă

Notă

- Doar pentru ref. **TGML-0250/TGML-0455**, utilizată cu software-ul Selectra TouchPro.
- **Vezi §PROCEDURĂ:** Risc de contaminare

Triglycerides   0
620   PIT-TGML

☛ESTABILIDADE
Conservar a 2-8 °C e ao abrigo da luz. Não congelar
Não utilizar após as datas de validade indicadas nos rótulos dos frascos.
O padrão deve ser imediatamente tampado para evitar a contaminação e evaporação.
Estabilidade em equipamentos:
A estabilidade a bordo é específica a cada equipamento (Consultar § DESEMPENHO)

PREPARAÇÃO
O reagente e o padrão estão prontos a usar.

DETERIORAÇÃO DO PRODUTO
- O produto deve ser clara. Qualquer turbidez seria sinal de deterioração do produto.
- Não use o produto se houver evidência visível de contaminação ou dano (por exemplo, partículas).
- Danos ao recipiente de producto podem afetar o desempenho do produto. Não use o producto se houver evidência física de deterioração (por exemplo, vazamentos ou recipiente perfurado).

☛AMOSTRAS
Amostras [(2)]
- Soro
- Plasma (heparina de lítio)
- Urina
- O uso de qualquer outro tipo de amostra deve ser validado pelo laboratório.

Aviso e precauções
- Para evitar a precipitação de urato, as amostras de urina podem ser ajustadas para pH> 8.0 com NaOH. [(2)]
- As amostras devem ser coletadas de acordo com as Boas Práticas de Laboratório e com as diretrizes apropriadas que podem estar em vigor.

Armazenamento e estabilidade [(2)]
Soro / plasma
- 3-5 dias a 2-8 ° C
- 6 meses a -20 ° C

Urina (Alcalinizada)
- 3 dias em temperatura ambiente

Não refrigerar amostras de urina

☛VALORES DE REFERÊNCIAS [(1)]

Soro / plasma	mg/dL	µmol/L
Homens	3.5 - 7.2	208 - 428
Mulheres	2.6 - 6.0	155 - 357
Urina (coleta de 24h)	mg/24h	mmol/24h
	250 - 750	1.48 - 4.43
	mg/dL*	mmol/L*
	16.7 - 50	0.99 - 2.97

* para um volume urinário de 1.5 L por 24 horas

Com uma dieta livre de purina, a excreção pode diminuir de 20 a 25%.

Observação: O intervalo citado deve servir apenas como guia. Recomenda-se que cada laboratório verifique esse intervalo ou estabeleça um intervalo de referência para a população pretendida.

PROCEDIMENTO
Procedimento manual
Comprimento de onda : 546 nm
Percurso óptico : 1 cm
Relação Amostra/Reagente : 1:40
Temperatura: 37 °C
As amostras de urina devem ser diluídas 1:10 com solução de NaCl 9 g/L antes da medição.

Ler comparando com o branco de reagente

	CALIBRAÇÃO	DOSAGEM
Reagente R	1 000 µL	1 000 µL
Padrão/Calibrador	25 µL	-
Amostra	-	25 µL

Misturar e ler as absorvâncias (A) após 5 minutos.

Procedimento automático
Estes reagentes podem ser utilizados em vários analisadores automáticos. Para os analisadores ELITech Selectra, as aplicações validadas estão disponíveis mediante solicitação. Com o Selectra TouchPro, utilize a aplicação incluída no código de barras disponível no final desde folheto.

As amostras de urina devem ser diluídas 1:10 com solução de NaCl 9 g/L antes da medição.
Para usuários do software Selectra TouchPro, a diluição da urina é realizada automaticamente.

☛CÁLCULO

$$\frac{(A)\ \text{Amostra}}{(A)\ \text{Padrão/calibrador}} \times n \quad n = \text{concentração do padrão/calibrador}$$

Para o cálculo da concentração do ácido úrico na urina, multiplique o resultado pelo fator de diluição (10). Para usuários do software Selectra TouchPro, os resultados levam em consideração o fator de diluição.

Fator de conversão: mg/dL x 59.48 = µmol/L
mg/dL x 0.059 = mmol/L

CALIBRAÇÃO
Para referências AUML-0427/0497/0507/0707: ELICAL 2 ou o padrão Uric Acid Standard 6 mg/dL são rastreáveis relativamente ao método de referência ID-MS (Diluição Isotópica por Espectrometria de Massa).
Para referências AUML-0250/0420/0500 : ELICAL 2. o é rastreável relativamente ao método de referência ID-MS (Diluição Isotópica por Espectrometria de Massa).

Frequência de calibração : A frequência de calibração é específica a cada equipamento (consultar § DESEMPENHO).

CONTROLE DE QUALIDADE
Recomenda-se o uso de soros de controle de qualidade, como ELITROL I e ELITROL II, para monitorar o desempenho do ensaio.
Os controles devem ser executados:
- antes de analisar amostras de pacientes,
- pelo menos uma vez por dia,
- após cada calibração,
- e/ou de acordo com os requisitos laboratoriais e regulamentares.

Os resultados devem estar dentro dos intervalos definidos. Se os valores ficarem fora dos intervalos definidos, cada laboratório deve tomar as medidas corretivas necessárias.

TRATAMENTO DOS RESÍDUOS
O descarte de todo material residual deve estar de acordo com os requisitos regulamentares locais, estaduais e federais (consulte a Ficha de dados de segurança (SDS)).

DESEMPENHO
Os desempenhos foram obtidos no Selectra ProM, seguindo as recomendações técnicas do CLSI, sob condições ambientais controladas.

- Precisão de medição
a) Soro / plasma
1.50 - 25.00 mg/dL (89 - 1487 µmol/L).
As amostras com maiores concentrações devem ser diluídas 1:5 com solução de NaCl 9 g/L e ensaiado novamente. Este procedimento estende a faixa de medição até 125.00 mg/dL (7436 µmol/L).
Não relatar resultados fora do intervalo de medição.
b) Urina
5.0 - 250.0 mg/dL (0.30 - 14.87 mmol/L)
As amostras com maiores concentrações devem ser diluídas 1:5 com solução de NaCl 9 g/L e ensaiado novamente. Este procedimento estende a faixa de medição até 800.0 mg/dL (47.59 mmol/L).
Não relatar resultados fora do intervalo de medição.

Para utilizadores do Selectra TouchPro, a função de «diluir» realiza a diluição do amostras automaticamente. Os resultados são tomados em consideração na diluição.

- Limite de detecção (LoD) e limite de quantificação (LoQ)
a) Soro / plasma
LoD = 0.09 mg/dL (5 µmol/L)
LoQ = 1.00 mg/dL (59 µmol/L)

b) Urina
LoD = 0.6 mg/dL (0.04 mmol/L)
LoQ = 5.0 mg/dL (0.30 mmol/L)

- Precisão
a) Soro / plasma
Dados de imprecisão foram obtidos em 2 analisadores Selectra ProM ao longo de 20 dias (2 corridas por dia, testes realizados em duplicata).
Os resultados representativos são apresentados na tabela a seguir.

		Média		Intra-série	Total
	n	mg/dL	µmol/L	CV (%)	
Nível baixo	80	2.41	143	0.5	2.8
Nível médio	80	4.95	294	0.7	2.3
Nível elevado	80	6.86	408	0.7	2.2

b) Urina
Dados de imprecisão foram obtidos em 2 analisadores Selectra ProM ao longo de 20 dias (2 corridas por dia, testes realizados em duplicata).
Os resultados representativos são apresentados na tabela a seguir.

		Média		Intra-série	Total
	n	mg/dL	mmol/L	CV (%)	
Nível baixo	80	10.3	0.61	1.8	6.6
Nível médio	80	23.9	1.42	1.1	3.8
Nível elevado	80	77.9	4.63	1.2	3.3

- Correlação
a) Soro / plasma
Foi realizado um estudo comparativo entre o reagente URIC ACID MONO SL em um analisador Selectra ProM e um sistema similar disponível comercialmente em 100 amostras de soro humano.
As concentrações da amostra variaram de 1.55 para 23.94 mg/dL (92 - 1424 µmol/L)..
Os resultados são os seguintes:
Coeficiente de correlação: (r) = 0.999
Regressão linear: y = 1.044x - 0.04 mg/dL (2 µmol/L)

b) Urina
Foi realizado um estudo comparativo entre o reagente URIC ACID MONO SL em um analisador Selectra ProM e um sistema similar disponível comercialmente em 49 amostras de urina humana.
As concentrações da amostra variaram de 5.6 para 220.2 mg/dL (0.33 - 13.10 mmol/L)
Os resultados são os seguintes:
Coeficiente de correlação: (r) = 0.996
Regressão linear: y = 1.061x + 0.1 mg/dL (0.01 mmol/L)

- Limitações/Interferências
- Não utilize amostras visivelmente turvas ou hemolizadas.

a) Soro / plasma
Estudos foram realizados para determinar o nível de interferência de diferentes compostos.
Os seguintes níveis ácido úrico foram testados : 2.52 mg/dL e 7.56 mg/dL
Uma interferência não significativa é definida por uma recuperação ≤±10% do valor inicial.
Bilirrubina não conjugada: Nenhuma interferência significativa até 30 mg/dL (513 µmol/L).
Bilirrubina conjugada: Nenhuma interferência significativa até 14.8 mg/dL (253 µmol/L).
Hemoglobina : Nenhuma interferência significativa até 50 mg/dL.
Glucose: Nenhuma interferência significativa até 500 mg/dL (27.8 mmol/L)
Triglicéridos : Nenhuma interferência significativa até 2095 mg/dL (23.7 mmol/L).
Turvação: Interferência ocorre em todos os níveis de Intralipid®
Ácido ascórbico: interferência significativa em amostras contendo ácido ascórbico.
Metildopa : Nenhuma interferência significativa até 1 mg/dL.
Dobesilato de cálcio: Induz resultados falsamente baixos em indivíduos que tomam dobesilato cálcio.

- Em casos muito raros, as gamopatias monoclonais (mieloma múltiplo), em particular, tipo IgM (macroglobulinemia de Waldenstrom) podem causar resultados não confiáveis.[(5)]

- Os resultados podem ser falsamente reduzidos em níveis significativos na amostra de NAC (*N*-acetilcisteína), NAPQI (metabólito do acetaminofeno (paracetamol)) ou metamizol.

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young. [(6-7)]

b) Urina
Estudos foram realizados para determinar o nível de interferência de diferentes compostos.
Os seguintes níveis ácido úrico foram testados : 10.0 e 75.0 mg/dL.
Bilirrubina conjugada: Nenhuma interferência significativa até 29.5 mg/dL (505 µmol/L).
Hemoglobina : Nenhuma interferência significativa até 300 mg/dL.
Urea: Nenhuma interferência significativa até 5000 mg/dlL (833 mmol/L)
Ácido ascórbico: Nenhuma interferência significativa até 20 mg/dL.
Metildopa : Em concentrações terapêuticas induz resultados falsamente elevados.

- Os resultados podem ser falsamente reduzidos em níveis significativos na amostra de NAC (*N*-acetilcisteína), NAPQI (metabólito do acetaminofeno (paracetamol)) ou metamizol.

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young. [(6-7)]

- Estabilidade a bordo / frequência de calibração
Estabilidade a bordo: 28 dias
Frequência de calibração: 28 dias
Recalibre quando os lotes de reagentes mudarem, quando os resultados do controle de qualidade estiverem fora da faixa estabelecida e após uma operação de manutenção.

Estes desempenhos foram obtidos utilizando o analisador ELITech Selectra ProM. Os resultados podem variar se um instrumento diferente ou um procedimento manual for usado.
Os desempenhos de aplicações não validados pela ELITech não são garantidos e devem ser definidos pelo usuário.

☛DECLARAÇÃO DE INCIDENTE GRAVE
Notifique o fabricante (através do seu distribuidor) e a autoridade competente do Estado-Membro da união europeia em que o usuário e / ou o paciente está estabelecido, de qualquer incidente grave que tenha ocorrido em relação ao dispositivo.
Para outras jurisdições, a declaração de incidente grave deve estar de acordo com os requisitos regulamentares locais, estaduais e federais.
Ao relatar um incidente grave, você fornece informações que podem contribuir para a segurança de dispositivos médicos *in vitro*.

☛ASSISTÊNCIA TÉCNICA
Entre em contato com o seu distribuidor local ou com a ELITech Clinical Systems SAS.
(CCsupport@elitechgroup.com).

☛BIBLIOGRAPHIE/BIBLIOGRAPHY BIBLIOGRAFÍA/BIBLIOGRAFIA

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SYMBOLES/SYMBOLS/ SÍMBOLOS/SÍMBOLOS
- Les symboles utilisés sont décrits dans la norme ISO 15223-1 hormis ceux présentés ci-dessous.
- Symbols used are defined on ISO 15223-1 standard, except those presented below.
- Los símbolos utilizados son descritos en la norma ISO 15223-1 a la excepción de los presentados a continuación.
- Os símbolos utilizados são definidos na norma ISO 15223-1, exceto os apresentados abaixo.

CONT	Contient Content Contiene Conteúdo
R	Réactif Reagent Reactivo Reagente
Std	Standard Standard Estándar Padrão
☛	Modification par rapport à la version précédente Modification from previous version Modificación con respecto a la versión anterior Modificação relativamente à versão anterior
CE	Conformité Européenne European Conformity Conformidad Europea Conformidade Europeia

Note/Nota
- Uniquement pour la réf. **AUML-0250,** utilisée avec le logiciel Selectra TouchPro.
- Only for ref. **AUML-0250,** used with Selectra TouchPro software.
- Únicamente para la ref. **AUML-0250,** utilizada(s) con el software Selectra TouchPro.
- Somente para ref. **AUML-0250,** usado(s) com o Selectra TouchPro.

AUML

Uric Acid 0
660 PIT-AUML

ELITechGroup
EMPOWERING IVD

URIC ACID MONO SL

AUML

AUML-0427	R 6 x 50 mL	+	Std	1 x 5 mL
AUML-0497	R 1 x 100 mL	+	Std	1 x 5 mL
AUML-0507	R 6 x 100 mL	+	Std	1 x 5 mL
AUML-0707	R 4 x 250 mL	+	Std	1 x 5 mL
AUML-0420	R 6 x 50 mL			
AUML-0500	R 6 x 100 mL			
AUML-0250	R 12 x 20 mL			

CE

PIT-AUML-4-v23 (09/2020)

Français - FR

☛USAGE PRÉVU
ELITech Clinical Systems URIC ACID MONO SL est un réactif de diagnostic *in vitro*, destiné au dosage quantitatif de l'acide urique dans les échantillons de sérum, de plasma et d'urine humains sur des automates ou semi-automates.
Le standard est destiné à la calibration du réactif.
Ces dispositifs de diagnostic *in vitro* sont uniquement destinés aux professionnels.

☛SIGNIFICATION CLINIQUE [(1-3)]
L'acide urique est le produit final du catabolisme des purines (adénosine et guanosine) endogènes et exogènes. L'acide urique est très peu soluble dans l'eau. Ainsi en cas de concentration sérique élevée, des cristaux d'urates peuvent se former et se déposer au niveau des articulations provoquant des inflammations douloureuses (goutte) et peuvent également endommager les reins. Une augmentation du taux d'acide urique sérique peut être provoquée soit par une production accrue (apport excessif de purines, augmentation du turn-over des acides nucléiques notamment dans le cadre de certains cancers ou à la suite de traitements anti-cancéreux, désordres métaboliques d'origine génétique tel que syndrome de Lesch-Nyhan, psoriasis), soit par une excrétion réduite (atteintes rénales, prise de certains médicaments comme les diurétiques). En cas de pré-éclampsie, l'acide urique sérique peut être augmenté selon ces deux mécanismes. Une diminution du taux d'acide urique sérique est plus rare. Elle peut être observée par exemple lors des troubles de l'élimination rénale tel que le syndrome de Fanconi, ou dans la maladie de Hodgkin.
Lorsque la concentration en acide urique est anormalement élevée dans les urines, il y a risque de formation de calculs.
En pratique, le dosage de l'acide urique dans le sérum est indiqué pour aider au diagnostic de la goutte, pour le suivi des patients sous radiothérapie ou chimiothérapie, et parfois dans l'aide au diagnostic de la pré-éclampsie. Le dosage de l'acide urique dans les urines est indiqué pour aider au diagnostic de la goutte et dans la prévention des récidives de calculs rénaux.

☛LIMITE D'UTILISATION
Le dosage de l'acide urique ne peut être utilisé seul pour diagnostiquer une maladie ou une pathologie spécifique.
Les résultats doivent toujours être confrontés aux résultats d'autres tests diagnostiques, aux examens cliniques, et à l'historique médical du patient.

☛MÉTHODE & PRINCIPE [(4)]
Enzymatique / PAP - Point Final.

$$\text{Acide urique} + 2H_2O + O_2 \xrightarrow{\text{Uricase}} \text{Allantoïne} + CO_2 + H_2O_2$$

$$2H_2O_2 + \text{4-AAP} + \text{EHSPT} \xrightarrow{\text{Peroxydase}} \text{Quinonéimine} + 4H_2O$$

EHSPT=*N*-Ethyl-*N*-(2-Hydroxy-3-Sulfopropyl)-*m*-Toluidine
4-AAP = Amino-4-antipyrine

☛COMPOSITION
Réactif : R
Tampon pH 7.00 (20-25°C)

EHSPT		0.72	mmol/L
Amino-4-antipyrine		0.37	mmol/L
Uricase	≥	150	U/L
Peroxydase	≥	12 000	U/L
Azide de sodium	<	0.1	% (p/p)

Standard: Std (ref : AUML-0427/0497/0507/0707)

Acide urique		6	mg/dL
		357	µmol/L
Azide de sodium	<	0.5	% (p/p)

MATÉRIELS REQUIS MAIS NON FOURNIS
- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solution saline normale (NaCl 9 g/L).
- Automates ou semi-automates.
- Equipement général de laboratoire (ex. pipette).
- Ne pas utiliser de matériel ne figurant pas ci-dessus.

☛PRÉCAUTIONS D'EMPLOI ET MISES EN GARDE
- Consulter la fiche de données de sécurité (FDS) pour une manipulation appropriée.
- Le réactif R et le standard Std contiennent de l'azide de sodium qui peut réagir avec le plomb ou le cuivre et former des azides métalliques potentiellement explosifs. Lors de l'élimination de ces réactifs toujours rincer abondamment avec de l'eau pour éviter l'accumulation d'azides.
- Respecter les précautions d'usage et les bonnes pratiques de laboratoire.
- Utiliser du matériel de laboratoire propre ou à usage unique afin d'éviter toute contamination.

☛STABILITÉ
Stocker à 2-8 °C et à l'abri de la lumière. Ne pas congeler.
Ne pas utiliser après la date d'expiration indiquée sur les étiquettes des flacons.
Le standard doit être immédiatement et correctement refermé afin d'éviter toute contamination ou évaporation.
Stabilité à bord :
La stabilité à bord est spécifique à chaque automate. (Se référer au § PERFORMANCES).

PRÉPARATION
Le réactif et le standard sont prêts à l'emploi.

DÉTÉRIORATION DU PRODUIT
- Le produit doit être limpide. Tout trouble serait le signe d'une détérioration du produit.
- Ne pas utiliser le produit s'il y a des signes évidents de contamination ou de détérioration (ex : particules).
- Un flacon endommagé peut avoir un impact sur les performances du produit. Ne pas utiliser le produit si les flacons présentent des signes physiques de détérioration (par exemple, fuite, flacon percé).

☛ÉCHANTILLONS
Echantillons requis [(2)]
- Sérum
- Plasma (héparine de lithium)
- Urine
- L'utilisation de toute autre type d'échantillon doit être validée par le laboratoire.

Avertissements et précautions
- Pour prévenir toute précipitation d'urate, les échantillons urinaires peuvent être ajustés à pH >8.0 avec du NaOH. [(2)]
- Les échantillons doivent être prélevés selon les Bonnes Pratiques de Laboratoire et les guides appropriés qui sont mis en place.

Stockage et stabilité [(2)]
Sérum/plasma
- 3-5 jours à 2-8°C
- 6 mois à -20°C

Urine (alcalinisée)
- 3 jours à température ambiante

Ne pas réfrigérer

☛VALEURS DE RÉFÉRENCE [(1)]

Sérum/plasma	mg/dL	µmol/L
Hommes	3.5 - 7.2	208 - 428
Femmes	2.6 - 6.0	155 - 357
Urine (recueil de 24 h)	mg/24h	mmol/24h
	250 - 750	1.48 - 4.43
	mg/dL*	mmol/L*
	16.7 - 50	0.99 - 2.97

*pour un volume urinaire de 1.5L par 24 heures.

Avec un régime sans purine, l'excrétion décroit de 20 à 25 %

Remarque : Les valeurs ci-dessus ne sont données qu'à titre indicatif. Il est recommandé à chaque laboratoire d'établir et de maintenir ses propres valeurs de référence par rapport à la population visée.

☛PROCÉDURE
Procédure manuelle
Longueur d'onde : 546 nm
Trajet optique : 1 cm
Ratio échantillon/réactif : 1:40
Température: 37 °C
Les échantillons urinaires doivent être dilués au 1/10 dans une solution de NaCl 9 g/L avant la mesure.

Lire contre le blanc réactif.

	CALIBRATION	DOSAGE
Réactif R	1 000 µL	1 000 µL
Standard/ Calibrant	25 µL	-
Echantillon	-	25 µL

Mélanger et lire les absorbances (A) après 5 minutes d'incubation.

Procédure sur automate
Ces réactifs peuvent être utilisés sur différents automates. Pour les automates ELITech Selectra, les applications validées sont disponibles sur demande. Avec le logiciel Selectra TouchPro, utilisez l'application incluse dans le code barre disponible à la fin de cette notice.

Les échantillons urinaires doivent être dilués au 1/10 dans une solution de NaCl 9 g/L avant la mesure. Pour les utilisateurs du logiciel Selectra TouchPro, la dilution des urines est réalisée automatiquement.

☛CALCUL

$$\frac{A\ \text{Echantillon}}{A\ \text{Standard/Calibrant}} \times n \quad n = \text{concentration du Standard/ calibrant}$$

Pour le calcul de la concentration de l'acide urique dans les urines, multiplier le résultat par le facteur de dilution (10). Pour les utilisateurs du logiciel Selectra TouchPro, les résultats tiennent compte du facteur de dilution.

Facteur de conversion : mg/dL x 59.48 = µmol/L
mg/dL x 0.059 = mmol/L

CALIBRATION
Pour les références AUML-0427/0497/0507/0707: ELICAL 2 et Uric Acid Standard 6 mg/dL sont traçables par rapport à la méthode de référence ID-MS (Dilution Isotopique - Spectrométrie de Masse).
Pour les références AUML-0250/0420/0500 : ELICAL 2 est traçable par rapport à la méthode de référence ID-MS (Dilution Isotopique - Spectrométrie de Masse).

Fréquence de calibration : La fréquence de calibration est spécifique à chaque automate (se référer au § PERFORMANCES).

CONTRÔLE QUALITÉ
Il est recommandé d'utiliser des sérums de contrôle tels que ELITROL I et ELITROL II pour surveiller les performances du dosage.
Ces contrôles doivent être effectués :
- avant que les échantillons de patients soient testés,
- au moins une fois par jour,
- après chaque calibration,
- et/ou en accord avec les requis du laboratoire et des exigences réglementaires.

Les résultats doivent être dans les intervalles définis. Si les valeurs se situent en dehors des plages définies, chaque laboratoire devra prendre les mesures correctives nécessaires.

TRAITEMENT DES DÉCHETS
L'élimination de tous les déchets doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales (veuillez vous référer à la la fiche de données de sécurité (FDS)).

PERFORMANCES
Les performances ont été obtenues sur l'automate Selectra ProM, en suivant les recommandations CLSI, dans des conditions environnementales contrôlées.

- Domaine de mesure
a) Sérum/Plasma
1.50 - 25.00 mg/dL (89 - 1487 µmol/L).
Les échantillons ayant des concentrations supérieures devront être dilués au 1/5 dans une solution de NaCl 9 g/L et redosés. Cette procédure étend le domaine de mesure jusqu'à 125.00 mg/dL (7436 µmol/L).
Ne pas communiquer de résultats en dehors du domaine de mesure étendu.

b) Urine
5.0 - 250.0 mg/dL (0.30 - 14.87 mmol/L)
Les échantillons ayant des concentrations supérieures devront être dilués au 1/5 dans une solution de NaCl 9 g/L et redosés. Cette procédure étend le domaine de mesure jusqu'à 800.0 mg/dL (47.59 mmol/L).
Ne pas communiquer de résultats en dehors du domaine de mesure étendu.

Pour les utilisateurs du logiciel Selectra TouchPro, la fonction « diluer » réalise la dilution des échantillons automatiquement. Les résultats tiennent compte de la dilution.

- Limite de Détection (LoD) et Limite de Quantification (LoQ)
a) Sérum/Plasma
LoD = 0.09 mg/dL (5 µmol/L)
LoQ = 1.00 mg/dL (59 µmol/L)

b) Urine
LoD = 0.6 mg/dL (0.04 mmol/L)
LoQ = 5.0 mg/dL (0.30 mmol/L)

- Précision
a) Sérum/Plasma
Les données d'imprécision ont été obtenues sur 2 automates Selectra ProM sur 20 jours (2 routines par jour, tests effectués en double).

Des résultats représentatifs sont présentés dans le tableau suivant :

		Moyenne		Intra-serie	Total
	n	mg/dL	µmol/L	CV (%)	
Niveau bas	80	2.41	143	0.5	2.8
Niveau moyen	80	4.95	294	0.7	2.3
Niveau haut	80	6.86	408	0.7	2.2

b) Urine
Les données d'imprécision ont été obtenues sur 2 automates Selectra ProM sur 20 jours (2 routines par jour, tests effectués en double).

Des résultats représentatifs sont présentés dans le tableau suivant :

		Moyenne		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Niveau bas	80	10.3	0.61	1.8	6.6
Niveau moyen	80	23.9	1.42	1.1	3.8
Niveau haut	80	77.9	4.63	1.2	3.3

- Corrélation
a) Sérum/Plasma
Une étude comparative a été réalisée entre le réactif URIC ACID MONO SL sur un automate Selectra ProM et un système similaire disponible sur le marché sur 100 échantillons sériques.
Les concentrations des échantillons s'échelonnent de 1.55 à 23.94 mg/dL (92 - 1424 µmol/L).
Les résultats sont les suivants :
Coefficient de corrélation: (r) = 0.999
Droite de régression : y = 1.044x - 0.04 mg/dL (2 µmol/L)

b) Urine
Une étude comparative a été réalisée entre le réactif URIC ACID MONO SL sur un automate Selectra ProM et un système similaire disponible sur le marché sur 49 échantillons urinaires.
Les concentrations des échantillons s'échelonnent de 5.6 à 220.2 mg/dL (0.33 - 13.10 mmol/L).
Les résultats sont les suivants :
Coefficient de corrélation: (r) = 0.996
Droite de régression : y = 1.061x + 0.1 mg/dL (0.01 mmol/L)

- Limitations/Interférences
- Ne pas utiliser d'échantillons hémolysés ou visiblement trouble.

a) Sérum/Plasma
- Des tests ont été réalisés pour déterminer le niveau d'interférence de différents composés.
Les niveaux suivants d'acide urique ont été testés : 2.52 mg/dL et 7.56 mg/dL.
L'absence d'interférence significative est définie par un recouvrement ≤±10% de la valeur initiale.
Bilirubine non-conjuguée : Aucune interférence significative jusqu'à 30.0 mg/dL (513 µmol/L).
Bilirubine conjuguée : Aucune interférence significative jusqu'à 14.8 mg/dL (253 µmol/L).
Hémoglobine : Aucune interférence significative jusqu'à 50 mg/dL.
Glucose: Aucune interférence significative jusqu'à 500 mg/dL (27.8mmol/L)
Triglycérides: Aucune interférence significative jusqu'à 2095 mg/dL (23.7 mmol/L).
Turbidité: Une interférence se produit à tous les niveaux d'Intralipid®
Acide ascorbique: Interférence importante sur des échantillons contenant de l'acide ascorbique.
Méthyl dopa: Aucune interférence significative jusqu'à 1 mg/dL.
Dobésilate de calcium : Induit des résultats faussement bas sur les personnes prenant du dobésilate de calcium.

- Dans des cas très rares, les gammapathies monoclonales (myélome multiple), en particulier de type IgM (Macroglobulinémie de Waldenström) peuvent être à l'origine de résultats peu fiables.[(5)]

- Les résultats peuvent être faussement abaissés dans les échantillons contenant des niveaux significatifs de NAC (*N*-Acétyl-Cystéine), de NAPQI (métabolite de l'acétaminophène (paracétamol)) ou de métamizole.

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.[(6-7)]

b) Urine
- Des tests ont été réalisés pour déterminer le niveau d'interférence de différents composés.
Les niveaux suivants d'acide urique ont été testés : 10.0 mg/dL et 75.0 mg/dL.
L'absence d'interférence significative est définie par un recouvrement ≤±10% de la valeur initiale.
Bilirubine conjuguée : Aucune interférence significative jusqu'à 29,5 mg/dL (505 µmol/L).
Hémoglobine : Aucune interférence significative jusqu'à 300 mg/dL.
Urée : Aucune interférence significative jusqu'à 5000 mg/dL (833 mmol/L).
Acide ascorbique: Aucune interférence significative jusqu'à 20 mg/dL.
Méthyl dopa: Induit des résultats faussement élevés aux concentrations thérapeutiques.

- Les résultats peuvent être faussement abaissés dans les échantillons contenant des niveaux significatifs de NAC (*N*-Acétyl-Cystéine), de NAPQI (métabolite de l'acétaminophène (paracétamol)) ou de métamizole.

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.[(6-7)]

- Stabilité à bord / fréquence de calibration
Stabilité à bord : 28 jours
Fréquence de calibration : 28 jours
Une nouvelle calibration doit être effectuée après chaque changement de lot de réactif, lorsque les résultats du ou des contrôles de qualité sont hors de l'intervalle établi, et après une opération de maintenance.

Ces performances ont été définies sur un automate ELITech Selectra ProM. Les résultats peuvent varier si le réactif est utilisé sur un automate différent ou en méthode manuelle.
Les performances obtenues à partir d'applications non validées par ELITech ne peuvent être garanties et doivent être définies par l'utilisateur.

☛DECLARATION DES INCIDENTS GRAVES
Veuillez notifier au fabricant (par l'intermédiaire de votre distributeur) et à l'autorité compétente de l'Etat membre de l'union européenne dans lequel l'utilisateur et/ou le patient est établi, les cas d'incident grave survenu en lien avec le dispositif.
Pour les autres juridictions, la déclaration d'incident grave doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales.
En signalant les incidents graves, vous contribuez à fournir davantage d'informations sur la sécurité des dispositifs médicaux de diagnostic *in vitro*.

☛ASSISTANCE TECHNIQUE
Contacter votre distributeur local ou ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

English - EN

☞INTENDED USE

ELITech Clinical Systems URIC ACID MONO SL is an *in vitro* diagnostic reagent intended for the quantitative determination of Uric Acid in human serum, plasma and urine samples on analyzers or semi-automatic analyzers.
The standard is intended for the calibration of reagent.
These *in vitro* diagnostic devices are for professional use only.

☞CLINICAL SIGNIFICANCE [1-3]

Uric acid is the major product of the catabolism of endogenous and exogenous purines (adenosine and guanosine). Uric acid is poorly soluble in water. Therefore, in case of high serum concentration, urate crystals can form and deposit in joints, triggering painful inflammations (gout), or can damage kidneys. Increased serum uric acid level can be caused either by increased production (increased intake of purines, increased nucleic acid turn-over particularly in case of certain cancers or following anti-cancer treatments, genetic metabolic disorders such as Lesch-Nyhan syndrome, psoriasis) or by decreased excretion (renal failure, drugs such as diuretics). In the case of pre-eclampsia, serum uric acid can be increased due to both mechanisms. Decreased serum uric acid is more uncommon. It can occur for example in impaired renal elimination such as in Fanconi syndrome or in Hodgkin's disease.
When uric acid concentration is abnormally high in urines, there is a risk of stone formation.
In practice, the determination of uric acid in serum is indicated to help diagnose gout, for the follow-up of patients under radiation or chemotherapy, and sometimes to help diagnose pre-eclampsia. The determination of uric acid in urines is indicated to help diagnose gout and in the prevention of recurring kidney stones.

☞LIMITATION OF USE

The quantitative assay of Uric Acid alone can not be used to diagnose a disease or a specific pathology.
The results must be interpreted in conjunction with other diagnostic test results, clinical findings and the patient's medical history.

☞METHOD & PRINCIPLE [4]

Enzymatic / PAP - End Point.

$$\text{Uric acid} + 2H_2O + O_2 \xrightarrow{\text{Uricase}} \text{Allantoine} + CO_2 + H_2O_2$$

$$2H_2O_2 + \text{4-AAP} + \text{EHSPT} \xrightarrow{\text{Peroxidase}} \text{Quinoneimine} + 4H_2O$$

EHSPT = N-Ethyl-N-(2-Hydroxy-3-Sulfopropyl) *m*-Toluidine
4-AAP = Amino-4-antipyrine

☞COMPOSITION

Reagent: R

Buffer pH 7.00 (20-25°C)			
EHSPT		0.72	mmol/L
Amino-4-antipyrine		0.37	mmol/L
Uricase	≥	150	U/L
Peroxidase	≥	12 000	U/L
Sodium azide	<	0.1	% (w/w)

Standard: Std (Ref : AUML-0427/0497/0507/0707)

Uric acid		6	mg/dL
		357	µmol/L
Sodium azide	<	0.5	% (w/w)

MATERIALS REQUIRED BUT NOT PROVIDED

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Normal saline solution (NaCl 9 g/L).
- Analyzers or semi-automatic analyzers.
- General Laboratory equipment (e.g. pipette).
- Do not use materials that are not required as indicated above.

☞PRECAUTIONS FOR USE AND WARNINGS

- Consult Safety Data Sheet (SDS) for a proper handling.
- Reagent R and Standard Std contain sodium azide which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of these reagents always flush with copious amounts of water to prevent azide buildup.
- Take normal precautions and adhere to good laboratory practice.
- Use clean or single use laboratory equipment only to avoid contamination.

☞STABILITY

Store at 2-8 °C and protect from light. Do not freeze.
Do not use after expiration dates indicated on the vial labels.
The standard should be immediately and tightly capped to prevent contamination and evaporation.
On board stability :
The on-board stability is specific for each analyzer. (Refer to § PERFORMANCE DATA).

PREPARATION

The reagent and standard are ready to use.

PRODUCT DETERIORATION

- The product should be clear. Cloudiness would indicate deterioration.
- Do not use the product if there is visible evidence of contamination or damage (e.g. particle matter).
- Damage to the product container may impact on product performance. Do not use the product if there is physical evidence of deterioration (e.g. leakages or punctured container).

☞SAMPLES

Specimen [2]
- Serum
- Plasma (lithium heparin)
- Urine
- Using any other specimen type should be validated by the laboratory.

Warnings and precautions
- To prevent urate precipitation, urine samples may be adjusted to pH>8.0 with NaOH.[2]
- Samples should be collected in accordance with Good Laboratory Practice and appropriate guidelines that may be in place.

Storage and stability [2]
Serum/ plasma
- 3-5 days at 2-8°C
- 6 months at -20°C
Urine (Alkalinized)
- 3 days at room temperature
Do not refrigerate urine samples

☞REFERENCE VALUES [1]

Serum/plasma	mg/dL	µmol/L
Men	3.5 - 7.2	208 - 428
Women	2.6 - 6.0	155 - 357
Urine (24 h collection)	mg/24h	mmol/24
	250 - 750	1.48 - 4.43
	mg/dL*	mmol/L*
	16.7 - 50	0.99 - 2.97

*for a urinary volume of 1.5 L per 24 hours

With a purine-free diet, excretion may decrease by 20 to 25%

Note : *The quoted range should serve as a guide only. It is recommended that each laboratory verifies this range or establishes a reference interval for the intended population.*

☞PROCEDURE

Manual Procedure
Wavelength : 546 nm
Optical path : 1 cm
Sample/ Reagent ratio : 1:40
Temperature: 37 °C
Urine samples must be diluted 1:10 with NaCl 9 g/L solution before measurement.

Read against reagent blank.

	CALIBRATION	TEST
Reagent R	1 000 µL	1 000 µL
Standard/ Calibrator	25 µL	-
Sample	-	25 µL

Mix and read the absorbances (A) after an incubation of 5 minutes.

Automatic Procedure
These reagents may be used on several automatic analyzers. For ELITech Selectra Analyzers, validated applications are available on request. For Selectra TouchPro software, use the application included in the barcode available at the end of this insert.

Urine samples must be diluted 1:10 with NaCl 9 g/L solution before measurement. For users of Selectra TouchPro software, urine dilution is performed automatically.

☞CALCULATION

$$\frac{A_{\text{Sample}}}{A_{\text{Calibrator/ Standard}}} \times n \quad n = \text{Calibrator/ standard concentration}$$

For the calculation of uric acid concentration in urine, multiply the result by the dilution factor (10). For users of Selectra TouchPro software, the results take the dilution factor into account.

Conversion factor : mg/dL x 59.48 = µmol/L
mg/dL x 0.059 = mmol/L

CALIBRATION

For the reference AUML-0427/0497/0507/0707 : ELICAL 2 and Uric Acid Standard 6 mg/dL are traceable to ID-MS (Isotope Dilution - Mass Spectrometry) reference method.
For the reference AUML-0250/0420/0500 : ELICAL 2 is traceable to ID-MS (Isotope Dilution - Mass Spectrometry) reference method.

Calibration frequency : The calibration is specific for each analyzer. (Refer to § PERFORMANCE DATA).

QUALITY CONTROL

It is recommended that quality control sera such as ELITROL I and ELITROL II be used to monitor the performance of the assay.
Controls have to be performed :
- prior to assaying patient samples,
- at least once per day,
- after every calibration,
- and/or in accordance with laboratory and regulatory requirements.

Results should be within the defined ranges. If values fall outside of the defined ranges, each laboratory should take necessary corrective measures.

WASTE MANAGEMENT

Disposal of all waste material should be in accordance with local, state and federal regulatory requirements (please refer to the Safety Data Sheet (SDS)).

PERFORMANCES

Performances were obtained on Selectra ProM, following CLSI technical recommendations, under controlled environmental conditions.

- Measuring range
a) Serum/Plasma
1.50 - 25.00 mg/dL (89 - 1487 µmol/L).
Samples having greater concentrations should be diluted 1:5 with NaCl 9 g/L solution and re-assayed.
This procedure extends the measuring range up to 125.00 mg/dL (7436 µmol/L).
Do not report results outside this extended range.

b) Urine
5.0 - 250.0 mg/dL (0.30 - 14.87 mmol/L)
Samples having greater concentrations should be diluted 1:5 with NaCl 9 g/L solution and re-assayed. This procedure extends the measuring range up to 800.0 mg/dL (47.59 mmol/L).
Do not report results outside this extended range.

For users with Selectra TouchPro software, the «dilute» function performs the sample dilution automatically. Results take the dilution into account.

Limit of Detection (LoD) and Limit of Quantification (LoQ)
a) Serum/Plasma
LoD = 0.09 mg/dL (5 µmol/L)
LoQ = 1.00 mg/dL (59 µmol/L)

b) Urine
LoD = 0.6 mg/dL (0.04 mmol/L)
LoQ = 5.0 mg/dL (0.30 mmol/L)

- Precision
a) Serum/Plasma
Imprecision data has been obtained on 2 Selectra ProM analyzers over 20 days (2 runs per day, tests performed in duplicate).
Representative results are presented in the following table.

		Mean		Within-run	Total
	n	mg/dL	µmol/L	CV (%)	
Low level	80	2.41	143	0.5	2.8
Medium level	80	4.95	294	0.7	2.3
High level	80	6.86	408	0.7	2.2

b) Urine
Imprecision data has been obtained on 2 Selectra ProM analyzers over 20 days (2 runs per day, tests performed in duplicate).
Representative results are presented in the following table.

		Mean		Within-run	Total
	n	mg/dL	mmol/L	CV (%)	
Low level	80	10.3	0.61	1.8	6.6
Medium level	80	23.9	1.42	1.1	3.8
High level	80	77.9	4.63	1.2	3.3

- Correlation
a) Serum/Plasma
A comparative study has been performed between URIC ACID MONO SL reagent on a Selectra ProM analyzer and a similar commercially available system on 100 human serum samples.
The sample concentrations ranged from 1.55 and 23.94 mg/dL (92 and 1424 µmol/L).
The results are as follows :
Correlation coefficient : (r) = 0.999
Linear regression: y = 1.044 x - 0.04 mg/dL (2 µmol/L)

b) Urine
A comparative study has been performed between URIC ACID MONO SL reagent on a Selectra ProM analyzer and a similar commercially available system on 49 human urine samples.
The sample concentrations ranged from 5.6 and 220.2 mg/dL (0.33 and 13.10 mmol/L).
The results are as follows :
Correlation coefficient : (r) = 0.996
Linear regression: y = 1.061 x + 0.1 mg/dL (0.01 mmol/L)

- Limitations/Interferences
- Do not use visibly turbid or hemolyzed samples.

a) Serum/Plasma
- Studies have been performed to determine the level of interference from different compounds.
The following uric acid levels were tested: 2.52 mg/dL and 7.56 mg/dL.
No significant interference is defined by a recovery ≤±10% of the initial value.
Unconjugated bilirubin: No significant interference up to 30.0 mg/dL (513 µmol/L).
Conjugated bilirubin: No significant interference up to 14.8 mg/dL (253 µmol/L).
Hemoglobin: No significant interference up to 50 mg/dL.
Glucose: No significant interference up to 500 mg/dL (27.8 mmol/L).
Triglycerides: No significant interference up to 2095 mg/dL (23.7 mmol/L).
Turbidity: Interference occurs at all levels of Intralipid®
Ascorbic acid: Significant interference on samples containing ascorbic acid.
Methyl-dopa: No significant interference up to 1 mg/dL.
Calcium dobesilate: Induces falsely low results on individuals taking calcium dobesilate.

- In very rare cases, monoclonal gammopathies (multiple myeloma), in particular IgM type (Waldenstrom's macroglobulinemia) can cause unreliable results.[5]

- Results can be falsely lowered by significant levels in the sample of NAC (*N*-Acetyl-Cysteine), NAPQI (metabolite of acetaminophene (paracetamol)) or metamizole.

- Many other substances and drugs may interfere. Some of them are listed in reviews published by Young.[6-7]

b) Urine
- Studies have been performed to determine the level of interference from different compounds.
The following uric acid levels were tested: 10.0 mg/dL and 75.0 mg/dL.
No significant interference is defined by a recovery ≤±10% of the initial value.
Conjugated bilirubin: No significant interference up to 29.5 mg/dL (505 µmol/L).
Hemoglobin: No significant interference up to 300 mg/dL.
Urea: No significant interference up to 5000 mg/dL (833 mmol/L).
Ascorbic acid: No significant interference up to 20 mg/dL.
Methyl-dopa: Induces falsely high results at therapeutic concentrations.

- Results can be falsely lowered by significant levels in the sample of NAC (*N*-Acetyl-Cysteine), NAPQI (metabolite of acetaminophene (paracetamol)) or metamizole.

- Many other substances and drugs may interfere. Some of them are listed in reviews published by Young.[6-7]

- On board stability/Calibration frequency
On Board Stability: 28 days
Calibration frequency: 28 days
Recalibrate when reagent lots change, when quality control results fall outside the established range and after a maintenance operation.

These performances have been obtained using ELITech Selectra ProM analyzer. Results may vary if a different instrument or a manual procedure is used. The performances of applications not validated by ELITech are not warranted and must be defined by the user.

☞DECLARATION OF SERIOUS INCIDENT

Please notify the manufacturer (through your distributor) and competent authority of the Member State of the european union in which the user and/or the patient is established, of any serious incident that has occurred in relation to the device. For other jurisdictions, the declaration of serious incident should be in accordance with local, state and federal regulatory requirements.
By reporting a serious incident, you provide information that can contribute to the safety of *in vitro* medical devices.

☞TECHNICAL ASSISTANCE

Contact your local distributor or ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

Español - ES

☞USO PREVISTO

ELITech Clinical Systems URIC ACID MONO SL es un reactivo de diagnóstico *in vitro* diseñado para la determinación cuantitativa del ácido úrico en muestras de suero, plasma y orina humanas en equipos automatizados o equipos semiautomáticos.
El estándar está diseñado para la calibración del reactivo.
Estos dispositivos de diagnóstico *in vitro* están destinados unicamente para los profesionales.

☞SIGNIFICADO CLÍNICO [1-3]

El aumento de la concentración sérica de ácido úrico puede deberse a un aumento de la producción (aumento de la ingesta de purinas, aumento del cambio de ácido nucleico, especialmente en casos de ciertos cánceres o después de tratamientos anticancerosos, trastornos metabólicos genéticos como el síndrome de Lesch-Nyhan, psoriasis) o por disminución de la excreción (insuficiencia renal, fármacos como los diuréticos). En el caso de la preeclampsia, el ácido úrico en suero puede incrementarse debido a ambos mecanismos. La disminución de la tasa de ácido úrico en suero es menos frecuente. Puede ocurrir, por ejemplo, en la eliminación renal deteriorada, como en el síndrome de Fanconi o en la enfermedad de Hodgkin.
Cuando la concentración de ácido úrico es anormalmente alta en orina, existe un riesgo de formación de cálculos.
En la práctica, la determinación del ácido úrico en suero es indicada para ayudar a diagnosticar la gota, para el seguimiento de los pacientes sometidos a radiación o quimioterapia, y algunas veces para ayudar a diagnosticar la preeclampsia. La determinación del ácido úrico en la orina es indicada para ayudar a diagnosticar la gota y en la prevención de cálculos renales recurrentes.

☞LÍMITE DE UTILIZACIÓN

La cuantificación del ácido úrico no puede ser utilizado solo para diagnosticar una enfermedad o patología específica.
Los resultados siempre deben compararse con los resultados de otras pruebas de diagnóstico, exámenes clínicos y el historial médico del paciente.

☞MÉTODO & PRINCIPIO [4]

Enzimático / PAP - Punto final.

$$\text{Ácido úrico} + 2H_2O + O_2 \xrightarrow{\text{Uricasa}} \text{Alantoína} + CO_2 + H_2O_2$$

$$2H_2O_2 + \text{4-AAP} + \text{EHSPT} \xrightarrow{\text{Peroxidasa}} \text{Quinoneimina} + 4H_2O$$

EHSPT = N- Etil-N-(2-Hidroxi-3-Sulfopropil) *m*-Toluidina
4-AAP = Amino-4-antipirina

☞COMPOSICIÓN

Reactivo : R

Tampón pH 7.00 (20-25°C)			
EHSPT		0.72	mmol/L
Amino-4-antipirina		0.37	mmol/L
Uricasa	≥	150	U/L
Peroxidasa	≥	12 000	U/L
Azida sódica	<	0.1	% (p/p)

Estándar : Std (Ref : AUML-0427/0497/0507/0707)

Ácido úrico		6	mg/dL
		357	µmol/L
Azida sódica	<	0.5	% (p/p)

MATERIALES REQUERIDOS PERO NO INCLUIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solución salina normal (NaCl 9 g/L).
- Equipos automatizados o equipos semiautomáticos.
- Equipamiento general de laboratorio (p. ej. pipeta).
- No utilice materiales que no se requieren, tal como se indica anteriormente.

☞PRECAUCIONES DE USO Y ADVERTENCIAS

- Consulte la Hoja de Datos de Seguridad (SDS) para un manejo adecuado.
- El reactivo R y el estándar Std contienen azida sódica que puede reaccionar con el plomo o el cobre de la tubería y formar potencialmente azidas metálicas explosivas. Cuando se elimine el reactivo enjuague con agua abundantemente para prevenir la acumulación de azidas.
- Tome las precauciones normales y respete las buenas prácticas de laboratorio.
- Para evitar contaminaciones utilizar equipo nuevo o completamente limpio.

☞ESTABILIDAD

Conservar a 2-8 °C y protegidos de la luz. No congelar.
No utilice después de la fecha de caducidad indicada en la etiqueta de los frascos.
El estándar debe cerrarse inmediatamente y correctamente para evitar contaminación y evaporación.
Estabilidad en el equipo:
La estabilidad es específica para cada equipo. (Referirse al § DATOS DE RENDIMIENTO).

PREPARACIÓN

El reactivo y el estándar están listos para su uso.

DETERIORACIÓN DEL PRODUCTO

- El producto debe ser claro. Turbidez indicaría deterioro.
- No utilice el producto si este presenta signos evidentes de contaminación o deterioro (p. ej partículas).
- Un frasco dañado puede tener un impacto en el rendimiento del producto. No utilice el producto si este tiene signos físicos de deterioro (p. ej, fugas, frasco perforado).

☞MUESTRAS

Muestras requeridas [2]
- Suero
- Plasma (heparina de litio)
- Orina
- El uso de cualquier otro tipo de muestra debe ser validado por el laboratorio.

Advertencias y precauciónes
- Para prevenir la precipitación de urato, las muestras de orina pueden ajustarse a pH> 8.0 con NaOH. [2]
- Las muestras deben de tomarse de acuerdo con las Buenas Prácticas de Laboratorio y las guías apropiadas establecidas.

Conservación y estabilidad [2]
Suero/plasma
- 3-5 días a 2-8°C
- 6 meses a -20°C
Orina (alcalinizada)
- 3 días a temperatura ambiente
No refrigere las muestras

☞VALORES DE REFERENCIA [1]

Suero/plasma	mg/dL	µmol/L
Hombres	3.5 - 7.2	208 - 428
Mujeres	2.6 - 6.0	155 - 357
Orina *(recolectada de 24h)*	mg/24h	mmol/24h
	250 - 750	1.48 - 4.43
	mg/dL*	mmol/L*
	16.7 - 50	0.99 - 2.97

*para un volumen de orina de 1.5 L por 24 horas.

Con una dieta sin purina, la excreción disminuye de 20 a 25%.

Nota : Los valores anteriores son solo indicativos. Se recomienda que cada laboratorio establezca y mantenga sus propios valores de referencia en relación con la población destinataria.

☞PROCEDIMIENTO

Procedimiento manual
Longitud de onda : 546 nm
Trayectoria óptica : 1 cm
Ratio muestra/reactivo : 1:40
Temperatura: 37 °C
Las muestras de orina deben diluirse 1:10 con una solución de NaCl 9 g/L antes de la medición

Leer contra blanco reactivo.

	CALIBRACIÓN	PRUEBA
Reactivo R	1 000 µL	1 000 µL
Estándar/Calibrador	25 µL	-
Muestra	-	25 µL

Mezcle y lea las absorbancias (A) después de una incubación de 5 minutos.

Procedimiento automático
Estos reactivos pueden ser utilizados en varios equipos. Para los equipos ELITech Selectra, las aplicaciones validadas están disponibles sobre pedido. Para el software Selectra TouchPro, use la aplicación incluida en el código de barras disponible al final de este inserto.

Las muestras de orina deben diluirse 1:10 con una solución de NaCl 9 g/L antes de la medición. Para los usuarios del software Selectra TouchPro, la dilución de orina se realiza automáticamente.

☞CÁLCULO

$$\frac{A_{\text{Muestra}}}{A_{\text{Estándar / calibrador}}} \times n \quad n = \text{concentración del estándar/ calibrador}$$

Para el cálculo de la concentración de ácido úrico en orina, multiplique el resultado por el factor de dilución (10). Para los usuarios del software Selectra TouchPro, los resultados toman en cuenta el factor de dilución.

Factor de conversión: mg/dL x 59.48 = µmol/L
mg/dL x 0.059 = mmol/L

CALIBRACIÓN

Para la referencia AUML-0427/0497/0507/0707 : ELICAL 2 o el estándar Uric Acid Standard 6 mg/dL son trazables al método de referencia DI-EM (Dilución Isotópica - Espectrometria de Masas)
Para la referencia AUML-0250/0420/0500 : ELICAL 2 es trazable al método de referencia DI-EM (Dilución Isotópica - Espectrometria de Masas).

Frecuencia de calibración : la frecuencia de calibración es específica para cada equipo (referirse al § DATOS DE RENDIMIENTO).

CONTROL DE CALIDAD

Es recomendado que sueros de control tales como ELITROL I y ELITROL II sean usados para monitorear el rendimiento de las pruebas.
Los controles deben realizarse :
- antes que las muestras del paciente sean evaluadas,
- por lo menos una vez al día,
- después de cada calibración,
- y/o en acuerdo con el laboratorio y los requerimientos regulatorios.

Los resultados deben de encontrarse en el rango definido. Si los valores se encuentran fuera del mismo, cada laboratorio deberá tomar las medidas correctivas necesarias.

TRATAMIENTO DE LOS RESIDUOS

Todos los materiales de desecho deben eliminarse de acuerdo con los requisitos regulatorios locales, estatales y federales. (diríjase a la hoja de seguridad (SDS)).

RENDIMIENTO

El rendimiento fue obtenido en un Selectra ProM, siguiendo las recomendaciones técnicas del CLSI, bajo condiciones ambientales controladas.

- Rango analítico
a) Suero/Plasma
1.50 - 25.00 mg/dL (89 - 1487 µmol/L)
Las muestras que tengan concentraciones mayores deben diluirse 1:5 con una solución de NaCl 9 g/L y volver a analizarse.
Este procedimiento extiende el rango analítico hasta 125.00 mg/dL (7436 µmol/L).
No tome en cuenta resultados fuera del rango analítico extendido.

b) Orina
5.0 - 250.0 mg/dL (0.30 - 14.87 mmol/L)
Las muestras que tengan concentraciones mayores deben diluirse 1:5 con una solución de NaCl 9 g/L y volver a analizarse.
Este procedimiento extiende el rango analítico hasta 800.0 mg/dL (47.59 mmol/L).
No tome en cuenta resultados fuera del rango analítico extendido.

Para los usuarios del software Selectra TouchPro, la función «diluir» realiza la dilución de las muestras automáticamente. Los resultados toman en cuenta la dilución.

- Límite de detección (LoD), límite de Cuantificación (LoQ)
a) Suero/Plasma
LoD = 0.09 mg/dL (5 µmol/L)
LoQ = 1.00 mg/dL (59 µmol/L)
b) Orina
LoD = 0.6 mg/dL (0.04 mmol/L)
LoQ = 5.0 mg/dL (0.30 mmol/L)

- Precisión
a) Suero/Plasma
Los datos de imprecisión fueron obtenidos en 2 equipos Selectra ProM durante 20 días (2 corridas por día, pruebas efectuadas en duplicado).
Resultados representativos se presentan en el cuadro siguiente:

		Media		Intra-serie	Total
	n	mg/dL	µmol/L	CV (%)	
Nivel bajo	80	2.41	143	0.5	2.8
Nivel medio	80	4.95	294	0.7	2.3
Nivel alto	80	6.86	408	0.7	2.2

b) Orina
Los datos de imprecisión fueron obtenidos en 2 equipos Selectra ProM durante 20 días (2 corridas por día, pruebas efectuadas en duplicado).
Resultados representativos se presentan en el cuadro siguiente:

		Media		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Nivel bajo	80	10.3	0.61	1.8	6.6
Nivel medio	80	23.9	1.42	1.1	3.8
Nivel alto	80	77.9	4.63	1.2	3.3

- Correlación
a) Suero/Plasma
Un estudio comparativo se llevó a cabo entre el reactivo URIC ACID MONO SL en el equipo Selectra ProM y un sistema comercial similar en 100 muestras séricas.
Las concentraciones de las muestras se encuentran entre 1.55 y 23.94 mg/dL (92 and 1424 µmol/L).
Los resultados son los siguientes :
Coeficiente de correlación: (r) = 0.999
Regresión linear : y = 1.044 x - 0.04 mg/dL (2 µmol/L)

b) Orina
Un estudio comparativo se llevó a cabo entre el reactivo URIC ACID MONO SL en el equipo Selectra ProM y un sistema comercial similar en 49 muestras de orina.
Las concentraciones de las muestras se encuentran entre 5.6 y 220.2 mg/dL (0.33 and 13.10 mmol/L).
Los resultados son los siguientes :
Coeficiente de correlación: (r) = 0.996
Regresión linear : y = 1.061 x + 0.1 mg/dL (0.01 mmol/L)

- Limitaciones/Interferencias
- No utilice muestras visiblemente turbias o hemolizadas.

a) Suero/Plasma
- Estudios fueron llevados a cabo para determinar el nivel de interferencia de diferentes componentes.
Los niveles siguientes del ácido úrico fueron probados: de 2.52 y 7.56 mg/dL.
Definimos una interferencia no significativa cuando se obtiene una recuperación de ≤±10% con respecto al valor inicial.
Bilirrubina no conjugada : No hay interferencia significativa hasta 30.0 mg/dL (513 µmol/L).
Bilirrubina conjugada : No hay interferencia significativa hasta 14.8 mg/dL (253 µmol/L).
Hemoglobina: No hay interferencia significativa hasta 50 mg/dL.
Glucosa: No hay interferencia significativa hasta 500 mg/dL (27.8 mmol/L).
Triglicéridos: No hay interferencia significativa hasta 2095 mg/dL (23.7 mmol/L).
Turbidez: Las interferencias ocurren a todos los niveles de Intralipid®.
Ácido ascórbico: Interferencias significativas en muestras que contienen ácido ascórbico.
Metildopa : No hay interferencia significativa hasta 1 mg/dL.
Calcio dobesilato : Induce a resultados falsamente bajos en personas que toman calcio dobesilato.

- En casos muy raros, las gammapatías monoclonales (mieloma múltiple), en particular el tipo IgM (macroglobulinemia de Waldenstrom) pueden producir resultados poco confiables.[5]

- Los resultados de dosificaciones pueden ser falsamente bajos cuando la muestra contiene niveles importantes de NAC (*N*-Acetil-cisteína), NAPQI (metabolito del acetaminofén (paracetamol)) o de Metamizol.

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en los artículos publicados por Young.[6-7]

b) Orina
- Estudios fueron llevados a cabo para determinar el nivel de interferencia de diferentes componentes.
Los niveles siguientes del ácido úrico fueron probados: 10.00 y 75.00 mg/dL.
Definimos una interferencia no significativa cuando se obtiene una recuperación de ≤±10% con respecto al valor inicial.
Bilirrubina conjugada : No hay interferencia significativa hasta 29.5 mg/dL (505 µmol/L).
Hemoglobina: No hay interferencia significativa hasta 300 mg/dL.
Urea: No hay interferencia significativa hasta 5000 mg/dL (833 mmol/L).
Ácido ascórbico: No hay interferencia significativa hasta 20 mg/dL.
Metildopa : Induce a resultados falsamente elevados a concentraciones terapéuticas.

- Los resultados de dosificaciones pueden ser falsamente bajos cuando la muestra contiene niveles importantes de NAC (*N*-Acetil-cisteína), NAPQI (metabolito del acetaminofén (paracetamol)) o de Metamizol.

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en los artículos publicados por Young.[6-7]

- Estabilidad en el equipo / frecuencia de calibración
Estabilidad en el equipo : 28 días
Frecuencia de calibración : 28 días
Recalibrar cuando los lotes de reactivo cambien, cuando los controles de calidad no se encuentren dentro del rango establecido, y después de operaciones de mantenimiento.

El rendimiento se ha obtenido utilizando el equipo ELITech Selectra ProM. Los resultados pueden variar si se utiliza un instrumento diferente o un procedimiento manual.
El rendimiento obtenido a partir de aplicaciones no validadas por ELITech no se garantiza y deben ser definidas por el usuario.

☞DECLARACIÓN DE INCIDENTES GRAVES

Por favor notifique al fabricante (por medio de su distribuidor) y autoridad competente del Estado miembro de la Unión Europea en donde el usuario o paciente radique, de cualquier incidente grave que se produzca con relación al dispositivo. Para otras jurisdicciones, la declaración de incidentes graves debe realizarse de acuerdo con los requisitos reglamentarios locales, estatales y federales. Reportando incidentes graves usted contribuye a proporcionar más información sobre la seguridad del dispositivo médico de diagnóstico *in vitro*.

☞ASISTENCIA TÉCNICA

Contacte a su distribuidor local o con ELITech Clinical Systems SAS (CCsupport@ elitechgroup.com)

Português – PT

☞UTILIZAÇÃO PREVISTA

ELITech Clinical Systems URIC ACID MONO SL é um reagente para diagnóstico *in vitro* destinado à determinação quantitativa do ácido úrico em amostras de soro, plasma e urina humanas em analisadores automáticos ou semi-automáticos.
O padrão é destinado à calibração do reagente.
Estes dispositivos de diagnóstico *in vitro* são apenas para uso profissional.

☞SIGNIFICADO CLÍNICO [1-3]

O ácido úrico é o principal produto do catabolismo de purinas endógenas e exógenas (adenosina e guanosina). O ácido úrico é pouco solúvel em água. Portanto, no caso de alta concentração sérica, os cristais de urato podem se formar e se depositar nas articulações, provocando inflamações dolorosas (gota) ou danificando os rins. O aumento do nível sérico de ácido úrico pode ser causado pelo aumento da produção (aumento da ingestão de purinas, aumento da renovação dos ácidos nucléicos, principalmente no caso de certos tipos de câncer ou após tratamentos anticâncer, distúrbios metabólicos genéticos, como síndrome de Lesch-Nyhan, psoríase) ou por excreção diminuída (insuficiência renal, medicamentos como diuréticos). No caso da pré-eclâmpsia, o ácido úrico sérico pode ser aumentado devido a ambos os mecanismos. A diminuição do ácido úrico sérico é mais incomum. Pode ocorrer, por exemplo, na eliminação renal prejudicada, como na síndrome de Fanconi ou na doença de Hodgkin.
Quando a concentração de ácido úrico é anormalmente alta nas urinas, existe o risco de formação de cálculos.
Na prática, a determinação do ácido úrico no soro é indicada para ajudar a diagnosticar a gota, para o acompanhamento de pacientes sob radiação ou quimioterapia e, às vezes, para ajudar a diagnosticar pré-eclâmpsia. A determinação do ácido úrico nas urinas é indicada para ajudar a diagnosticar a gota e na prevenção de cálculos renais recorrentes.

☞LIMITAÇÃO DE USO

O ensaio quantitativo de ácido úrico sozinho não pode ser usado para diagnosticar uma doença ou uma patologia específica.
Os resultados devem ser interpretados em conjunto com outros resultados de testes de diagnóstico, achados clínicos e histórico médico do paciente.

☞MÉTODO & PRINCÍPIO [4]

Enzimática / PAP - Ponto final.

$$\text{Ácido úrico} + 2H_2O + O_2 \xrightarrow{\text{Uricase}} \text{Alantoína} + CO_2 + H_2O_2$$

$$2H_2O_2 + \text{4-AAP} + \text{EHSPT} \xrightarrow{\text{Peroxidase}} \text{Quinoneimina} + 4H_2O$$

EHSPT = N-etil-N-(2-hidroxi-3-sulfopropil) m-toluidina
4-AAP = amino-4-antipirina

☞COMPOSIÇÃO

Reagente : R

Tampão pH 7.00 (20-25°C)			
EHSPT		0.72	mmol/L
Amino-4-antipirina		0.37	mmol/L
Uricase	≥	150	U/L
Peroxidase	≥	12 000	U/L
Azida de sódio	<	0.1	% (p/p)

Padrão: Std (Ref : AUML-0427/0497/0507/0707)

Ácido úrico		6	mg/dL
		357	µmol/L
Azida de sódio	<	0.5	% (p/p)

MATERIAIS NECESSÁRIOS MAS NÃO FORNECIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solução salina normal (NaCl 9 g/L).
- Analisador automáticos ou semi-automáticos.
- Equipamento geral de laboratório (por exemplo, pipeta ...).
- Não utilize materiais que não são necessários, tal como indicado acima.

☞PRECAUÇÕES DE USO E AVISOS

- Consulte a ficha de dados de segurança (SDS) para obter um manuseio adequado.
- O reagente R e o padrão Std contém azida de sódio que pode reagir com o chumbo ou cobre das canalizações formando azidas metálicas explosivas. Ao manusear estes reagentes lave as mãos sempre com grandes quantidades de água para evitar a produção de azida.
- Utilize as precauções normais e siga as boas práticas de laboratório.
- Utilizar material de laboratório limpo ou destinado a uma única utilização de modo a evitar qualquer contaminação.

CHOLINESTERASE

Références/References/ Referencias/ Referências:
CHES-0053

Composition du coffret/ Kit composition/ Composición del kit/ Conteúdo da embalagem :
R1 16 x 3 mL + R2 4 x 1,5 mL

PIT-CHES-4-v18 (07/2020)

CE

Français - FR

USAGE PRÉVU
ELITech Clinical Systems CHOLINESTERASE est un réactif de diagnostic *in vitro*, destiné au dosage quantitatif de de la cholinestérase dans les échantillons de sérum humains.

SIGNIFICATION CLINIQUE (1,2,3)
La cholinestérase sérique (ChE) (pseudocholinestérase ou cholinestérase II, EC3.1.1.8) est principalement retrouvée dans le foie mais aussi dans la substance blanche du cerveau, le pancréas, le cœur et le sérum. Son rôle biologique est inconnu. Le dosage de la cholinestérase sert d'indicateur d'une éventuelle intoxication par inhalation ou contact avec la peau par des composés organophosphorés (dont certains insecticides et gaz neurologiques); dans les maladies du foie ; ou avant une anesthésie avec la succinylcholine afin d'éliminer un déficit congénital de ces enzymes qui entraînerait une apnée prolongée due à la dégradation lente du myorelaxant.
Une chute de 15-25 % se rencontre lors d'une intoxication faible, de 25-35 % lors d'une intoxication modérée, de 30 à 50 % lors d'une intoxication sévère par des composés organophosphorés, mais aussi chez des patients avec une hépatite chronique ou en phase aiguë. Une chute de 50 à 70 % se rencontre lors de cirrhose, de cancer avec métastases hépatiques.

MÉTHODE
Enzymatique. Cinétique.

PRINCIPE (4)
Sous l'action catalytique de la cholinestérase, l'iodure de butyrylthiocholine est hydrolysé en iodure de thiocholine :

$$\text{Butyrylthiocholine} + H_2O \xrightarrow{\textit{Cholinesterase}} \text{Iodure de thiocholine} + \text{Butyrate}$$

Les thiols réagissent avec le 5,5'-Dithiobis-(2-nitrobenzoate) ou DNTB en donnant un produit coloré jaune, le 2-Nitrobenzoate-5-mercaptothiocholine :

Thiocholine +5,5'-Dithiobis-(2-nitrobenzoate) ⟶ 2-Nitrobenzoate-5-mercaptothiocholine + 5-Thio-2-nitrobenzoate

COMPOSITION
Réactif 1 : R1

Tampon phosphate, pH 7,40	52	mmol/L
5,5'-Dithio-bis-2-nitrobenzoate	0,24	mmol/L

Réactif 2 : R2

Iodure de S-butyrylthiocholine	218	mmol/L

MATÉRIELS REQUIS MAIS NON FOURNIS
- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Equipement général de laboratoire.
- Ne pas utiliser de matériel ne figurant pas ci-dessus.

☞AVERTISSEMENTS ET PRÉCAUTIONS
- Ce dispositif de diagnostic *in vitro* est uniquement destiné aux professionnels.
- Le réactif R2 est classé comme dangereux (iodure de (propylcarbonylthioéthyl)triméthylammonium) :

- Le réactif R1 contient 2-méthyl-2H-isothiazole-3-one, chlorhydrate. Peut produire une réaction allergique.
- Se procurer la fiche de données de sécurité (FDS) avant manipulation pour une utilisation appropriée.
- Respecter les précautions d'usage et les bonnes pratiques de laboratoire.
- Utiliser du matériel de laboratoire propre ou à usage unique afin d'éviter toute contamination.
- Ne pas échanger les flacons réactifs des différents kits.

STABILITÉS
Stocker à 2-8 °C et à l'abri de la lumière. Ne pas congeler.
Ne pas utiliser après la date d'expiration indiquée sur les étiquettes des flacons.
Stabilité à bord :
La stabilité à bord est spécifique à chaque automate. (Se réferer au § PERFORMANCES).

☞PRÉPARATION
- Réactif de travail 1 :
Dissoudre le réactif R1 avec de l'eau distillée comme indiqué sur le flacon de réactif 1.
Attendre environ 15 minutes avant utilisation.
Stabilité : Se réferer au § PERFORMANCES/Stabilité à bord.

- Réactif de travail 2 :
Dissoudre le réactif R2 avec de l'eau distillée comme indiqué sur le flacon de réactif 2.
Attendre environ 15 minutes avant utilisation.
Stabilité : Se réferer au § PERFORMANCES/Stabilité à bord.

DÉTÉRIORATION DU PRODUIT
- Le produit doit être limpide. Tout trouble serait le signe d'une détérioration du produit.
- Ne pas utiliser le produit s'il y a des signes évidents de détérioration biologique, chimique ou physique.
- Ne pas utiliser le produit si les dommages de l'emballage peuvent avoir un effet sur les performances du produit (fuites).

ÉCHANTILLONS (2,3)
Echantillons requis
- Sérum
- Ne pas utiliser d'autres échantillons.

Avertissements et précautions
Selon les Bonnes Pratiques de Laboratoire, tout prélèvement devrait être réalisé avant l'administration de médicaments.
Stockage et stabilité
Le sérum est stable jusqu'à 6 heures à température ambiante, une semaine à 4 °C et 6 mois congelés à -70 °C.

VALEURS DE RÉFÉRENCE (5,6)
à 37 °C
- Enfants, hommes et femmes (> 40 ans) :
5320-12920 U/L
- Femmes de 16 à 39 ans, non enceintes et ne prenant pas de contraceptifs oraux :
4260-11250 U/L
- Femmes de 16 à 39 ans, enceintes ou sous contraceptifs oraux:
3650-9120 U/L

Remarque : Il est recommandé à chaque laboratoire d'établir et de maintenir ses propres valeurs de référence par rapport à la population visée. Les valeurs ci-dessus ne sont données qu'à titre indicatif.

PROCÉDURE
Procédure manuelle

Longueur d'onde : 405 nm
Trajet optique : 1 cm
Ratio échantillon/réactif : 1:155
Température: 37 °C
Lire contre l'eau distillée.

Réactif de travail R1	1500 µL
Echantillon	10 µL
Réactif de travail R2	50 µL

Mélanger et mesurer la variation d'absorbance toutes les 30 secondes (ΔA/30 s.) pendant 90 secondes.

Procédure sur automate
Ces réactifs peuvent être utilisés sur différents automates. Pour les automates ELITech Selectra, les applications validées sont disponibles sur demande.

CALCUL
Activité (U/L)= ΔA/30 s. x 23460

Facteur de conversion : U/L x 0,0167 = µkat/L

CALIBRATION
Pour la calibration, le calibrant multiparamétrique ELICAL 2 doit être utilisé. Sa valeur est traçable par rapport à la méthode manuelle.

Fréquence de calibration : La fréquence de calibration est spécifique à chaque automate (se référer au § PERFORMANCES).

CONTRÔLE QUALITÉ
Pour vérifier l'exactitude des résultats, les sérums de contrôle ELITROL I et ELITROL II doivent être utilisés. Ces contrôles doivent être effectués et validés avant que les échantillons des patients soient testés. La fréquence de contrôle doit être au moins une fois par jour, après chaque calibration et doit être adaptée aux procédures de contrôle de qualité de chaque laboratoire et aux exigences réglementaires. Les résultats doivent être dans les intervalles définis. Si les valeurs se situent en dehors des plages définies, chaque laboratoire doit prendre des mesures correctives. Les matériaux de contrôle qualité doivent être utilisés conformément aux directives locales.

TRAITEMENT DES DÉCHETS
L'élimination de tous les déchets doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales.

PERFORMANCES à 37 °C sur ELITech Clinical Systems Selectra E
- Domaine de mesure
Le réactif est linéaire de 1200 à 8000 U/L.

- Limite de détection (7)
Déterminée selon le protocole recommandé par la SFBC, la limite de détection est égale à 5 U/L.

- Précision

	Reproductibilité intrasérielle			Reproductibilité intersérielle		
	n	Moy. (U/L)	CV %	n	Moy. (U/L)	CV %
Niveau bas	20	1532	0,9	20	1344	3,5
Niveau moyen	20	4227	0,8	20	4412	3,6
Niveau élevé	20	7929	1,6	20	7469	3,4

- Corrélation
Une étude comparative a été réalisée entre la méthode ELITech et un autre réactif du commerce (méthode Butyrylthiocholine) sur 60 échantillons sériques.
Les valeurs s'échelonnent dans le domaine de mesure.
Les paramètres de la droite de régression pour les échantillons sériques sont les suivants :
Coefficient de corrélation : (r) = 0,9991
Droite de régression linéaire : y = 1,0119 x - 36,57 U/L

- Limitations/Interférences(7,8)
- Ne pas communiquer de résultats en dehors du domaine de mesure testé.

- Selon les recommandations de la SFBC, des tests ont été réalisés pour déterminer le niveau d'interférence de différents composés :
Bilirubine conjuguée : Biais négatif à partir de 17 mg/dL (300 µmol/L).
Bilirubine non-conjuguée : Biais négatif à partir de 30 mg/dL (513 µmol/L).
Hémoglobine : Aucune interférence significative jusqu'à 500 mg/dL (5 g/L).
Turbidité : Aucune interférence significative jusqu'à 614 mg/dL (6,94 mmol/L) équivalent triglycérides.

- Dans des cas très rares, les gammapathies monoclonales (myélome multiple), en particulier de type IgM (Macroglobulinémie de Waldenström) peuvent être à l'origine de résultats peu fiables.(9)

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.(10-11)

- Pour le diagnostic, les résultats doivent toujours être confrontés aux résultats d'autres tests diagnostiques, aux examens cliniques, et aux données de l'anamnèse du patient.

☞- Stabilité à bord / fréquence de calibration
Stabilité à bord : 14 jours pour un réactif de travail nouvellement préparé.
Fréquence de calibration : 14 jours pour un réactif de travail nouvellement préparé.
Une nouvelle calibration doit être effectuée après chaque changement de lot de réactif, lorsque les résultats du ou des contrôles de qualité sont hors de l'intervalle établi, et après une opération de maintenance.

Ces performances ont été définies sur un automate ELITech Selectra E. Les résultats peuvent varier si le réactif est utilisé sur un automate différent ou en méthode manuelle.
Les performances obtenues à partir d'applications non validées par ELITech ne peuvent être garanties et doivent être définies par l'utilisateur.

English - EN

INTENDED USE
ELITech Clinical Systems CHOLINESTERASE is an *in vitro* diagnostic reagent intended for the quantitative determination of cholinesterase in human serum samples.

CLINICAL SIGNIFICANCE (1,2,3)
Serum cholinesterase (ChE) (pseudocholinesterase or cholinesterase II, EC3.1.1.8) is found primarily in the liver but also in the white matter of the brain, pancreas, heart and serum. Its biological role is unknown. Serum ChE levels can be assayed as an indicator of liver potential poisoning by inhalation or contact with skin with some organophosphorus compounds (including some insectisides or neurological gases) ; in liver diseases; or before an anesthesia with succinylcholine so as to eliminate a congenital deficiency of these enzymes which could lead to a prolonged apnea due to a slow degradation of myorelaxant.
A 15-25 % decrease is observed in slight poisoning, a 25-35 % decrease in moderate poisononig, a 30-50 % decrease in serious poisoning by organophosphorus compounds, but also in patients with acute or chronic hepatitis. A 50-70 % decrease occurs in those with advanced cirrhosis and carcinoma metastases to the liver.

METHOD
Enzymatic. Kinetic.

PRINCIPLE (4)
Under the catalytic action of cholinesterase, butyrylthiocholine iodide is hydrolised in thiocholine iodide :

$$\text{Butyrylthiocholine} + H_2O \xrightarrow{\textit{Cholinesterase}} \text{Thiocholine iodide} + \text{Butyrate}$$

Thiols react with 5,5'-Dithiobis-(2-nitrobenzoate) or DNTB giving a yellow compound, 2-Nitrobenzoate-5-mercaptothiocholine :

Thiocholine+5,-5'-Dithio-bis-(2-nitrobenzoate) ⟶ 2-Nitrobenzoate-5-mercaptothiocholine + 5-Thio-2-nitrobenzoate

COMPOSITION
Reagent 1: R1

Phosphate buffer, pH 7.40	52	mmol/L
5,-5'-Dithiobis-2-nitrobenzoate	0.24	mmol/L

Reagent 2 : R2

S-Butyrylthiocholine iodide	218	mmol/L

MATERIALS REQUIRED BUT NOT PROVIDED
- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- General Laboratory equipment.
- Do not use materials that are not required as indicated above.

☞WARNINGS AND PRECAUTIONS
- This *in vitro* diagnostic device is for professional use only.
- The reagent R2 is classified as hazardous (propylcarbonylthioethyl)trimethylammonium iodide) :

- Reagent R1 contains 2-methyl-2H-isothiazol-3-one hydrochloride. May produce an allergic reaction.
- Obtain Safety data sheet (SDS) before use for a proper handling.
- Take normal precautions and adhere to good laboratory practice.
- Use clean or single use laboratory equipment only to avoid contamination.
- Do not interchange reagent vials from different kits.

STABILITIES
Store at 2-8 °C and protect from light. Do not freeze.
Do not use after expiration dates indicated on the vial labels.
On board stability :
The on-board stability is specific for each analyzer. (Refer to § PERFORMANCE DATA).

☞PREPARATION
- Working reagent 1
Dissolve reagent R1 with the suitable volume of distilled water as stated on the label.
Wait about 15 minutes before use.
Stability : Refer to § PERFORMANCE DATA/On board stability

- Working reagent 2
Dissolve reagent R2 with the suitable volume of distilled water as stated on the label.
Wait about 15 minutes before use.
Stability : Refer to § PERFORMANCE DATA/On board stability

PRODUCT DETERIORATION
- The product should be clear. Cloudiness would indicate deterioration.
- Do not use the product if there is visible evidence of biological, chemical or physical deterioration.
- Do not use the product if the damages of packaging might have an effect on the product performances (leakages).

SAMPLES (2,3)
Specimen
- Serum
- Do not use other specimens.

Warnings and precautions
According to Good Laboratory Practice, sampling should be performed prior to the administration of drugs.
Storage
Serum is stable up to 6 hours at room temperature, one week at 4 °C and 6 months frozen at -70 °C.

REFERENCE VALUES (5,6)

at 37 ° C

- Children, males and females (> 40 years) :
5320 -12920 U/L
- Females 16-39 years, not pregnant, not taking hormonal contraceptives :
4260 - 11250 U/L
- Females 16-39 years, pregnant or taking hormonal contraceptives :
3650 - 9120 U/L

Note : *The quoted range should serve as a guide only. It is recommended that each laboratory verifies this range or establishes a reference interval for the intended population.*

PROCEDURE

Manual Procedure

Wavelength : 405 nm
Optical path : 1 cm
Sample/ Reagent ratio : 1:155
Temperature: 37 °C
Read against distilled water.

Working reagent R1	1500 µL
Sample	10 µL
Working reagent R2	50 µL

Mix and measure the change of absorbance every 30 seconds (ΔA/30 s.) during 90 seconds.

Automatic Procedure

These reagents may be used in several automatic analyzers. For ELITech Selectra Analyzers, validated applications are available on request.

CALCULATION

Activity (U/L)= ΔA/30 s. x 23460

Conversion factor : U/L x 0.0167 = µkat/L

CALIBRATION

For calibration, multiparametric calibrator ELICAL 2 must be used. Its value is traceable to the manual measurement.

Calibration frequency : The calibration is specific for each analyzer. (Refer to § PERFORMANCE DATA).

QUALITY CONTROL

To check the accuracy of assays, control sera such as ELITROL I and ELITROL II should be used. These controls must be performed and validated before the patient samples are assayed. The control frequency must be at least once a day, after each calibration and should be adapted to Quality Control procedures of each laboratory and the regulatory requirements. Results should be within the defined ranges. If values fall outside of the defined ranges, each laboratory should take corrective measures. Quality control materials should be used in accordance with local guidelines.

WASTE MANAGEMENT

Disposal of all waste material should be in accordance with local, state and federal regulatory requirements

PERFORMANCE DATA at 37 °C on ELITech Clinical Systems Selectra E

- Measuring range

The reagent is linear from 1200 to 8000 U/L.

- Limit of Detection (7)

Determined according to SFBC protocol, the detection limit is equal to 5 U/L.

- Precision

	Within-run reproducibility			Between-run reproducibility		
	n	Mean (U/L)	CV %	n	Mean (U/L)	CV %
Low level	20	1532	0.9	20	1344	3.5
Medium level	20	4227	0.8	20	4412	3.6
High level	20	7929	1.6	20	7469	3.4

- Correlation

A comparative study has been performed between ELITech method and another commercial reagent (Butyrylthiocholine method) on 60 human serum samples.
The values are distributed in the measuring range.
The parameters of the linear regressions are as follows
Correlation coefficient : (r) = 0.9991
Linear regression : y = 1.0119 x - 36.57 U/L

- Limitations/Interferences (7,8)

- Do not report results outside of the usable range.
- According to SFBC recommendations, studies have been performed to determine the level of interference from different compound :
Conjugated Bilirubin : Negative bias from 17 mg/dL (300 µmol/L).
Unconjugated Bilirubin : Negative bias from 30 mg/dL (513 µmol/L).
Haemoglobin : No significant interference up to 500 mg/dL (5 g/L).
Turbidity : No significant interference up to 614 mg/dL (6.94 mmol/L) Triglycérides equivalent.

- In very rare cases, monoclonal gammopathies (multiple myeloma), in particular IgM type (Waldenstrom's macroglobulinemia) can cause unreliable results.(9)

- Many other substances and drugs may interfere. Some of them are listed in Young.(10,11)

- The results of this assay should only be interpreted in conjunction with other diagnostic test results, clinical findings and the patient's medical history.

☞- On board stability/Calibration frequency

On Board Stability: 14 days for a freshly prepared working reagent
Calibration frequency: 14 days for a freshly prepared working reagent
Recalibrate when reagent lots change, when quality control results fall outside the established range, and after a maintenance operation.

These performances have been obtained using ELITech Selectra E analyzer. Results may vary if a different instrument or a manual procedure is used. The performances of applications not validated by ELITech are not warranted and must be defined by the user.

Español - ES

USO PREVISTO

ELITech Clinical Systems CHOLINESTERASE es un reactivo de diagnóstico *in vitro* diseñado para la determinación cuantitativa de la colinesterasa en muestras de suero humano.

SIGNIFICADO CLÍNICO (1,2,3)

La colinesterasa sérica (CE) (pseudocolinesterasa o colinesterasa II, EC3.1.1.8) se encuentra principalmente en el hígado, pero también en la sustancia blanca del cerebro, el páncreas, el corazón y el suero. Su papel biológico es desconocido. La dosificación de la colinesterasa sirve como indicador en una posible intoxicación por inhalación o contacto con la piel por compuestos organofosforados (entre ellos ciertos insecticidas y gases neurológicos); en las enfermedades del hígado; o antes de una anestesia con succinilcolina para descartar un déficit congénito de estas enzimas que podría producir una apnea prolongada debido a la degradación lenta del miorrelajante.
Una caída del 15 al 25% se observa durante una intoxicación leve, del 25 al 35% durante una intoxicación moderada, del 30 al 50% durante una intoxicación grave por compuestos organofosforados, pero también en pacientes con una hepatitis crónica o en fase aguda. Una caída del 50 al 70% se observa en la cirrosis y en el cáncer con metástasis hepáticas.

MÉTODO

Enzimático. Cinético.

PRINCIPIO (4)

Debido a la acción catalítica de la colinesterasa, el yoduro de butirilcolina se hidroliza a yoduro de tiocolina:

$$\text{Butiriltiocolina} + H_2O \xrightarrow{\text{Colinesterasa}} \text{Yoduro de tiocolina} + \text{Butirato}$$

Los tioles reaccionan con el 5,5'-ditiobis-(2-nitrobenzoato) o DNTB dando un producto de color amarillo, el 2-nitrobenzoato-5-mercaptotiocolina:

Tiocolina +5,5'-ditiobis-(2-nitrobenzoato) ⟶ 2-nitrobenzoato-5-mercaptotiocolina + 5-tio-2-nitrobenzoato

COMPOSICIÓN

Reactivo 1 : R1
Tampón fosfato, pH 7,40 52 mmol/L
5,5'-ditio-bis-2-nitrobenzoato 0,24 mmol/L
Reactivo 2 : R2
Yoduro de S-butiriltiocolina 218 mmol/L

MATERIALES REQUERIDOS PERO NO INCLUIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Equipamiento general de laboratorio.
- No utilice materiales que no se requieren, tal como se indica anteriormente.

☞ATENCIÓN Y PRECAUCIONES

- Este dispositivo de diagnóstico *in vitro* está destinado únicamente para uso profesional.
- El reactivo R2 está clasificado como peligroso (ioduro de(propilcarboniltioetil)trimetilamonio) .

- Reactivo R1 contiene 2-metil-2H-isotiazol-3-ona, clorhidrato. Puede provocar una reacción alérgica.
- Obtenga la Hoja de datos de seguridad (FDS) previo a la utilización para un manejo adecuado.
- Tome las precauciones normales y respete las buenas prácticas de laboratorio.
- Para evitar contaminaciones utilizar equipo nuevo o completamente limpio.
- No intercambie los frascos de reactivos de diferentes kits.

ESTABILIDADES

Conservar a 2-8 °C y protegidos de la luz. No congelar.
No utilice después de la fecha de caducidad indicada en la etiqueta de los frascos.
Estabilidad en el equipo:
La estabilidad es específica para cada equipo. (Referirse al § DATOS DE RENDIMIENTO).

☞PREPARACIÓN

Reactivo de trabajo 1 :
Disolver el reactivo R1 con agua destilada como se indica en el frasco de reactivo 1.
Esperar unos 15 minutos antes de usarlo.
Estabilidad: Referirse al § DATOS DE RENDIMIENTO/ Estabilidad en el equipo.

Reactivo de trabajo 2 :
Disolver el reactivo R2 con agua destilada como se indica en el frasco de reactivo 2.
Esperar unos 15 minutos antes de usarlo.
Estabilidad: Referirse al § DATOS DE RENDIMIENTO/ Estabilidad en el equipo.

DETERIORACIÓN DEL PRODUCTO

- El producto debe ser claro. Turbidez indicaría deterioro.
- No utilice el producto si este presenta signos evidentes de deterioración biológica, química o física.
- No utilice el producto si los daños al embalaje pudiesen tener un efecto sobre el rendimiento del producto (fugas).

MUESTRAS (2,3)

Muestra requeridas
- Suero
- No utilice otras muestras.

Advertencias y precauciones
De acuerdo con las buenas prácticas de laboratorio, la toma de muestra debe ser llevada a cabo antes de la administración de medicamentos.
Conservación y estabilidad
El suero es estable hasta 6 horas a temperatura ambiente, una semana a 4 °C y 6 meses congelado a -70 °C.

VALORES DE REFERENCIA (5,6)

a 37 °C
- Niños, hombres y mujeres (> 40 años):
5320-12920 U/L
- Mujeres de 16 a 39 años, no embarazadas y que no toman anticonceptivos orales:
4260-11250 U/L
- Mujeres de 16 a 39 años, embarazadas o que toman anticonceptivos orales:
3650-9120 U/L

Nota : *Se recomienda que cada laboratorio establezca y mantenga sus propios valores de referencia con respecto a la poblacion destinataria. Los datos aquí proporcionados son únicamente una indicación.*

PROCEDIMIENTO

Procedimiento manual

Longitud de onda : 405 nm
Trayectoria óptica : 1 cm
Ratio muestra/reactivo : 1:155
Temperatura: 37 °C
Leer contra agua destilada.

Reactivo de trabajo R1	1500 µL
Muestra	10 µL
Reactivo de trabajo R2	50 µL

Mezcle y mida el cambio de absorbancia cada 30 segundos (ΔA/30 s.) durante 90 segundos.

Procedimiento automático

Estos reactivos pueden ser utilizados en varios equipos. Para los equipos ELITech Selectra, las aplicaciones validadas están disponibles sobre pedido.

CÁLCULO

Actividad (U/L)= ΔA/30 s. x 23460

Factor de conversión : U/L x 0,0167 = µkat/L

CALIBRACIÓN

Para la calibración, el calibrador multiparametrico ELICAL 2 debe ser utilizado. El valor es trazable a la medición manual.

Frecuencia de calibración : la frecuencia de calibración es específica para cada equipo (referirse al § DATOS DE RENDIMIENTO).

CONTROL DE CALIDAD

Para asegurar la exactitud de los resultados, sueros de control tales como ELITROL I y ELITROL II deben ser utilizados. Los controles deben ser realizados y validados antes de que las muestras del paciente sean probadas. La frecuencia de control debe ser al menos una vez al día, después de cada calibración y debe ser adaptada a los procedimientos de control de calidad de cada laboratorio y las exigencias regulatorias.
Los resultados deben estar dentro del rango analítico definido. Si los valores quedan fuera del rango analítico definido, cada laboratorio debera de tomar las medidas correctivas. Los materiales de control de calidad deben ser usados conforme a las directivas locales.

TRATAMIENTO DE LOS RESIDUOS

Todos los materiales de desecho deben eliminarse de acuerdo con los requisitos reglamentarios locales, estatales y federales.

DATOS DE RENDIMIENTO a 37 °C en equipo ELITech Clinical Systems Selectra E

- Rango analítico
El reactivo es lineal de 1200 a 8000 U/L.

- Límite de detección (7)
Se determinó de acuerdo al protocolo de SFBC, el límite de detección es igual a 5 U/L.

- Precisión

	Reproducibilidad intraserial			Reproducibilidad interserial		
	n	Media (U/L)	CV %	n	Media (U/L)	CV %
Nivel bajo	20	1532	0,9	20	1344	3,5
Nivel medio	20	4227	0,8	20	4412	3,6
Nivel elevado	20	7929	1,6	20	7469	3,4

- Correlación
Un estudio comparativo fue llevado a cabo entre el método Elitech y otro método comercial (método de la butiriltiocolina) en 60 muestras de suero.
Los valores se distribuyen en el rango analítico.
Los parámetros de la regresión lineal son los siguientes :
Coeficiente de correlación : (r) = 0,9991
Regresión lineal : y = 1,0119 x - 36,57 U/L

- Limitaciones/Interferencias (7,8)
- No reporte resultados fuera del rango analítico.
- De acuerdo con las recomendaciones de SFBC, se han realizado algunos estudios para determinar el nivel de interferencia de diferentes componentes :
Bilirrubina conjugada : Desviación negativa desde 17 mg/dL (300 µmol/L).
Bilirrubina no conjugada : Desviación negativa desde 30 mg/dL (513 µmol/L).
Hemoglobina : No hay interferencia significativa hasta 500 mg/dL (5 g/L).
Turbidez : No hay interferencia significativa hasta 614 mg/dL (6,94 mmol/L) equivalente triglicéridos.

- En casos muy raros, las gammapatías monoclonales (mieloma múltiple), en particular el tipo IgM (macroglobulinemia de Waldenstrom) pueden producir resultados poco confiables.(9)

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en Young.(10-11)

- Los resultados de este ensayo deben ser interpretados en conjunción con otros resultados de exámenes de diagnóstico, resultados clínicos, así como el historial médico del paciente.

☞- Estabilidad en el equipo / frecuencia de calibración
Estabilidad en el equipo : 14 días para un reactivo de trabajo recién preparado.
Frecuencia de calibración : 14 días para un reactivo de trabajo recién preparado.
Se debe ejecutar una nueva calibración si se cambia de lote de reactivo, si los resultados de uno o varios controles de calidad exceden el intervalo establecido y después de una operación de mantenimiento.

El rendimiento se ha obtenido utilizando el equipo ELITech Selectra E. Los resultados pueden variar si se utiliza un instrumento diferente o un procedimiento manual.
El rendimiento obtenido a partir de aplicaciones no validadas por ELITech no se garantizan y deben ser definidas por el utilizador.

Português – PT

UTILIZAÇÃO PREVISTA

ELITech Clinical Systems CHOLINESTERASE é um reagente para diagnóstico *in vitro* destinado à determinação quantitativa de colinesterase em amostras de soro humano.

SIGNIFICADO CLÍNICO (1,2,3)

Colinesterase Sérica (ChE) (pseudocolinesterase ou colinesterase II, EC3.1.1.8) é encontrada principalmente no fígado, mas também na matéria branca do cérebro, pâncreas, coração e soro. O seu papel biológico é desconhecido. Os níveis séricos de ChE podem ser avaliados como um indicador do potencial envenenamento do fígado por inalação ou contato com a pelo com alguns compostos organofosforados (incluindo alguns inseticidas ou gases neurológicos); em doenças hepáticas; ou antes de uma anestesia com succinilcolina, de modo a eliminar uma deficiência congénita dessas enzimas que poderiam conduzir a uma apneia prolongada devido a uma lenta degradação do miorrelaxante.
Uma redução de 15-25% pode ser observada na intoxicação ligeira, uma redução de 25-35% na intoxicação moderada, uma redução de 30-50% nas intoxicações graves por compostos organofosforados, mas também em pacientes com hepatite aguda ou crónica. Uma redução de 50-70% ocorre em pacientes com cirrose avançada e carcinoma e metástases para o fígado.

MÉTODO

Enzimático. Cinético.

PRINCÍPIO (4)

Sob a ação catalítica de colinesterase, iodeto Butiriltiocolina é hidrolisado em Iodeto de Tiocolina.

$$\text{Butiriltiocolina} + H_2O \xrightarrow{\text{Colinesterase}} \text{Iodeto de Tiocolina} + \text{Butirato}$$

Os tióis reagem com 5,5' –ditiobis- (2-nitrobenzoato) ou DNTB dando um composto amarelo, 2-nitrobenzoato-5-mercaptotiocolina.

Tiocolina + 5, -5' –Ditio-bis-(2-nitrobenzoato) ⟶ 2-nitrobenzoato-5-mercaptotiocolina + 5-tio-2-nitrobenzoato

COMPOSIÇÃO

Reactivo 1 : R1
Tampão fosfato, pH 7,40 52 mmol/L
5, -5' –ditiobis-2-nitrobenzoato 0,24 mmol/L
Reactivo 2 : R2
Iodeto de S-butiriltiocolina 218 mmol/L

MATERIAIS NECESSÁRIO MAS NÃO FORNECIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Equipamento geral de laboratório.
- Não utilize materiais que não são necessários, tal como indicado acima.

☞AVISO E PRECAUÇÕES

- Este dispositivo de diagnóstico *in vitro* é apenas para uso profissional.
- A reagente R2 é classificado como perigoso (iodet de(propilcarboniltioetil)trimetilamónio).

- A reagente R1 contém 2-metil-2H-isotiazole-3-ona cloridrato. Pode provocar uma reacção alérgica.
- Antes de utilizar, obtenha a ficha de dados de segurança (FDS) para um manuseio adequado.
- Utilize as precauções normais e siga as boas práticas de laboratório.
- Utilizar material de laboratório limpo ou destinado a uma única utilização de modo a evitar qualquer contaminação.
- Não trocar os frascos de reagentes de diferentes kits.

ESTABILIDADES

Conservar a 2-8 °C e ao abrigo da luz. Não congelar
Não utilizar após as datas de validade indicadas nos rótulos dos frascos.
Estabilidade em equipamento:
A estabilidade a bordo é específica a cada autómato (Consultar § DESEMPENHO)

☞PREPARAÇÃO

- Reagente de Trabalho 1
Dissolver o reagente R1 com o volume adequado de água destilada como indicado no rótulo R1.
Espere cerca de 15 minutos antes da utilização.
Estabilidade : Consultar § DESEMPENHO/ Estabilidade a bordo.

- Reagente de Trabalho 2 :
Dissolver o reagente R2 com o volume adequado de água destilada como indicado no rótulo R2.
Espere cerca de 15 minutos antes da utilização.
Estabilidade : Consultar § DESEMPENHO/ Estabilidade a bordo.

DETERIORAÇÃO DO PRODUTO

- O produto deve ser clara. Qualquer turbidez seria sinal de deterioração do produto.
- Não use o produto se houver evidência visível de deterioração física, biológica ou química.
- Não utilizar o produto caso haja danos na embalagem que possam causar algum efeito sobre o desempenho do produto (vazamentos).

AMOSTRAS (2,3)

Amostras
- Soro.
- Não utilize outras amostras.

Aviso e precauções
- De acordo com as boas praticas de laboratório, a amostragem deve ser executada antes da administração de drogas.

Armazenamento e estabilidade
O soro é estável até 6 horas à temperatura ambiente, uma semana a 4 ° C e 6 meses congeladas a -70 ° C.

VALORES DE REFERÊNCIAS (5,6)

a 37 °C
- Crianças, homens e mulheres (> 40 anos):
5320-12920 U/L
- Mulheres 16-39 anos, que não estejam grávidas, e não estejam tomando contraceptivos hormonais:
4260-11250 U/L
- Mulheres 16-39 anos, grávidas ou tomando contraceptivos hormonais:
3650-9120 U/L

Observação: Recomenda-se que cada laboratório estabeleça e mantenha os seus próprios valores de referência para a população desejada. Os valores anteriores são apenas fornecidos a título indicativo.

PROCEDIMENTO

Procedimento manual

Comprimento de onda : 405 nm
Percurso óptico : 1 cm
Relação Amostra/Reagente : 1:155
Temperatura: 37 °C
Ler comparando com o água destilada

Reagente de trabalho R1	1500 µL
Amostra	10 µL
Reagente de trabalho R2	50 µL

Misture e meça a alteração de absorbância a cada 30 segundos (ΔA / 30 s.), durante 90 segundos.

Procedimento automático

Estes reagentes podem ser utilizados em vários analisadores automáticos. Para os analisadores ELITech Selectra, as aplicações validadas estão disponíveis mediante solicitação.

CÁLCULO

Atividad (U/L)= ΔA/30 s. x 23460

Fator de conversão: U/L x 0,0167 = µkat/L

CALIBRAÇÃO

Para a calibração, deve ser utilizado o calibrador multiparamétrico ELICAL 2. O seu valor é rastreável em relação ao método manual.

Frequência de calibração : A frequência de calibração é especif ca a cada equipamento (consultar § DESEMPENHO).

CONTROLE DE QUALIDADE

Para verificar a exatidão dos resultados, os soros controle, tal como ELITROL I e ELITROL II devem ser usados. Esses controles devem ser realizados e validados antes das amostras dos pacientes serem testadas. A frequência do controle deve ser efetuada, pelo menos, uma vez por dia, após cada calibração e deve ser adaptada aos procedimentos de controle de qualidade de cada laboratório e aos requisitos regulamentares. Os resultados devem estar dentro dos limites definidos. Se os valores se estiverem fora dos limites definidos, cada laboratório deve tomar as devidas medidas corretivas. Os controles de qualidade devem ser utilizados de acordo com os procedimentos habituais.

TRATAMENTO DOS RESÍDUOS

Todos os resíduos devem ser eliminados de acordo com as exigências locais de regulamentação local, estadual e federal.

DESEMPENHO a 37 °C no ELITech Clinical Systems Selectra E

- Precisão de medição
O reagente é linear de 1200 a 8000 U/L.

- Limite de detecção(7)
Determinado de acordo com o protocolo recomendado pela SFBC, o limite de detecção é igual a 5 U/L.

- Precisão

	Reprodutibilidade intrasérie			Reprodutibilidade intersérie		
	n	Media (U/L)	CV %	n	Media (U/L)	CV %
Nível baixo	20	1532	0,9	20	1344	3,5
Nível médio	20	4227	0,8	20	4412	3,6
Nível elevado	20	7929	1,6	20	7469	3,4

- Correlação
Foi realizado um estudo comparativo entre o reagente Elitech e um outro reagente disponível no mercado (método butiriltiocolina) em 60 amostras séricas.
Os valores são distribuídos no intervalo de medição.
Os parâmetros da linha de regressão são os seguintes :
Coeficiente de correlação : (r) = 0,9991
Linha de regressão: y = 1,0119 x - 36,57 U/L

- Limitações/Interferências (7,8)
- Não relatam resultados fora do alcance útil.

- Segundo as recomendações da SFBC, foram realizados testes para determinar o nível de interferência de diferentes compostos:
Bilirrubina não conjugada: Desvio negativo a partir de 17 mg/dL (300 µmol/L).
Bilirrubina conjugada: Desvio negativo a partir de 30 mg/dL (513 µmol/L).
Hemoglobina: Nenhuma interferência significativa até 500 mg/dL (5 g/L).
Turvação : Nenhuma interferência significativa até 614 mg/dL equivalente de triglicérides (6,94 mmol/L).

- Em casos muito raros, as gamopatias monoclonais (mieloma múltiplo), em particular, tipo IgM (macroglobulinemia de Waldenstrom) podem causar resultados não confiáveis.(9)

- Muitas outras substâncias e drogas podem interferir. Algumas delas estão listadas em Young (10-11).

- Os resultados deste teste só devem ser interpretados em conjunto com outros resultados de testes de diagnóstico, que constem no historico médico e clínico do paciente

☞- Estabilidade a bordo / frequência de calibração
Estabilidade a bordo: 14 dias para um reagente de trabalho recém preparado.
Frequência de calibração: 14 diaspara um reagente de trabalho recém preparado.
Uma nova calibração deve ser efetuada após cada mudança de lote de reagente, quando os resultados do(s) controle(s) de qualidade estiverem fora do intervalo estabelecido e após uma operação de manutenção.

Estes desempenhos foram obtidos utilizando o analisador ELITech Selectra E. Os resultados podem variar se um instrumento diferente ou um procedimento manual for usado.
Os desempenhos de aplicações não validados pela ELITech não são garantidos e devem ser definidos pelo usuário.

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11. Young, D. S., Effects of drugs on clinical laboratory tests, 4th Ed., AACC Press, (1995).

SYMBOLES/SYMBOLS/ SÍMBOLOS/SÍMBOLOS

- Les symboles utilisés sont décrits dans la norme ISO-15223-1 hormis ceux présentés ci-dessous.
- Symbols used are defined on ISO-15223-1 standard, except those presented below.
- Los símbolos utilizados son descritos en la norma ISO-15223-1 a la excepción de los presentados a continuación.
- Os símbolos utilizados são definidos na norma ISO-15223-1, exceto os apresentados abaixo.

CONT	Contient Content Contiene Conteúdo
R1	Réactif R1 Reagent R1 Reactivo R1 Reagente R1
R2	Réactif R2 Reagent R2 Reactivo R2 Reagente R2
RCNS x mL	Reconstituer avec x mL Reconstitute with x mL Reconstituir con x mL Reconstituir com x mL
CE	Conformité Européenne European Conformity Conformidad Europea Conformidade Europeia

☞: Modification par rapport à la version précédente/Modification from previous version/ Modificación con respecto a la versión anterior/Modificação relativamente à versão anterior

Informação de configuração importante :
O Reagente CHOLESTEROL SL pode ser levemente contaminado pelo MAGNESIUM XB en Selectra ProM e ProXL.
Para evitar a contaminação nestes equipamentos , programe as seguintes incompatibilidades :

Logiciel	Menu	Parametro
TouchPro	Incompatibilidades de Agulha	incompatibilidade/ CHOLESTEROL - MAGNESIUM
Autres	Incompatibilidade de Agulha	CHOLESTEROL: MAGNESIUM

Para outros analisadores Selectra Pro: repita qualquer resultado muito fora do intervalo esperado após programar uma lavagem com agulha.

CÁLCULO

$$\frac{(A)\ \text{Amostra}}{(A)\ \text{Padrão/Calibrador}} \times n$$ n = concentração do padrão/ Calibrador

Fator de conversão: mg/dL x 0.0259 = mmol/L
mg/dL x 0.01 = g/L

CALIBRAÇÃO

Para referências CHSL-0497/0507/0707 : ELICAL 2 ou o padrão Cholesterol Standard 200 mg/dL são rastreáveis relativamente ao método de referência ID-GC-MS (Diluição de Isótopos - Cromatografia Gasosa - Espectrometria de Massa).
Para referências CHSL-0250/0455/0500/0700: ELICAL 2. e é rastreável relativamente ao método de referência ID-GC-MS (Diluição de Isótopos - Cromatografia Gasosa - Espectrometria de Massa).

Frequência de calibração : A frequência de calibração é específica a cada equipamento (consultar § DESEMPENHO).

CONTROLE DE QUALIDADE

Recomenda-se o uso de soros de controle de qualidade, como ELITROL I e ELITROL II, para monitorar o desempenho do ensaio.
Os controles devem ser executados:
- antes de analisar amostras de pacientes,
- pelo menos uma vez por dia,
- após cada calibração,
- e/ou de acordo com os requisitos laboratoriais e regulamentares.

Os resultados devem estar dentro dos intervalos definidos. Se os valores ficarem fora dos intervalos definidos, cada laboratório deve tomar as medidas corretivas necessárias.

TRATAMENTO DOS RESÍDUOS

O descarte de todo material residual deve estar de acordo com os requisitos regulamentares locais, estaduais e federais (consulte a Ficha de dados de segurança (SDS)).

DESEMPENHO

Os desempenhos foram obtidos no Selectra ProM, seguindo as recomendações técnicas do CLSI, sob condições ambientais controladas.

- Precisão de medição
20 - 600 mg/dL (0.52 - 15.52 mmol/L).
As amostras com maiores concentrações devem ser diluídas 1:5 com solução de NaCl 9 g/L e ensaiado novamente. Este procedimento estende a faixa de medição até 3000 mg/dL. (77.59 mmol/L).
Não relatar resultados fora do intervalo de medição.

Para utilizadores do Selectra TouchPro, a função de «diluir» realiza a diluição do amostras automaticamente. Os resultados são tomados em consideração na diluição.

☞- Limite de detecção (LoD) e limite de quantificação (LoQ)
LoD = 1 mg/dL (0.03 mmol/L)
LoQ = 10 mg/dL (0.26 mmol/L)

- Precisão
Dados de imprecisão foram obtidos em 2 analisadores Selectra ProM ao longo de 20 dias (2 corridas por dia, testes realizados em duplicata).
Os resultados representativos são apresentados abaixo.

		Média		Intra-série	Total
	n	mg/dL	mmol/L	CV (%)	
Nível 1	80	115	2.97	1.1	2.1
Nível 2	80	184	4.76	0.7	1.9
Nível 3	80	292	7.55	1.9	2.7

☞- Correlação
Foi realizado um estudo comparativo entre o reagente CHOLESTEROL SL em um analisador Selectra ProM e um sistema semelhante disponível com o certificado CRMLN em 100 amostras de soro humano.
As concentrações da amostra variaram de 20 para 575 mg/dL (0.52 - 14.87 mmol/L).
Os resultados são os seguintes:
Coeficiente de correlação: (r) = 0.999
Regressão linear: y = 1.016 x + 0 mg/dL

☞- Limitações/Interferências
Estudos foram realizados para determinar o nível de interferência de diferentes compostos.
Os seguintes níveis de colesterol total foram testados: 116 e 309 mg/dL.
Uma interferência não significativa é definida por uma recuperação ≤±10% do valor inicial.
Bilirrubina não conjugada: Nenhuma interferência significativa até 6.0 mg/dL (103 µmol/L).
Bilirrubina conjugada: Nenhuma interferência significativa até 5.9 mg/dL (101 µmol/L).
Hemoglobina: Nenhuma interferência significativa até 300 mg/dL.
Turvação: Nenhuma interferência significativa até 614 mg/dL (6.94 mmol/L) equivalente de triglicérides.
Ácido ascórbico: Nenhuma interferência significativa até 4.0 mg/dL.
.Metildopa : Nenhuma interferência significativa até 1.6 mg/dL.
Ácido úrico : Nenhuma interferência significativa até 23.7 mg/dL (1410 µmol/L).
- Não use amostras ictéricas ou hemolisadas.

- Em casos muito raros, as gamopatias monoclonais (mieloma múltiplo), em particular, tipo IgM (macroglobulinemia de Waldenstrom) podem causar resultados não confiáveis.[6]

- Os resultados podem ser falsamente reduzidos em níveis significativos na amostra de NAC (*N*-acetilcisteína), NAPQI (metabólito do acetaminofeno (paracetamol)) ou metamizol.

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young. [7-8].

- Estabilidade a bordo / frequência de calibração
Estabilidade a bordo: 28 dias
Frequência de calibração: 28 dias
Recalibre quando os lotes de reagentes mudarem, quando os resultados do controle de qualidade estiverem fora da faixa estabelecida e após uma operação de manutenção.

Estes desempenhos foram obtidos utilizando o analisador ELITech Selectra ProM. Os resultados podem variar se um instrumento diferente ou um procedimento manual for usado.
Os desempenhos de aplicações não validados pela ELITech não são garantidos e devem ser definidos pelo usuário.

☞DECLARAÇÃO DE INCIDENTE GRAVE

Notifique o fabricante (através do seu distribuidor) e a autoridade competente do Estado-Membro da união europeia em que o usuário e / ou o paciente está estabelecido, de qualquer incidente grave que tenha ocorrido em relação ao dispositivo.
Para outras jurisdições, a declaração de incidente grave deve estar de acordo com os requisitos regulamentares locais, estaduais e federais.
Ao relatar um incidente grave, você fornece informações que podem contribuir para a segurança de dispositivos médicos *in vitro*.

☞ASSISTÊNCIA TÉCNICA

Entre em contato com o seu distribuidor local ou com a ELITech Clinical Systems SAS. (CCsupport@elitechgroup.com).

☞BIBLIOGRAPHIE/BIBLIOGRAPHY BIBLIOGRAFÍA/BIBLIOGRAFIA

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- Os símbolos utilizados são definidos na norma ISO 15223-1, exceto os apresentados abaixo.

CONT	Contient Content Contiene Conteúdo
R	Réactif Reagent Reactivo Reagente
Std	Standard Standard Estándar Padrão
☞	Modification par rapport à la version précédente Modification from previous version Modificación con respecto a la versión anterior Modificação relativamente à versão anterior
CE	Conformité Européenne European Conformity Conformidad Europea Conformidade Europeia

☞Importante Note /Nota importante

- Uniquement pour les réf. **CHSL-0250/0455,** utilisée(s) avec le logiciel Selectra TouchPro.
- voir § PROCEDURE: Risque de contamination

- Only for ref. **CHSL-0250/0455,** used with Selectra TouchPro software.
- see § PROCEDURE: Contamination risk

- Únicamente para la (las) ref. **CHSL-0250/0455,** utilizada(s) con el software Selectra TouchPro.
- vea § PROCEDIMIENTO: Riesgo de contaminación

- Somente para ref. **CHSL-0250/0455,** usado(s) com o Selectra TouchPro.
- verificar § PROCEDIMENTO: Risco de contaminação

CHSL

Cholesterol 0
280 PIT-CHSL

ELITechGroup
EMPOWERING IVD

CHOLESTEROL SL

CHSL

CHSL-0497	R 1 x 100 mL + Std 1 x 5 mL	
CHSL-0507	R 6 x 100 mL + Std 1 x 5 mL	
CHSL-0707	R 4 x 250 mL + Std 1 x 5 mL	
CHSL-0250	R 12 x 20 mL	
CHSL-0455	R 6 x 45 mL	
CHSL-0500	R 6 x 100 mL	
CHSL-0700	R 4 x 250 mL	

CE

PIT-CHSL-4-v27 (02/2021)

Français - FR

☞USAGE PRÉVU

ELITech Clinical Systems CHOLESTEROL SL est un réactif de diagnostic *in vitro*, destiné au dosage quantitatif du cholestérol total dans les échantillons de sérum et de plasma humains sur des automates ou semi-automates.
Le standard est destiné à la calibration du réactif.
Ces dispositifs de diagnostic *in vitro* sont uniquement destinés aux professionnels.

☞SIGNIFICATION CLINIQUE [1-3]

Le cholestérol total dans le sérum est issu de l'alimentation ou est synthétisé de façon endogène, principalement dans les cellules hépatiques et intestinales. Le cholestérol est un composant structurel important des membranes des cellules et organelles. Le cholestérol est également un précurseur des acides biliaires, de la vitamine D et des hormones stéroïdiennes. Le cholestérol, étant une molécule insoluble dans l'eau, circule en étant associé à des lipoprotéines (HDL, LDL, VLDL et chylomicrons).
En pratique le dosage du cholestérol total est effectué pour évaluer la prédisposition des patients aux risques cardiovasculaires dans le cadre du bilan lipidique ainsi que pour le suivi des stratégies thérapeutiques associées. La mesure du cholestérol total est également importante pour l'aide au diagnostic des hyperlipoprotéinémies.

☞LIMITE D'UTILISATION

Le dosage du cholestérol total ne peut être utilisé seul pour diagnostiquer une maladie ou une pathologie spécifique.
Les résultats doivent toujours être confrontés aux résultats d'autres tests diagnostiques, aux examens cliniques, et à l'historique médical du patient.

☞MÉTHODE & PRINCIPE [4]

Enzymatique / PAP - Point final.

$$\text{Cholestérol estérifié} + H_2O \xrightarrow{\text{Cholestérol estérase}} \text{Cholestérol} + \text{Acides gras}$$

$$\text{Cholestérol} + O_2 \xrightarrow{\text{Cholestérol oxydase}} \text{Cholest-4-èn-3-one} + H_2O_2$$

$$2H_2O_2 + \text{Phénol} + \text{4-AAP} \xrightarrow{\text{Peroxydase}} \text{Quinonéimine} + 4H_2O$$

4-AAP = Amino-4-antipyrine

COMPOSITION

Réactif : R

Tampon de Good, pH 6.7			
Phénol		24	mmol/L
Amino-4-antipyrine		0.5	mmol/L
Cholestérol estérase	≥	180	U/L
Cholestérol oxydase	≥	200	U/L
Peroxydase	≥	1 000	U/L
Azide de sodium	<	0.1	% (p/p)

Contient aussi des surfactants et des sels de magnésium pour des performances optimales.
Standard : Std (Ref : CHSL-0497/0507/0707)
Cholestérol 200 mg/dL
5.17 mmol/L

MATÉRIELS REQUIS MAIS NON FOURNIS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solution saline normale (NaCl 9 g/L).
- Automates ou semi-automates.
- Equipement général de laboratoire (ex. pipette).
- Ne pas utiliser de matériel ne figurant pas ci-dessus.

☞PRÉCAUTIONS D'EMPLOI ET MISES EN GARDE

- Consulter la fiche de données de sécurité (FDS) pour une manipulation appropriée.
- Le réactif R contient de l'azide de sodium qui peut réagir avec le plomb ou le cuivre et former des azides métalliques potentiellement explosifs. Lors de l'élimination de ces réactifs toujours rincer abondamment avec de l'eau pour éviter l'accumulation d'azides.
- Respecter les précautions d'usage et les bonnes pratiques de laboratoire.
- Utiliser du matériel de laboratoire propre ou à usage unique afin d'éviter toute contamination.

☞STABILITÉ

Stocker à 2-8 °C et à l'abri de la lumière. Ne pas congeler.
Ne pas utiliser après la date d'expiration indiquée sur les étiquettes des flacons.
Le standard doit être immédiatement et correctement refermé afin d'éviter toute contamination ou évaporation.

Stabilité à bord :
La stabilité à bord est spécifique à chaque automate. (Se référer au § PERFORMANCES).

PRÉPARATION

Le réactif et le standard sont prêts à l'emploi.

DÉTÉRIORATION DU PRODUIT

- Le produit doit être limpide. Tout trouble serait le signe d'une détérioration du produit.
- Ne pas utiliser le produit s'il y a des signes évidents de contamination ou de détérioration (ex : particules).
- Un flacon endommagé peut avoir un impact sur les performances du produit. Ne pas utiliser le produit si les flacons présentent des signes physiques de détérioration (par exemple, fuite, flacon percé).

☞ÉCHANTILLONS

Echantillons requis [1,2]
- Sérum
- Plasma (héparine de lithium)
- L'utilisation de toute autre type d'échantillon doit être validée par le laboratoire.

Avertissements et précautions
- Les échantillons stockés doivent être suffisamment vortexés avant dosage.[2]
- Le prélèvement des échantillons sanguins pour la réalisation d'un bilan lipidique peut être réalisé sur des patients à jeun ou non à jeun. Un bilan sur échantillon de patient à jeun peut être répété lorsqu'un dosage sur échantillon prélevé non à jeun a conduit à une triglycéridémie > 400 mg/dL (4.5 mmol/L) ou lorsqu'une hypertriglycéridémie est connue.[3]
- Les échantillons doivent être prélevés selon les Bonnes Pratiques de Laboratoire et les guides appropriés qui sont mis en place.

Stockage et stabilité [5]
- 7 jours à 2-8°C
- 3 mois à -20°C

☞VALEURS DE RÉFÉRENCE [3]

Les publications les plus récentes recommandent d'adapter les seuils décisionnels de cholestérol total dans le cadre d'une évaluation globale des risques. Au niveau des laboratoires, l'EFLM (European Federation of Clinical Chemistry and Laboratory Medicine) recommande de signaler les concentrations suivantes comme anormales:

Sérum/plasma	mg/dL	mmol/L
	≥ 190	≥ 5.0

Remarque : *Les laboratoires doivent suivre les recommandations applicables localement pour les seuils lipidiques s'ils diffèrent de ceux indiqués ci-dessus.*

☞PROCÉDURE

Procédure manuelle

Longueur d'onde :	*505 nm*
Trajet optique :	*1 cm*
Ratio échantillon/réactif :	*1:100*
Température:	*37 °C*

Lire contre le blanc réactif.

	CALIBRATION	DOSAGE
Réactif R	1 000 µL	1 000 µL
Standard/ Calibrant	10 µL	-
Echantillon	-	10 µL

Mélanger et lire les absorbances (A) après 5 minutes d'incubation.

Procédure sur automate
Ces réactifs peuvent être utilisés sur différents automates. Pour les automates ELITech Selectra, les applications validées sont disponibles sur demande. Avec le logiciel Selectra TouchPro, utilisez l'application incluse dans le code barre disponible à la fin de cette notice.

Information importante de programmation:
Le réactif CHOLESTEROL SL peut être faiblement contaminé par le réactif MAGNESIUM XB sur les Selectra ProM et ProXL.
Afin d'éviter une contamination sur ces instruments, programmer les incompatibilités suivantes:

Logiciel	Menu	Paramètre
TouchPro	Incompatibilités Aiguille	incompatibilité/ CHOLESTEROL - MAGNESIUM
Autres	Incompatibilité Aiguille	CHOLESTEROL: MAGNESIUM

Pour les autres instruments Selectra Pro: répétez les résultats aberrantes après avoir programmé un lavage d'aiguille.

CALCUL

$$\frac{(A)\ \text{Echantillon}}{(A)\ \text{Standard/Calibrant}} \times n$$ n = concentration du standard/ Calibrant

Facteur de conversion : mg/dL x 0.0259 = mmol/L
mg/dL x 0.01 = g/L

CALIBRATION

Pour les références CHSL-0497/0507/0707 : ELICAL 2 et Cholesterol Standard 200 mg/dL sont traçables par rapport à la méthode de référence ID-GC-MS (Dilution Isotopique - Chromatographie en phase gazeuse - Spectrométrie de Masse).
Pour les références CHSL-0250/0455/0500/0700 : ELICAL 2 est traçable par rapport à la méthode de référence ID-GC-MS (Dilution Isotopique - Chromatographie en phase gazeuse - Spectrométrie de Masse).
Fréquence de calibration : La fréquence de calibration est spécifique à chaque automate (se référer au § PERFORMANCES).

CONTRÔLE QUALITÉ

Il est recommandé d'utiliser des sérums de contrôle tels que ELITROL I et ELITROL II pour surveiller les performances du dosage.
Ces contrôles doivent être effectués :
- avant que les échantillons de patients soient testés,
- au moins une fois par jour,
- après chaque calibration,
- et/ou en accord avec les requis du laboratoire et des exigences réglementaires.

Les résultats doivent être dans les intervalles définis. Si les valeurs se situent en dehors des plages définies, chaque laboratoire devra prendre les mesures correctives nécessaires.

TRAITEMENT DES DÉCHETS

L'élimination de tous les déchets doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales (veuillez vous référer à la fiche de données de sécurité (FDS)).

PERFORMANCES

Les performances ont été obtenues sur l'automate Selectra ProM, en suivant les recommandations CLSI, dans des conditions environnementales contrôlées.

- Domaine de mesure
20 - 600 mg/dL (0.52 - 15.52 mmol/L).
Les échantillons ayant des concentrations supérieures devront être dilués au 1/5 dans une solution de NaCl 9 g/L et redosés. Cette procédure étend le domaine de mesure jusqu'à 3000 mg/dL. (77.59 mmol/L).
Ne pas communiquer de résultats en dehors du domaine de mesure étendu.

Pour les utilisateurs du logiciel Selectra TouchPro, la fonction « diluer » réalise la dilution des échantillons automatiquement. Les résultats tiennent compte de la dilution.

☞- Limite de Détection (LoD) et Limite de Quantification (LoQ)
LoD = 1 mg/dL (0.03 mmol/L)
LoQ = 10 mg/dL (0.26 mmol/L)

- Précision
Les données d'imprécision ont été obtenues sur 2 automates Selectra ProM sur 20 jours (2 routines par jour, tests effectués en double).
Des résultats représentatifs sont présentés ci dessous :

		Moyenne		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Niveau 1	80	115	2.97	1.1	2.1
Niveau 2	80	184	4.76	0.7	1.9
Niveau 3	80	292	7.55	1.9	2.7

☞- Corrélation
Une étude comparative a été réalisée entre le réactif CHOLESTEROL SL sur un automate Selectra ProM et un système similaire certifié par le CRMLN, sur 100 échantillons sériques.
Les concentrations des échantillons s'échelonnent de 20 à 575 mg/dL (0.52 - 14.87 mmol/L).
Les résultats sont les suivants :
Coefficient de corrélation: (r) = 0.999
Droite de régression : y = 1.016 x + 0 mg/dL

☞- Limitations/Interférences
- Des tests ont été réalisés pour déterminer le niveau d'interférence de différents composés.
Les niveaux suivants du cholestérol total ont été testés: 116 et 309 mg/dL.
L'absence d'interférence significative est définie par un recouvrement ≤±10% de la valeur initiale.
Bilirubine non-conjuguée : Aucune interférence significative jusqu'à 6.0 mg/dL (103 µmol/L).
Bilirubine conjuguée : Aucune interférence significative jusqu'à 5.9 mg/dL (101 µmol/L).
Hémoglobine : Aucune interférence significative jusqu'à 300 mg/dL.
Turbidité : Aucune interférence significative jusqu'à 614 mg/dL (6.94 mmol/L) équivalent Triglycérides.
Acide ascorbique: Aucune interférence significative jusqu'à 4.0 mg/dL. .
Méthyl Dopa : Aucune interférence significative jusqu'à 1.6 mg/dL.
Acide urique : Aucune interférence significative jusqu'à 23.7 mg/dL (1410 µmol/L).
- Ne pas utiliser d'échantillons ictériques ou hémolysés.

- Dans des cas très rares, les gammapathies monoclonales (myélome multiple), en particulier de type IgM (Macroglobulinémie de Waldenström) peuvent être à l'origine de résultats peu fiables.[6]

- Les résultats peuvent être faussement abaissés dans les échantillons contenant des niveaux significatifs de NAC (*N*-Acétyl-Cystéine), de NAPQI (métabolite de l'acétaminophène (paracétamol)) ou de métamizole.

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.[7-8]

- Stabilité à bord / fréquence de calibration
Stabilité à bord : 28 jours
Fréquence de calibration : 28 jours
Une nouvelle calibration doit être effectuée après chaque changement de lot de réactif, lorsque les résultats du ou des contrôles de qualité sont hors de l'intervalle établi, et après une opération de maintenance.

Ces performances ont été définies sur un automate ELITech Selectra ProM. Les résultats peuvent varier si le réactif est utilisé sur un automate différent ou en méthode manuelle.
Les performances obtenues à partir d'applications non validées par ELITech ne peuvent être garanties et doivent être définies par l'utilisateur.

☞DECLARATION DES INCIDENTS GRAVES

Veuillez notifier au fabricant (par l'intermédiaire de votre distributeur) et à l'autorité compétente de l'Etat membre de l'union européenne dans lequel l'utilisateur et/ou le patient est établi, les cas d'incident grave survenu en lien avec le dispositif.
Pour les autres juridictions, la déclaration d'incident grave doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales.
En signalant les incidents graves, vous contribuez à fournir davantage d'informations sur la sécurité des dispositifs médicaux de diagnostic *in vitro*.

☞ASSISTANCE TECHNIQUE

Contacter votre distributeur local ou ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

English - EN

☞INTENDED USE

ELITech Clinical Systems CHOLESTEROL SL is an *in vitro* diagnostic reagent intended for the quantitative determination of total cholesterol in human serum and plasma samples on analyzers or semi-automatic analyzers.
The standard is intended for the calibration of reagent.
These *in vitro* diagnostic devices are for professional use only.

☞CLINICAL SIGNIFICANCE [1-3]

Total cholesterol in the serum is derived from dietary sources or is synthesized endogenously, mainly in hepatic and intestinal cells. Cholesterol is an important structural component of cell and organelle membranes. It is a precursor of bile acids, vitamin D and steroid hormones. Cholesterol, being insoluble in water, circulates in association with lipoproteins (HDL, LDL, VLDL and chylomicrons).
In practice, total cholesterol measurement is requested to assess predisposition of patients to cardiovascular risk as part of a lipid profile and to monitor associated therapeutic strategies. Total Cholesterol measurement is also important to help diagnose hyperlipoproteinaemias.

☞LIMITATION OF USE

The quantitative assay of total cholesterol alone can not be used to diagnose a disease or a specific pathology.
The results must be interpreted in conjunction with other diagnostic test results, clinical findings and the patient's medical history.

☞METHOD & PRINCIPLE [4]

Enzymatic / PAP - End point.

$$\text{Cholesterol ester} + H_2O \xrightarrow{\textit{Cholesterol esterase}} \text{Cholesterol} + \text{Fatty acids}$$

$$\text{Cholesterol} + O_2 \xrightarrow{\textit{Cholesterol oxidase}} \text{Cholest-4-en-3-one} + H_2O_2$$

$$2H_2O_2 + \text{Phenol} + \text{4-AAP} \xrightarrow{\textit{Peroxidase}} \text{Quinoneimine} + 4H_2O$$

4-AAP = 4-Aminoantipyrine

COMPOSITION

Reagent: R

Good's buffer, pH 6.7

Phenol		24	mmol/L
4-Aminoantipyrine		0.5	mmol/L
Cholesterol esterase	≥	180	U/L
Cholesterol oxidase	≥	200	U/L
Peroxidase	≥	1 000	U/L
Sodium azide	<	0.1	% (w/w)

Also contains surfactants and magnesium salts for optimal performance.

Standard: Std (Ref : CHSL-0497/0507/0707)

Cholesterol	200	mg/dL
	5.17	mmol/L

MATERIALS REQUIRED BUT NOT PROVIDED

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Normal saline solution (NaCl 9 g/L).
- Analyzers or semi-automatic analyzers.
- General Laboratory equipment (e.g. pipette).
- Do not use materials that are not required as indicated above.

☞PRECAUTIONS FOR USE AND WARNINGS

- Consult Safety Data Sheet (SDS) for a proper handling.
- Reagent R contains sodium azide which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of these reagents always flush with copious amounts of water to prevent azide buildup.
- Take normal precautions and adhere to good laboratory practice.
- Use clean or single use laboratory equipment only to avoid contamination.

☞STABILITY

Store at 2-8 °C and protect from light. Do not freeze.
Do not use after expiration dates indicated on the vial labels.
The standard should be immediately and tightly capped to prevent contamination and evaporation.
On board stability :
The on-board stability is specific for each analyzer. (Refer to § PERFORMANCE DATA).

PREPARATION

The reagent and standard are ready to use.

PRODUCT DETERIORATION

- The product should be clear. Cloudiness would indicate deterioration.
- Do not use the product if there is visible evidence of contamination or damage (e.g. particle matter).
- Damage to the product container may impact on product performance. Do not use the product if there is physical evidence of deterioration (e.g. leakages or punctured container).

☞SAMPLES

Specimen [1,2]
- Serum.
- Plasma (lithium heparin).
- Using any other specimen type should be validated by the laboratory.

Warnings and precautions
- Stored samples must be adequately mixed on a vortex mixer before being tested.[2]
- A non-fasting or fasting sample is suitable for the determination of a lipid profile. A repeat of lipid profile on a fasting sample could be performed in cases where a non-fasting Triglyceride result > 400 mg/dL (4.5 mmol/L) or hypertriglyceridemia is known.[3]
- Samples should be collected in accordance with Good Laboratory Practice and appropriate guidelines that may be in place.

Storage and stability [5]
- 7 days at 2-8°C.
- 3 months at -20°C.

☞REFERENCE VALUES [3]

Most recent publications recommend adapting total cholesterol thresholds as part of an overall risk assessment. At the laboratory level, the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) recommends that the following concentrations be reported as abnormal:

Serum/plasma	mg/dL	mmol/L
	≥ 190	≥ 5.0

Note : *Laboratories should follow locally applicable recommendations for lipid targets if they differ from those reported above.*

☞PROCEDURE

Manual Procedure

Wavelength : 505 nm
Optical path : 1 cm
Sample/ Reagent ratio : 1:100
Temperature: 37 °C
Read against reagent blank.

	CALIBRATION	TEST
Reagent R	1 000 µL	1 000 µL
Standard/ Calibrator	10 µL	-
Sample	-	10 µL

Mix and read the absorbances (A) after an incubation of 5 minutes.

Automatic Procedure

These reagents may be used on several automatic analyzers. For ELITech Selectra Analyzers, validated applications are available on request. For Selectra TouchPro software, use the application included in the barcode available at the end of this insert.

Important set-up information:
CHOLESTEROL SL reagent can be weakly contaminated by MAGNESIUM XB on Selectra ProM and ProXL.
In order to avoid contamination on these instruments, program the following incompatibilities:

Software	Menu	Parameter
TouchPro	Probe incompatibilities	incompatibility/ CHOLESTEROL - MAGNESIUM
Other	Needle incompatibility	CHOLESTEROL: MAGNESIUM

For other Selectra Pro instruments: repeat any absurd results after programming a needle wash.

CALCULATION

$$\frac{(A)\ \text{Sample}}{(A)\ \text{Calibrator/ Standard}} \times n \qquad n = \text{Calibrator/ standard concentration}$$

Conversion factor : mg/dL x 0.0259 = mmol/L
mg/dL x 0.01 = g/L

CALIBRATION

For the references CHSL-0497/0507/0707 : ELICAL 2 and Cholesterol Standard 200 mg/dL are traceable to ID-GC-MS (Isotope Dilution - Gas Chromatography - Mass Spectrometry) reference method.
For the references CHSL-0250/0455/0500/0700 : ELICAL 2 is traceable ID-GC-MS (Isotope Dilution - Gas Chromatography - Mass Spectrometry) reference method.

Calibration frequency : The calibration is specific for each analyzer. (Refer to § PERFORMANCE DATA).

QUALITY CONTROL

It is recommended that quality control sera such as ELITROL I and ELITROL II be used to monitor the performance of the assay.
Controls have to be performed :
- prior to assaying patient samples,
- at least once per day,
- after every calibration,
- and/or in accordance with laboratory and regulatory requirements.

Results should be within the defined ranges. If values fall outside of the defined ranges, each laboratory should take necessary corrective measures.

WASTE MANAGEMENT

Disposal of all waste material should be in accordance with local, state and federal regulatory requirements (please refer to the Safety Data Sheet (SDS)).

PERFORMANCES

Performances were obtained on Selectra ProM, following CLSI technical recommendations, under controlled environmental conditions.

- Measuring range

20 - 600 mg/dL (0.52 - 15.52 mmol/L).
Samples having greater concentrations should be diluted 1:5 with NaCl 9 g/L solution and re-assayed. This procedure extends the measuring range up to 3000 mg/dL. (77.59 mmol/L).

Do not report results outside this extended range.

For users with Selectra TouchPro software, the «dilute» function performs the sample dilution automatically. Results take the dilution into account.

☞Limit of Detection (LoD) and Limit of Quantification (LoQ)

LoD = 1 mg/dL (0.03 mmol/L)
LoQ = 10 mg/dL (0.26 mmol/L)

- Precision

Imprecision data has been obtained on 2 Selectra ProM analyzers over 20 days (2 runs per day, tests performed in duplicate).

Representative results are presented below.

		Mean		Within-run	Total
	n	**mg/dL**	**mmol/L**	**CV (%)**	
Level 1	80	115	2.97	1.1	2.1
Level 2	80	184	4.76	0.7	1.9
Level 3	80	292	7.55	1.9	2.7

☞- Correlation

A comparative study has been performed between CHOLESTEROL SL reagent on a Selectra ProM analyzer and a similar available system CRMLN certified on 100 human serum samples.
The sample concentrations ranged from 20 to 575 mg/dL (0.52 - 14.87 mmol/L).
The results are as follows :
Correlation coefficient : (r) = 0.999
Linear regression: y = 1.016 x + 0 mg/dL

☞- Limitations/Interferences

- Studies have been performed to determine the level of interference from different compounds.
The following total cholesterol levels were tested: 116 and 309 mg/dL.
No significant interference is defined by a recovery ≤±10% of the initial value.
Unconjugated Bilirubin: No significant interference up to 6.0 mg/dL (103 µmol/L).
Conjugated Bilirubin: No significant interference up to 5.9 mg/dL (101 µmol/L).
Hemoglobin : No significant interference up to 300 mg/dL.
Turbidity: No significant interference up to 614 mg/dL (6.94 mmol/L) triglyceride equivalent.
Ascorbic acid : No significant interference up to 4.0 mg/dL.
Methyl-dopa: No significant interference up to 1.6 mg/dL.
Uric acid: No significant interference up to 23.7 mg/dL (1410 µmol/L).

- Do not use icteric or hemolyzed samples.

- In very rare cases, monoclonal gammopathies (multiple myeloma), in particular IgM type (Waldenstrom's macroglobulinemia) can cause unreliable results.[6]

- Results can be falsely lowered by significant levels in the sample of NAC (*N*-Acetyl-Cysteine), NAPQI (metabolite of acetaminophene (paracetamol)) or metamizole.

- Many other substances and drugs may interfere. Some of them are listed in reviews published by Young.[7-8]

- On board stability/Calibration frequency

On Board Stability: 28 days
Calibration frequency: 28 days
Recalibrate when reagent lots change, when quality control results fall outside the established range and after a maintenance operation.

These performances have been obtained using ELITech Selectra ProM analyzer. Results may vary if a different instrument or a manual procedure is used.
The performances of applications not validated by ELITech are not warranted and must be defined by the user.

☞DECLARATION OF SERIOUS INCIDENT

Please notify the manufacturer (through your distributor) and competent authority of the Member State of the european union in which the user and/or the patient is established, of any serious incident that has occurred in relation to the device. For other jurisdictions, the declaration of serious incident should be in accordance with local, state and federal regulatory requirements.
By reporting a serious incident, you provide information that can contribute to the safety of *in vitro* medical devices.

☞TECHNICAL ASSISTANCE

Contact your local distributor or ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

Español - ES

☞USO PREVISTO

ELITech Clinical Systems CHOLESTEROL SL es un reactivo de diagnóstico *in vitro* diseñado para la determinación cuantitativa de colesterol total en muestras de suero y plasma humanos en equipos automatizados o equipos semiautomáticos.
El estándar está diseñado para la calibración del reactivo.
Estos dispositivos de diagnóstico *in vitro* están destinados unicamente para los profesionales.

☞SIGNIFICADO CLÍNICO [1-3]

El colesterol total sérico se deriva de la dieta o se sintetiza endógenamente, principalmente en las células hepáticas e intestinales. El colesterol es un componente estructural importante de las membranas de las células y los orgánelos. El colesterol también es un precursor de los ácidos biliares, la vitamina D y las hormonas esteroides. El colesterol, al ser una molécula insoluble en el agua, circula en asociación con las lipoproteínas (HDL, LDL, VLDL y quilomicrones).
En la práctica, la determinación del colesterol total se lleva a cabo para evaluar la susceptibilidad de los pacientes a los riesgos cardiovasculares como parte de la evaluación de los lípidos, así como para controlar las estrategias terapéuticas asociadas. La medición del colesterol total también es importante para el diagnóstico de hiperlipoproteinemias.

☞LÍMITE DE UTILIZACIÓN

La cuantificación de colesterol total no puede ser utilizado solo para diagnosticar una enfermedad o patología específica.
Los resultados siempre deben compararse con los resultados de otras pruebas de diagnóstico, exámenes clínicos y el historial médico del paciente.

☞MÉTODO & PRINCIPIO [4]

Enzimático / PAP - Punto final.

$$\text{Colesterol ester} + H_2O \xrightarrow{\textit{Colesterol esterasa}} \text{Colesterol} + \text{Ácidos grasos}$$

$$\text{Colesterol} + O_2 \xrightarrow{\textit{Colesterol oxidasa}} \text{Cholest-4-en-3-one} + H_2O_2$$

$$2H_2O_2 + \text{Fenol} + \text{4-AAP} \xrightarrow{\textit{Peroxidasa}} \text{Quinonemina} + 4H_2O$$

4-AAP = Amino-4-antipirina

COMPOSICIÓN

Reactivo : R

Tampón de Good, pH 6.7

Fenol		24	mmol/L
Amino-4-antipirina		0.5	mmol/L
Colesterol esterase	≥	180	U/L
Colesterol oxidasa	≥	200	U/L
Peroxidasa	≥	1 000	U/L
Azida sódica	<	0.1	(p/p)

También contiene surfactantes y sales de magnesio para un rendimiento óptimo.

Estándar : Std (Ref : CHSL-0497/0507/0707)

Colesterol	200	mg/dL
	5.17	mmol/L

MATERIALES REQUERIDOS PERO NO INCLUIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solución salina normal (NaCl 9 g/L).
- Equipos automatizados o equipos semiautomáticos.
- Equipamiento general de laboratorio (p. ej. pipeta).
- No utilice materiales que no se requieren, tal como se indica anteriormente.

☞PRECAUCIONES DE USO Y ADVERTENCIAS

- Consulte la Hoja de Datos de Seguridad (SDS) para un manejo adecuado.
- El reactivo R contiene azida sódica que puede reaccionar con el plomo o el cobre de la tubería y formar potencialmente azidas metálicas explosivas. Cuando se elimine el reactivo enjuague con agua abundantemente para prevenir la acumulación de azidas.
- Tome las precauciones normales y respete las buenas prácticas de laboratorio.
- Para evitar contaminaciones utilizar equipo nuevo o completamente limpio.

☞ESTABILIDAD

Conservar a 2-8 °C y protegidos de la luz. No congelar.
No utilice después de la fecha de caducidad indicada en la etiqueta de los frascos.
El estándar debe cerrarse inmediatamente y correctamente para evitar contaminación y evaporación.
Estabilidad en el equipo:
La estabilidad es específica para cada equipo. (Referirse al § DATOS DE RENDIMIENTO).

PREPARACIÓN

El reactivo y el estándar están listos para su uso.

DETERIORACIÓN DEL PRODUCTO

- El producto debe ser claro. Turbidez indicaría deterioro.

- No utilice el producto si este presenta signos evidentes de contaminación o deterioro (p. ej partículas).
- Un frasco dañado puede tener un impacto en el rendimiento del producto. No utilice el producto si este tiene signos físicos de deterioro (p. ej, fugas, frasco perforado).

☞MUESTRAS

Muestras requeridas [1,2]
- Suero.
- Plasma (heparina de litio).
- El uso de cualquier otro tipo de muestra debe ser validado por el laboratorio.

Advertencias y precauciónes
- Las muestras almacenadas deben agitarse lo suficiente antes de la dosificación. [2]
- Una muestra en ayunas o no en ayunas es adecuada para la determinación de un perfil lipídico. Se podría repetir el perfil lipídico en una muestra en ayunas en los casos en que se encuentre un resultado de triglicéridos sin ayuno> 400 mg/dL (4.5 mmol/L) o hipertrigliceridemia. [3]
- Las muestras deben de tomarse de acuerdo con las Buenas Prácticas de Laboratorio y las guías apropiadas establecidas.

Conservación y estabilidad [5]
- 7 días a 2-8°C
- 3 meses a -20°C.

☞VALORES DE REFERENCIA [3]

Las publicaciones más recientes recomiendan adaptar los umbrales de colesterol total como parte de una evaluación general del riesgo. A nivel de laboratorio, la Federación Europea de Química Clínica y Medicina de Laboratorio (EFLM) recomienda que las siguientes concentraciones se notifiquen como anormales:

Suero/plasma	mg/dL	mmol/L
	≥ 190	≥ 5.0

Nota : *Los laboratorios deben seguir las recomendaciones localmente aplicables para los valores de lípidos si difieren de los informados anteriormente.*

☞PROCEDIMIENTO

Procedimiento manual

Longitud de onda : 505 nm
Trayectoria óptica : 1 cm
Ratio muestra/reactivo : 1:100
Temperatura: 37 °C
Leer contra blanco reactivo.

	CALIBRACIÓN	PRUEBA
Reactivo R	1 000 µL	1 000 µL
Estándar/Calibrador	10 µL	-
Muestra	-	10 µL

Mezcle y lea las absorbancias (A) después de una incubación de 5 minutos.

Procedimiento automático

Estos reactivos pueden ser utilizados en varios equipos. Para los equipos ELITech Selectra, las aplicaciones validadas están disponibles sobre pedido. Para el software Selectra TouchPro, use la aplicación incluida en el código de barras disponible al final de este inserto.

Información importante de programación:
El reactivo CHOLESTEROL SL puede ser ligeramente contaminado con el reactivo MAGNESIUM XB en Selectra ProM y ProXL.
Con el fin de evitar contaminaciones en estos analizadores, programe incompatibilidades de la siguiente manera :

Software	Menú	Parámetro
TouchPro	compatibilidades de las sondas	incompatibilidad/ CHOLESTEROL - MAGNESIUM
Otros	Incompatibilidad de aguja	CHOLESTEROL: MAGNESIUM

Para otros equipos Selectra Pro: repita cualquier resultado aberrante después de programar un lavado de aguja.

CÁLCULO

$$\frac{(A)\ \text{Muestra}}{(A)\ \text{Estándar / Calibrador}} \times n \qquad n = \text{concentración del estándar/ Calibrador}$$

Factor de conversión: mg/dL x 0.0259 = mmol/L
mg/dL x 0.01 = g/L

CALIBRACIÓN

Para las referencias CHSL-0497/0507/0707 : ELICAL 2 o el estándar Cholesterol Standard 200 mg/dL son trazables al método de referencia ID-GC-MS (Dilución isotópica - Cromatografía en fase gaseosa - Espectrometría de masas).
Para las referencias CHSL-0250/0455/0500/0700 : ELICAL 2 es trazable al método de referencia ID-GC-MS (Dilución isotópica - Cromatografía en fase gaseosa - Espectrometría de masas).

Frecuencia de calibración : la frecuencia de calibración es específica para cada equipo (referirse al § DATOS DE RENDIMIENTO).

CONTROL DE CALIDAD

Es recomendado que sueros de control tales como ELITROL I y ELITROL II sean usados para monitorear el rendimiento de las pruebas.
Los controles deben realizarse :
- antes que las muestras del paciente sean evaluadas,
- por lo menos una vez al día,
- después de cada calibración,
- y/o en acuerdo con el laboratorio y los requerimientos regulatorios.

Los resultados deben de encontrarse en el rango definido. Si los valores se encuentran fuera del mismo, cada laboratorio deberá tomar las medidas correctivas necesarias.

TRATAMIENTO DE LOS RESIDUOS

Todos los materiales de desecho deben eliminarse de acuerdo con los requisitos regulatorios locales, estatales y federales. (diríjase a la hoja de seguridad (SDS)).

RENDIMIENTO

El rendimiento fue obtenido en un Selectra ProM, siguiendo las recomendaciones técnicas del CLSI, bajo condiciones ambientales controladas.

- Rango analítico

20 - 600 mg/dL (0.52 - 15.52 mmol/L).
Las muestras que tengan concentraciones mayores deben diluirse 1:5 con una solución de NaCl 9 g/L y volver a analizarse.
Este procedimiento extiende el rango analítico hasta 3000 mg/dL. (77.59 mmol/L).
No tome en cuenta resultados fuera del rango analítico extendido.

Para los usuarios del software Selectra TouchPro, la función «diluir» realiza la dilución de las muestras automáticamente. Los resultados toman en cuenta la dilución.

☞- Límite de detección (LoD), límite de Cuantificación (LoQ)

LoD = 1 mg/dL (0.03 mmol/L)
LoQ = 10 mg/dL (0.26 mmol/L)

- Precisión

Los datos de imprecisión fueron obtenidos en 2 equipos Selectra ProM durante 20 días (2 corridas por día, pruebas efectuadas en duplicado).

Resultados representativos se presentan a continuación :

		Media		Intra-serie	Total
	n	**mg/dL**	**mmol/L**	**CV (%)**	
Nivel 1	80	115	2.97	1.1	2.1
Nivel 2	80	184	4.76	0.7	1.9
Nivel 3	80	292	7.55	1.9	2.7

☞- Correlación

Un estudio comparativo se llevó a cabo entre el reactivo CHOLESTEROL SL en el equipo Selectra ProM y un sistema comercial similar certificado por el CRMLN en 100 muestras séricas.
Las concentraciones de las muestras se encuentran entre 20 y 575 mg/dL (0.52 - 14.87 mmol/L)
Los resultados son los siguientes :
Coeficiente de correlación: (r) = 0.999
Regresión linear : y = 1.016 x + 0 mg/dL

☞- Limitaciones/Interferencias

Estudios fueron llevados a cabo para determinar el nivel de interferencia de diferentes componentes.
Los niveles siguientes de colesterol total fueron probados: 116 y 309 mg/dL.
Definimos una interferencia no significativa cuando se obtiene una recuperación de ≤±10% con respecto al valor inicial.
Bilirrubina no conjugada: No hay interferencia significativa hasta 6.0 mg/dL (103 µmol/L).
Bilirrubina conjugada: No hay interferencia significativa hasta 5.9 mg/dL (101 µmol/L).
Hemoglobina: No hay interferencia significativa hasta 300 mg/dL.
Turbidez: No hay interferencia significativa hasta 614 mg/dL (6.94 mmol/L) de triglicéridos equivalente.
Ácido ascórbico: No hay interferencia significativa hasta 4.0 mg/dL.
Metildopa : No hay interferencia significativa hasta 1.6 mg/dL.
Ácido úrico : No hay interferencia significativa hasta 23.7 mg/dL (1410 µmol/L).

- No utilizar muestras ictéricas o hemolizadas.

- En casos muy raros, las gammapatías monoclonales (mieloma múltiple), en particular el tipo IgM (macroglobulinemia de Waldenstrom) pueden producir resultados poco confiables.[6]

- Los resultados de dosificaciones pueden ser falsamente bajos cuando la muestra contiene niveles importantes de NAC (*N*-Acetil-cisteína), NAPQI (metabolito del acetaminofén (paracetamol)) o de Metamizol.

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en los artículos publicados por Young.[7-8]

- Estabilidad en el equipo / frecuencia de calibración

Estabilidad en el equipo : 28 días
Frecuencia de calibración : 28 días
Recalibrar cuando los lotes de reactivo cambien, cuando los controles de calidad no se encuentren dentro del rango establecido, y después de operaciones de mantenimiento.

El rendimiento se ha obtenido utilizando el equipo ELITech Selectra ProM. Los resultados pueden variar si se utiliza un instrumento diferente o un procedimiento manual.
El rendimiento obtenido a partir de aplicaciones no validadas por ELITech no se garantiza y deben ser definidas por el usuario.

☞DECLARACIÓN DE INCIDENTES GRAVES

Por favor notifique al fabricante (por medio de su distribuidor) y autoridad competente del Estado miembro de la Unión Europea en donde el usuario o paciente radique, de cualquier incidente grave que se produzca con relación al dispositivo. Para otras jurisdicciones, la declaración de incidentes graves debe realizarse de acuerdo con los requisitos reglamentarios locales, estatales y federales. Reportando incidentes graves usted contribuye a proporcionar más información sobre la seguridad del dispositivo médico de diagnóstico *in vitro*.

☞ASISTENCIA TÉCNICA

Contacte a su distribuidor local o con ELITech Clinical Systems SAS (CCsupport@ elitechgroup.com)

Português – PT

☞UTILIZAÇÃO PREVISTA

ELITech Clinical Systems CHOLESTEROL SL é um reagente para diagnóstico *in vitro* destinado à determinação quantitativa do colesterol total em amostras de soro e plasma humanos em analisadores automáticos ou semi-automáticos
O padrão é destinado à calibração do reagente.
Estes dispositivos de diagnóstico *in vitro* são apenas para uso profissional.

☞SIGNIFICADO CLÍNICO [1-3]

O colesterol total no soro é derivado de fontes alimentares ou sintetizado endogenamente, principalmente nas células hepáticas e intestinais. O colesterol é um componente estrutural importante das membranas celulares e organelares. É um precursor dos ácidos biliares, vitamina D e hormônios esteróides. O colesterol, sendo insolúvel em água, circula em associação com lipoproteínas (HDL, LDL, VLDL e quilomícrons).
Na prática, a medição do colesterol total é solicitada para avaliar a predisposição dos pacientes ao risco cardiovascular como parte de um perfil lipídico e para monitorar estratégias terapêuticas associadas. A medição total do colesterol também é importante para ajudar a diagnosticar hiperlipoproteinemias.

☞LIMITAÇÃO DE USO

O ensaio quantitativo de colesterol total sozinho não pode ser usado para diagnosticar uma doença ou uma patologia específica.
Os resultados devem ser interpretados em conjunto com outros resultados de testes de diagnóstico, achados clínicos e histórico médico do paciente.

☞MÉTODO & PRINCÍPIO [4]

Enzimático / PAP – Ponto final.

$$\text{Colesterol esterificado} + H_2O \xrightarrow{\textit{Colesterol esterase}} \text{Colesterol} + \text{Ácidos gordos}$$

$$\text{Colesterol} + O_2 \xrightarrow{\textit{Colesterol oxidase}} \text{Colest-4-en-3-ona} + H_2O_2$$

$$2H_2O_2 + \text{Fenol} + \text{4-AAP} \xrightarrow{\textit{Peroxidase}} \text{Quinoneimina} + 4H_2O$$

4-AAP = Amino-4-antipirina

COMPOSIÇÃO

Reagente : R

Tampão de Good, pH 6.7

Fenol		24	mmol/L
Amino-4-antipirina		0.5	mmol/L
Colesterol esterase	≥	180	U/L
Colesterol oxidase	≥	200	U/L
Peroxidase	≥	1 000	U/L
Azida de sódio	<	0.1	% (p/p)

Também contém surfactantes e sais de magnésio para um ótimo desempenho.

Padrão: Std (Ref : CHSL-0497/0507/0707)

Colesterol	200	mg/dL
	5.17	mmol/L

MATERIAIS NECESSÁRIOS MAS NÃO FORNECIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solução salina normal (NaCl 9 g/L).
- Analisador automáticos ou semi-automáticos.
- Equipamento geral de laboratório (por exemplo, pipeta ...).
- Não utilize materiais que não são necessários, tal como indicado acima.

☞PRECAUÇÕES DE USO E AVISOS

- Consulte a ficha de dados de segurança (SDS) para obter um manuseio adequado.
- O reagente R contém azida de sódio que pode reagir com o chumbo ou cobre das canalizações formando azidas metálicas explosivas. Ao manusear estes reagentes lave as mãos sempre com grandes quantidades de água para evitar a produção de azida.
- Utilize as precauções normais e siga as boas práticas de laboratório.
- Utilizar material de laboratório limpo ou destinado a uma única utilização de modo a evitar qualquer contaminação.

☞ESTABILIDADE

Conservar a 2-8 °C e ao abrigo da luz. Não congelar
Não utilizar após as datas de validade indicadas nos rótulos dos frascos.
O padrão deve ser imediatamente tampado para evitar a contaminação e evaporação.
Estabilidade em equipamentos:
A estabilidade a bordo é específica a cada equipamento (Consultar § DESEMPENHO)

PREPARAÇÃO

O reagente e o padrão estão prontos a usar.

DETERIORAÇÃO DO PRODUTO

- O produto deve ser clara. Qualquer turbidez seria sinal de deterioração do produto.
- Não use o produto se houver evidência visível de contaminação ou dano (por exemplo, partículas).
- Danos ao recipiente de producto podem afetar o desempenho do produto. Não use o producto se houver evidência física de deterioração (por exemplo, vazamentos ou recipiente perfurado).

☞AMOSTRAS

Amostras [1,2]
- Soro.
- Plasma (heparina de lítio).
- O uso de qualquer outro tipo de amostra deve ser validado pelo laboratório.

Aviso e precauções
- As amostras armazenadas devem ser adequadamente misturadas em um misturador de vórtice antes de serem testadas.[2]
- Uma repetição do perfil lipídico em uma amostra de jejum pode ser realizada nos casos em que um resultado de triglicerídeos sem jejum> 400 mg/dL (4.5 mmol/L) ou hipertrigliceridemia é conhecido.[3]
- As amostras devem ser coletadas de acordo com as Boas Práticas de Laboratório e com as diretrizes apropriadas que podem estar em vigor.

Armazenamento e estabilidade [5]
- 7 dias a 2-8°C.
- 3 meses a -20°C.

☞VALORES DE REFERÊNCIAS [3]

As publicações mais recentes recomendam a adaptação dos limites de colesterol total como parte de uma avaliação de risco geral. A nível laboratorial, a Federação Europeia de Química Clínica e Medicina Laboratorial (EFLM) recomenda que as seguintes concentrações sejam comunicadas como anormais:

Soro/plasma	mg/dL	mmol/L
	≥ 190	≥ 5.0

Nota: *Os laboratórios devem seguir as recomendações aplicáveis localmente para alvos lipídicos, caso sejam diferentes dos relatados acima.*

☞PROCEDIMENTO

Procedimento manual

Comprimento de onda : 505 nm
Percurso óptico : 1 cm
Relação Amostra/Reagente : 1:100
Temperatura: 37 °C
Ler comparando com o branco de reagente

	CALIBRAÇÃO	DOSAGEM
Reagente R	1 000 µL	1 000 µL
Padrão/Calibrador	10 µL	-
Amostra	-	10 µL

Misturar e ler as absorvâncias (A) após 5 minutos.

Procedimento automático

Estes reagentes podem ser utilizados em vários analisadores automáticos. Para os analisadores ELITech Selectra, as aplicações validadas estão disponíveis mediante solicitação. Com o Selectra TouchPro, utilize a aplicação incluída
no código de barras disponível no final desde folheto.

Os resultados devem estar dentro dos intervalos definidos. Se os valores ficarem fora dos intervalos definidos, cada laboratório deve tomar as medidas corretivas necessárias.

TRATAMENTO DOS RESÍDUOS

O descarte de todo material residual deve estar de acordo com os requisitos regulamentares locais, estaduais e federais (consulte a Ficha de dados de segurança (SDS)).

DESEMPENHO

Os desempenhos foram obtidos no Selectra ProM, seguindo as recomendações técnicas do CLSI, sob condições ambientais controladas.

- Precisão de medição

20.0 - 400.0 mg/dL (1.11 - 22.20 mmol/L).
As amostras com maiores concentrações devem ser diluídas 1:5 com solução de NaCl 9 g/L e ensaiado novamente. Este procedimento estende a faixa de medição até 2 000.0 mg/dL (111.01 mmol/L).

Não relatar resultados fora do intervalo de medição.

Para utilizadores do Selectra TouchPro, a função de «diluir» realiza a diluição do amostras automaticamente. Os resultados são tomados em consideração na diluição.

- Limite de detecção (LoD) e limite de quantificação (LoQ)

LoD = 0.2 mg/dL (0.01 mmol/L)
LoQ = 10.0 mg/dL (0.56 mmol/L)

- Precisão

Dados de imprecisão foram obtidos em 2 analisadores Selectra ProM ao longo de 20 dias (2 corridas por dia, testes realizados em duplicata).
Os resultados representativos são apresentados abaixo :

		Média		Intra-série	Total
	n	mg/dL	mmol/L	CV (%)	
Nível 1	80	37.4	2.08	0.7	1.6
Nível 2	80	113.1	6.28	0.5	0.9
Nível 3	80	284.0	15.76	0.7	1.3

- Correlação

Foi realizado um estudo comparativo entre o reagente GLUCOSE PAP SL em um analisador Selectra ProM e um sistema similar disponível comercialmente em 100 amostras de soro humano.
As concentrações da amostra variaram de 22.2 para 384.9 mg/dL (1.23 - 21.36 mmol/L).
Os resultados são os seguintes:
Coeficiente de correlação: (r) = 1.000
Regressão linear: y = 0.989x + 1.1 mg/dL (0.06 mmol/L)

☞- Limitações/Interferências

Estudos foram realizados para determinar o nível de interferência de diferentes compostos.
Os seguintes níveis de glicose foram testados : 36.0 mg/dL, 108.1 mg/dL e 400.0 mg/dL.
Uma interferência não significativa é definida por uma recuperação ≤±10% do valor inicial.
Bilirrubina não conjugada: Nenhuma interferência significativa até 6.0 mg/dL (103 µmol/L).
Bilirrubina conjugada: Nenhuma interferência significativa até 5.9 mg/dL (101 µmol/L).
Hemoglobina: Nenhuma interferência significativa até 300 mg/dL.
Triglicéridos : Nenhuma interferência significativa até 920 mg/dL (10.40 mmol/L).
Ácido ascórbico: Nenhuma interferência significativa até 2.0 mg/dL.
Ácido úrico : Nenhuma interferência significativa até 23.0 mg/dL (1 368 µmol/L).
Metil dopa: Nenhuma interferência significativa até 0.8 mg/dL.
L-Dopa: Induz falsamente resultados baixos em concentrações terapêuticas.
Tolazamida: Nenhuma interferência significativa até 40.0 mg/dL.
Acetaminofeno : Nenhuma interferência significativa até 30.0 mg/dL.
Não use amostras ictéricas ou hemolisadas.

- Em casos muito raros, as gamopatias monoclonais (mieloma múltiplo), em particular, tipo IgM (macroglobulinemia de Waldenstrom) podem causar resultados não confiáveis.[7]

- Os resultados podem ser falsamente reduzidos em níveis significativos na amostra de NAC (*N*-acetilcisteína), NAPQI (metabólito do acetaminofeno (paracetamol)) ou metamizol.

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young.[8-9].

- Estabilidade a bordo / frequência de calibração

Estabilidade a bordo: 28 dias
Frequência de calibração: 28 dias
Recalibre quando os lotes de reagentes mudarem, quando os resultados do controle de qualidade estiverem fora da faixa estabelecida e após uma operação de manutenção.

Estes desempenhos foram obtidos utilizando o analisador ELITech Selectra ProM. Os resultados podem variar se um instrumento diferente ou um procedimento manual for usado.
Os desempenhos de aplicações não validados pela ELITech não são garantidos e devem ser definidos pelo usuário.

☞DECLARAÇÃO DE INCIDENTE GRAVE

Notifique o fabricante (através do seu distribuidor) e a autoridade competente do Estado-Membro da união europeia em que o usuário e / ou o paciente está estabelecido, de qualquer incidente grave que tenha ocorrido em relação ao dispositivo.
Para outras jurisdições, a declaração de incidente grave deve estar de acordo com os requisitos regulamentares locais, estaduais e federais.
Ao relatar um incidente grave, você fornece informações que podem contribuir para a segurança de dispositivos médicos *in vitro.*

☞ASSISTÊNCIA TÉCNICA

Entre em contato com o seu distribuidor local ou com a ELITech Clinical Systems SAS.
(CCsupport@elitechgroup.com).

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SYMBOLES/SYMBOLS/ SÍMBOLOS/SÍMBOLOS

- Les symboles utilisés sont décrits dans la norme ISO 15223-1 hormis ceux présentés ci-dessous.
- Symbols used are defined on ISO 15223-1 standard, except those presented below.
- Los símbolos utilizados son descritos en la norma ISO 15223-1 a la excepción de los presentados a continuación.
- Os símbolos utilizados são definidos na norma ISO 15223-1, exceto os apresentados abaixo.

CONT	Contient Content Contiene Conteúdo
R	Réactif Reagent Reactivo Reagente
Std	Standard Standard Estándar Padrão
☞	Modification par rapport à la version précédente Modification from previous version Modificación con respecto a la versión anterior Modificação relativamente à versão anterior
CE	Conformité Européenne European Conformity Conformidad Europea Conformidade Europeia

Note/Nota

- Uniquement pour les réf. **GPSL-0455/GPSL-0250,** utilisées avec le logiciel Selectra TouchPro.
- Only for ref. **GPSL-0455/GPSL-0250,** used with Selectra TouchPro software.
- Únicamente para las ref. **GPSL-0455/GPSL-0250,** utilizadas con el software Selectra TouchPro.
- Somente para ref. **GPSL-0455/GPSL-0250,** usados com o Selectra TouchPro.

GPSL

Glucose 0
480 PIT-GPSL

ELITechGroup
EMPOWERING IVD

GLUCOSE PAP SL

GPSL

GPSL-0497	**R** 1 x 100 mL	+	**Std** 1 x 5 mL	
GPSL-0507	**R** 6 x 100 mL	+	**Std** 1 x 5 mL	
GPSL-0707	**R** 4 x 250 mL	+	**Std** 1 x 5 mL	
GPSL-0250	**R** 12 x 20 mL			
GPSL-0455	**R** 6 x 45 mL			
GPSL-0500	**R** 6 x 100 mL			
GPSL-0700	**R** 4 x 250 mL			CE

PIT-GPSL-4-v20 (01/2021)

Français - FR

☞USAGE PRÉVU

ELITech Clinical Systems GLUCOSE PAP SL est un réactif de diagnostic *in vitro*, destiné au dosage quantitatif du glucose dans les échantillons de sérum et de plasma sur des automates ou semi-automates.
Le standard est destiné à la calibration du réactif.
Ces dispositifs de diagnostic *in vitro* sont uniquement destinés aux professionnels.

☞SIGNIFICATION CLINIQUE [1-3]

Le glucose est la principale source d'énergie pour le corps humain. Le glucose d'origine alimentaire est converti en glycogène ou en triglycérides pour pouvoir être stocké. Le taux de glucose sanguin est principalement régulé par deux hormones antagonistes : l'insuline et le glucagon.
Les troubles de la glycémie sont principalement rencontrés dans les diabètes de type I et II ou le diabète gestationnel. Ils peuvent aussi être associés à divers désordres endocrinologiques, pancréatiques, hépatiques, ou être d'origine médicamenteuse.
En conditions normales, le glucose est filtré puis réabsorbé par les reins et n'est pas retrouvé dans les urines. Des concentrations anormalement élevées sont observées lorsque la concentration sanguine est élevée ou en cas de réabsorption tubulaire altérée.
En pratique, la mesure du glucose sérique est indiquée dans le diabète, que ce soit pour le dépistage, le diagnostic ou le suivi des patients. Elle est aussi utilisée pour le suivi de patients ayant des symptômes évoquant une hyperglycémie ou une hypoglycémie.

☞LIMITE D'UTILISATION

Pour l'évaluation du diabète, les conditions de prélèvement et l'interprétation des concentrations sériques de glucose doivent suivre les recommandations locales en vigueur telles que celles publiées par l'OMS.[4]
Le dosage du glucose ne peut être utilisé seul pour diagnostiquer une maladie ou une pathologie spécifique.
Les résultats doivent toujours être confrontés aux résultats d'autres tests diagnostiques, aux examens cliniques, et à l'historique médical du patient.

☞MÉTHODE & PRINCIPE [5]

Enzymatique / PAP - Point final.

$$\text{Glucose} + O_2 \xrightarrow{\text{Glucose oxydase}} \text{Acide gluconique} + H_2O_2$$

$$2H_2O_2 + \text{Phénol} + \text{Amino-4-antipyrine} \xrightarrow{\text{Peroxydase}} \text{Quinonéimine} + 4H_2O$$

☞COMPOSITION

Réactif : R

Tampon Phosphate, pH 7.4		
Phénol		10 mmol/L
Amino-4-antipyrine		0.3 mmol/L
Glucose oxydase	≥	10 000 U/L
Peroxydase	≥	700 U/L
Azide de sodium	<	0.1 % (p/p)

Standard: Std (ref : GPSL-0497/0507/0707)

D-Glucose 100 mg/dL
5.55 mmol/L

MATÉRIELS REQUIS MAIS NON FOURNIS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solution saline normale (NaCl 9 g/L).
- Automates ou semi-automates.
- Equipement général de laboratoire (ex. pipette).
- Ne pas utiliser de matériel ne figurant pas ci-dessus.

PRÉCAUTIONS D'EMPLOI ET MISES EN GARDE

- Consulter la fiche de données de sécurité (FDS) pour une manipulation appropriée.
- Le réactif R contient de l'azide de sodium qui peut réagir avec le plomb ou le cuivre et former des azides métalliques potentiellement explosifs. Lors de l'élimination de ces réactifs toujours rincer abondamment avec de l'eau pour éviter l'accumulation d'azides.
- Respecter les précautions d'usage et les bonnes pratiques de laboratoire.
- Utiliser du matériel de laboratoire propre ou à usage unique afin d'éviter toute contamination.

☞STABILITÉ

Stocker à 2-8 °C et à l'abri de la lumière. Ne pas congeler.
Ne pas utiliser après la date d'expiration indiquée sur les étiquettes des flacons.
Le standard doit être immédiatement et correctement refermé afin d'éviter toute contamination ou évaporation.
Stabilité à bord :
La stabilité à bord est spécifique à chaque automate. (Se référer au § PERFORMANCES).

PRÉPARATION

Le réactif et le standard sont prêts à l'emploi.

DÉTÉRIORATION DU PRODUIT

- Le produit doit être limpide. Tout trouble serait le signe d'une détérioration du produit.
- Ne pas utiliser le produit s'il y a des signes évidents de contamination ou de détérioration (ex : particules).
- Un flacon endommagé peut avoir un impact sur les performances du produit. Ne pas utiliser le produit si les flacons présentent des signes physiques de détérioration (par exemple, fuite, flacon percé).

☞ÉCHANTILLONS

Echantillons requis [1]
- Sérum.
- Plasma (héparine de lithium).
- Plasma (fluorure de sodium / oxalate de potassium (inhibiteurs de la glycolyse)).
- L'utilisation de toute autre type d'échantillon doit être validée par le laboratoire.

Avertissements et précautions
- Les échantillons prélevés sans inhibiteur de la glycolyse doivent être séparés des cellules rapidement après le prélèvement pour limiter la perte de glucose (diminution de 5-7% par heure dans le sang total à température ambiante). [1]
- La méthode PAP n'est pas appropriée pour la mesure du glucose dans l'urine en raison des quantités importantes d'interférents endogènes présents dans cette matrice. [1,2]
- Les échantillons doivent être prélevés selon les Bonnes Pratiques de Laboratoire et les guides appropriés qui sont mis en place.

Stockage et stabilité [1,6]
Sérum / Plasma (héparine de lithium)
- 8 heures à température ambiante
- 3 jours à 2-8°C
Plasma (fluorure de sodium / oxalate de potassium)
- 2 jours à température ambiante
- 7 jours à 2-8°C

☞VALEURS DE RÉFÉRENCE [3]

Sérum/plasma	mg/dL	mmol/L
Nouveau-nés	30 – 60	1.7 – 3.3
Enfants	60 – 100	3.3 – 5.6
Adultes 18-60 ans	74 – 106	4.1 – 5.9
Adultes 60-90 ans	82 – 115	4.6 – 6.4

Remarque : Les valeurs ci-dessus ne sont données qu'à titre indicatif. Il est recommandé à chaque laboratoire d'établir et de maintenir ses propres valeurs de référence par rapport à la population visée.

PROCÉDURE

Procédure manuelle

Longueur d'onde : *505 nm*
Trajet optique : *1 cm*
Ratio échantillon/réactif : *1:100*
Température: *37 °C*
Lire contre le blanc réactif.

	CALIBRATION	DOSAGE
Réactif R	1 000 µL	1 000 µL
Calibrant/ Standard	10 µL	-
Echantillon	-	10 µL

Mélanger et lire les absorbances (A) après 10 minutes d'incubation.

Procédure sur automate

Ces réactifs peuvent être utilisés sur différents automates. Pour les automates ELITech Selectra, les applications validées sont disponibles sur demande. Avec le logiciel Selectra TouchPro, utilisez l'application incluse dans le code barre disponible à la fin de cette notice.

CALCUL

$$\frac{A_{\text{Echantillon}}}{A_{\text{Standard/Calibrant}}} \times n \qquad n = \text{concentration du standard/Calibrant}$$

Facteur de conversion : mg/dL x 0.0555= mmol/L

CALIBRATION

Pour les références GPSL-0497/0507/0707 : ELICAL 2 et Glucose Standard 100 mg/dL sont traçables par rapport à la méthode de référence ID-MS (Dilution Isotopique - Spectrométrie de Masse).

Pour les références 0250/0455/0500/0700 : ELICAL 2 est traçable par rapport à la méthode de référence ID-MS (Dilution Isotopique - Spectrométrie de Masse).

Fréquence de calibration : La fréquence de calibration est spécifique à chaque automate (se référer au § PERFORMANCES).

CONTRÔLE QUALITÉ

Il est recommandé d'utiliser des sérums de contrôle tels que ELITROL I et ELITROL II pour surveiller les performances du dosage.
Ces contrôles doivent être effectués :
- avant que les échantillons de patients soient testés,
- au moins une fois par jour,
- après chaque calibration,
- et/ou en accord avec les requis du laboratoire et des exigences réglementaires.
Les résultats doivent être dans les intervalles définis. Si les valeurs se situent en dehors des plages définies, chaque laboratoire devra prendre les mesures correctives nécessaires.

TRAITEMENT DES DÉCHETS

L'élimination de tous les déchets doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales (veuillez vous référer à la la fiche de données de sécurité (FDS)).

PERFORMANCES

Les performances ont été obtenues sur l'automate Selectra ProM, en suivant les recommandations CLSI, dans des conditions environnementales contrôlées.

- Domaine de mesure

20.0 - 400.0 mg/dL (1.11 - 22.20 mmol/L).
Les échantillons ayant des concentrations supérieures devront être dilués au 1/5 dans une solution de NaCl 9 g/L et redosés. Cette procédure étend le domaine de mesure jusqu'à 2 000.0 mg/dL (111.01 mmol/L).

Ne pas communiquer de résultats en dehors du domaine de mesure étendu.

Pour les utilisateurs du logiciel Selectra TouchPro, la fonction « diluer » réalise la dilution des échantillons automatiquement. Les résultats tiennent compte de la dilution.

- Limite de Détection (LoD) et Limite de Quantification (LoQ)

LoD = 0.2 mg/dL (0.01 mmol/L)
LoQ = 10.0 mg/dL (0.56 mmol/L)

- Précision

Les données d'imprécision ont été obtenues sur 2 automates Selectra ProM sur 20 jours (2 routines par jour, tests effectués en double).

Des résultats représentatifs sont présentés ci-dessous :

		Moyenne		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Niveau 1	80	37.4	2.08	0.7	1.6
Niveau 2	80	113.1	6.28	0.5	0.9
Niveau 3	80	284.0	15.76	0.7	1.3

- Corrélation

Une étude comparative a été réalisée entre le réactif GLUCOSE PAP SL sur un automate Selectra ProM et un système similaire disponible sur le marché sur 100 échantillons sériques.
Les concentrations des échantillons s'échelonnent de 22.2 à 384.9 mg/dL (1.23 - 21.36 mmol/L).
Les résultats sont les suivants :
Coefficient de corrélation: (r) = 1.000
Droite de régression : y = 0.989x + 1.1 mg/dL (0.06 mmol/L)

☞- Limitations/Interférences

- Des tests ont été réalisés pour déterminer le niveau d'interférence de différents composés.
Les niveaux suivants de glucose ont été testés: 36.0 mg/dL, 108.1 mg/dL et 400.0 mg/dL.
L'absence d'interférence significative est définie par un recouvrement ≤±10% de la valeur initiale.
Bilirubine non-conjuguée : Aucune interférence significative jusqu'à 6.0 mg/dL (103 µmol/L).
Bilirubine conjuguée : Aucune interférence significative jusqu'à 5.9 mg/dL (101 µmol/L).
Hémoglobine : Aucune interférence significative jusqu'à 300 mg/dL.
Triglycérides: Aucune interférence significative jusqu'à 920 mg/dL (10.40 mmol/L).
Acide ascorbique: Aucune interférence significative jusqu'à 2.0 mg/dL.
Acide urique : Aucune interférence significative jusqu'à 23.0 mg/dL (1 368 µmol/L).
Méthyl dopa: Aucune interférence significative jusqu'à 0.8 mg/dL.
L-Dopa : Induit des résultats faussement bas aux concentrations thérapeutiques.
Tolazamide: Aucune interférence significative jusqu'à 40.0 mg/dL.
Acétaminophène: Aucune interférence significative jusqu'à 30.0 mg/dL.
Ne pas utiliser d'échantillons ictériques ou hémolysés.

- Dans des cas très rares, les gammapathies monoclonales (myélome multiple), en particulier de type IgM (Macroglobulinémie de Waldenström) peuvent être à l'origine de résultats peu fiables.[7]

- Les résultats peuvent être faussement abaissés dans les échantillons contenant des niveaux significatifs de NAC (*N*-Acétyl-Cystéine), de NAPQI (métabolite de l'acétaminophène (paracétamol)) ou de métamizole.

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.[8-9]

- Stabilité à bord / fréquence de calibration

Stabilité à bord : 28 jours
Fréquence de calibration : 28 jours
Une nouvelle calibration doit être effectuée après chaque changement de lot de réactif, lorsque les résultats du ou des contrôles de qualité sont hors de l'intervalle établi, et après une opération de maintenance.

Ces performances ont été définies sur un automate ELITech Selectra ProM. Les résultats peuvent varier si le réactif est utilisé sur un automate différent ou en méthode manuelle.
Les performances obtenues à partir d'applications non validées par ELITech ne peuvent être garanties et doivent être définies par l'utilisateur.

☞DECLARATION DES INCIDENTS GRAVES

Veuillez notifier au fabricant (par l'intermédiaire de votre distributeur) et à l'autorité compétente de l'Etat membre de l'union européenne dans lequel l'utilisateur et/ou le patient est établi, les cas d'incident grave survenu en lien avec le dispositif.
Pour les autres juridictions, la déclaration d'incident grave doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales.
En signalant les incidents graves, vous contribuez à fournir davantage d'informations sur la sécurité des dispositifs médicaux de diagnostic *in vitro*.

☞ASSISTANCE TECHNIQUE

Contacter votre distributeur local ou ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

English - EN

☞INTENDED USE

ELITech Clinical Systems GLUCOSE PAP SL is an *in vitro* diagnostic reagent intended for the quantitative determination of glucose in human serum and plasma samples on analyzers or semi-automatic analyzers.
The standard is intended for the calibration of the reagent.
These *in vitro* diagnostic devices are for professional use only.

☞CLINICAL SIGNIFICANCE [1-3]

Glucose is the main source of energy for the human body. Glucose is converted either into glycogen or into triglycerides to be stored. Glucose blood level is mainly regulated by two antagonist hormones: insulin and glucagon.
Glycemia disorders appear mostly in type I or type II diabetes as well as in gestational diabetes. They can be also associated to various endocrinal, pancreatic or hepatic disorders, or linked to drugs.
In normal health condition, glucose is filtered then reabsorbed by kidneys and is therefore not present in urine. Elevated concentrations in urine are observed when the blood concentration is high or in case of impaired tubular reabsorption.
Glucose measurement in blood is indicated for diabetes, in screening, diagnosis or follow-up of patients. It is also indicated to monitor patients with symptoms of hyperglycemia or hypoglycemia.

☞LIMITATION OF USE

For diabetes assessment, the collection conditions and interpretation of serum glucose concentrations should follow local recommendations such as those published by WHO.[4]
The quantitative assay of glucose alone can not be used to diagnose a disease or a specific pathology.
The results must be interpreted in conjunction with other diagnostic test results, clinical findings and the patient's medical history.

☞METHOD & PRINCIPLE [5]

Enzymatic / PAP - End Point.

$$Glucose + O_2 \xrightarrow{Glucose\ oxidase} Gluconic\ acid + H_2O_2$$

$$2H_2O_2 + Phenol + 4\text{-}Aminoantipyrine \xrightarrow{Peroxidase} Quinoneimine + 4H_2O$$

☞COMPOSITION

Reagent: R

Phosphate buffer, pH 7.4		
Phenol	10	mmol/L
4-Aminoantipyrine	0.3	mmol/L
Glucose Oxidase	≥ 10 000	U/L
Peroxidase	≥ 700	U/L
Sodium azide	< 0.1	% (w/w)

Standard: Std (ref : GPSL-0497/0507/0707)

D-Glucose	100	mg/dL
	5.55	mmol/L

MATERIALS REQUIRED BUT NOT PROVIDED

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Normal saline solution (NaCl 9 g/L).
- Analyzers or semi-automatic analyzers.
- General Laboratory equipment (e.g. pipette).
- Do not use materials that are not required as indicated above.

PRECAUTIONS FOR USE AND WARNINGS

- Consult Safety Data Sheet (SDS) for a proper handling.
- Reagent R contains sodium azide which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of these reagents always flush with copious amounts of water to prevent azide buildup.
- Take normal precautions and adhere to good laboratory practice.
- Use clean or single use laboratory equipment only to avoid contamination.

☞STABILITY

Store at 2-8 °C and protect from light. Do not freeze.

Do not use after expiration dates indicated on the vial labels.

The standard should be immediately and tightly capped to prevent contamination and evaporation.

On board stability :

The on-board stability is specific for each analyzer. (Refer to § PERFORMANCE DATA).

PREPARATION

The reagent and standard are ready to use.

PRODUCT DETERIORATION

- The product should be clear. Cloudiness would indicate deterioration.
- Do not use the product if there is visible evidence of contamination or damage (e.g. particle matter).
- Damage to the product container may impact on product performance. Do not use the product if there is physical evidence of deterioration (e.g. leakages or punctured container).

☞SAMPLES

Specimen [1]

-- Serum.
- Plasma (lithium heparin).
- Plasma (Sodium fluoride / potassium oxalate (glycolysis inhibitors)).
- Using any other specimen type should be validated by the laboratory.

Warnings and precautions

- In samples collected without glycolysis inhibitors, blood cells must be removed rapidly to prevent the glucose loss (5% to 7% per hour in whole blood at room temperature).[1]
- PAP method is not suitable for glucose measurement in urine due to the large amount of interfering endogenous substances present in this matrix. [1,2]
- Samples should be collected in accordance with Good Laboratory Practice and appropriate guidelines that may be in place.

Storage and stability [1,6]

Serum / Plasma (lithium heparin)
- 8 hours at room temperature
- 3 days at 2-8°C

Plasma (sodium fluoride / potassium oxalate)
- 2 days at room temperature
- 7 days at 2-8°C

☞REFERENCE VALUES [3]

Serum/plasma	mg/dL	mmol/L
Neonates	30 – 60	1.7 – 3.3
Children	60 – 100	3.3 – 5.6
Adults 18-60 y/o	74 – 106	4.1 – 5.9
Adults 60-90 y/o	82 – 115	4.6 – 6.4

Note : The quoted range should serve as a guide only. It is recommended that each laboratory verifies this range or establishes a reference interval for the intended population.

PROCEDURE

Manual Procedure

Wavelength : 505 nm
Optical path : 1 cm
Sample/ Reagent ratio : 1:100
Temperature: 37 °C
Read against reagent blank.

	CALIBRATION	TEST
Reagent R	1 000 µL	1 000 µL
Standard/ Calibrator	10 µL	-
Sample	-	10 µL

Mix and read the absorbances (A) after an incubation of 10 minutes.

Automatic Procedure

These reagents may be used on several automatic analyzers. For ELITech Selectra Analyzers, validated applications are available on request. For Selectra TouchPro software, use the application included in the barcode available at the end of this insert.

CALCULATION

$$\frac{A\ Sample}{A\ Calibrator/\ Standard} \times n \qquad n = \text{Calibrator/ standard concentration}$$

Conversion factor : mg/dL x 0.0555 = mmol/L

CALIBRATION

For the references GPSL-0497/0507/0707 : ELICAL 2 and Glucose Standard 100 mg/dL are traceable to ID-MS (Isotope Dilution - Mass Spectrometry) reference method.

For the references GPSL-0250/0455/0500/0700 : ELICAL 2 is traceable to ID-MS (Isotope Dilution - Mass Spectrometry) reference method.

Calibration frequency : The calibration is specific for each analyzer. (Refer to § PERFORMANCE DATA).

QUALITY CONTROL

It is recommended that quality control sera such as ELITROL I and ELITROL II be used to monitor the performance of the assay.

Controls have to be performed :
- prior to assaying patient samples,
- at least once per day,
- after every calibration,
- and/or in accordance with laboratory and regulatory requirements.

Results should be within the defined ranges. If values fall outside of the defined ranges, each laboratory should take necessary corrective measures.

WASTE MANAGEMENT

Disposal of all waste material should be in accordance with local, state and federal regulatory requirements (please refer to the Safety Data Sheet (SDS)).

PERFORMANCES

Performances were obtained on Selectra ProM, following CLSI technical recommendations, under controlled environmental conditions.

- Measuring range

20.0 - 400.0 mg/dL (1.11 - 22.20 mmol/L)

Samples having greater concentrations should be diluted 1:5 with NaCl 9 g/L solution and re-assayed. This procedure extends the measuring range up to 2 000.0 mg/dL (111.01 mmol/L).

Do not report results outside this extended range.

For users with Selectra TouchPro software, the «dilute» function performs the sample dilution automatically. Results take the dilution into account.

Limit of Detection (LoD) and Limit of Quantification (LoQ)

LoD = 0.2 mg/dL (0.01 mmol/L)
LoQ = 10.0 mg/dL (0.56 mmol/L)

- Precision

Imprecision data has been obtained on 2 Selectra ProM analyzers over 20 days (2 runs per day, tests performed in duplicate).

Representative results are presented below :

		Mean		Within-run	Total
	n	mg/dL	mmol/L	CV (%)	
Level 1	80	37.4	2.08	0.7	1.6
Level 2	80	113.1	6.28	0.5	0.9
Level 3	80	284.0	15.76	0.7	1.3

- Correlation

A comparative study has been performed between GLUCOSE PAP SL reagent on a Selectra ProM analyzer and a similar commercially available system on 100 human serum samples.

The sample concentrations ranged from 22.2 to 384.9 mg/dL (1.23 - 21.36 mmol/L).

The results are as follows :

Correlation coefficient : (r) = 1.000
Linear regression: y = 0.989x + 1.1 mg/dL (0.06 mmol/L)

☞- Limitations/Interferences

- Studies have been performed to determine the level of interference from different compounds.

The following glucose levels were tested: 36.0 mg/dL, 108.1 mg/dL and 400.0 mg/dL.

No significant interference is defined by a recovery ≤±10% of the initial value.

Unconjugated bilirubin: No significant interference up to 6.0 mg/dL (103 µmol/L).
Conjugated bilirubin: No significant interference up to 5.9 mg/dL (101 µmol/L).
Hemoglobin: No significant interference up to 300 mg/dL.
Triglycerides: No significant interference up to 920 mg/dL (10.40 mmol/L).
Ascorbic acid: No significant interference up to 2.0 mg/dL.
Uric acid: No significant interference up to 23.0 mg/dL (1 368 µmol/L).
Methyl dopa: No significant interference up to 0.8 mg/dL.
L-Dopa: Induces falsely low results at therapeutic concentrations.
Tolazamide: No significant interference up to 40.0 mg/dL.
Acetaminophen: No significant interference up to 30.0 mg/dL.
Do not use icteric or hemolyzed samples.

- In very rare cases, monoclonal gammopathies (multiple myeloma), in particular IgM type (Waldenström's macroglobulinemia) can cause unreliable results.[7]

- Results can be falsely lowered by significant levels in the sample of NAC (*N*-Acetyl-Cysteine), NAPQI (metabolite of acetaminophene (paracetamol)) or metamizole.

- Many other substances and drugs may interfere. Some of them are listed in reviews published by Young.[8-9]

- On board stability/Calibration frequency

On Board Stability: 28 days
Calibration frequency: 28 days

Recalibrate when reagent lots change, when quality control results fall outside the established range and after a maintenance operation.

These performances have been obtained using ELITech Selectra ProM analyzer. Results may vary if a different instrument or a manual procedure is used. The performances of applications not validated by ELITech are not warranted and must be defined by the user.

☞DECLARATION OF SERIOUS INCIDENT

Please notify the manufacturer (through your distributor) and competent authority of the Member State of the european union in which the user and/or the patient is established, of any serious incident that has occurred in relation to the device. For other jurisdictions, the declaration of serious incident should be in accordance with local, state and federal regulatory requirements. By reporting a serious incident, you provide information that can contribute to the safety of *in vitro* medical devices.

☞TECHNICAL ASSISTANCE

Contact your local distributor or ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

Español - ES

☞USO PREVISTO

ELITech Clinical Systems GLUCOSE PAP SL es un reactivo de diagnóstico *in vitro* diseñado para la determinación cuantitativa de glucosa en muestras de suero y plasma humanos en equipos automatizados o equipos semiautomáticos.

El estándar está diseñado para la calibración del reactivo.

Estos dispositivos de diagnóstico *in vitro* están destinados únicamente para los profesionales.

☞SIGNIFICADO CLÍNICO [1-3]

La glucosa es la principal fuente de energía para el cuerpo humano. La glucosa se convierte en glucógeno o en triglicéridos para ser almacenados. El nivel de glucosa en sangre está regulado principalmente por dos hormonas antagonistas: la insulina y glucagon.

Los trastornos de la glucemia aparecen principalmente en la diabetes tipo I o tipo II, así como en la diabetes gestacional. Pueden ser tambien asociado a diversos trastornos endocrinos, pancreáticos o hepáticos, o vinculado a fármacos.

En condición de salud normal, la glucosa se filtra y luego es absorbida por los riñones y, por lo tanto, no está presente en la orina. Se observan concentraciones elevadas en la orina cuando la concentración en sangre es alta o en caso de reabsorción tubular alterada.

La medición de glucosa en sangre es indicada para la diabetes, en la detección, el diagnóstico o el seguimiento de los pacientes. Tambien es adecuada para monitorear pacientes con síntomas de hiperglucemia o hipoglucemia.

☞LÍMITE DE UTILIZACIÓN

Para la evaluación de la diabetes, las condiciones de muestreo y la interpretación de las concentraciones de glucosa en suero deben seguir las recomendaciones locales publicadas por la OMS (WHO). [4]

La cuantificación de glucosa no puede ser utilizado solo para diagnosticar una enfermedad o patología específica.

Los resultados siempre deben compararse con los resultados de otras pruebas de diagnóstico, exámenes clínicos y el historial médico del paciente.

☞MÉTODO & PRINCIPIO [5]

Enzimático / PAP - Point final.

$$Glucosa + O_2 \xrightarrow{Glucosa\ oxidasa} \text{Ácido glucónico} + H_2O_2$$

$$2H_2O_2 + Fenol + Amino\text{-}4\text{-}antipirina \xrightarrow{Peroxidasa} Quinoneimina + 4\ H_2O$$

☞COMPOSICIÓN

Reactivo : R

Tampón Fosfato pH 7.4		
Fenol	10	mmol/L
Amino-4-antipirina	0.3	mmol/L
Glucosa oxidasa	≥ 10 000	U/L
Peroxidasa	≥ 700	U/L
Azida sódica	< 0.1	% (p/p)

Estándar : Std (ref : GPSL-0497/0507/0707)

D-Glucosa	100	mg/dL
	5.5	mmol/L

MATERIALES REQUERIDOS PERO NO INCLUIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solución salina normal (NaCl 9 g/L).
- Equipos automatizados o equipos semiautomáticos.
- Equipamiento general de laboratorio (p. ej. pipeta).
- No utilice materiales que no se requieren, tal como se indica anteriormente.

PRECAUCIONES DE USO Y ADVERTENCIAS

- Consulte la Hoja de Datos de Seguridad (SDS) para un manejo adecuado.
- El reactivo R contiene azida sódica que puede reaccionar con el plomo o el cobre de la tubería y formar potencialmente azidas metálicas explosivas. Cuando se elimine el reactivo enjuague con agua abundantemente para prevenir la acumulación de azidas.
- Tome las precauciones normales y respete las buenas prácticas de laboratorio.
- Para evitar contaminaciones utilizar equipo nuevo o completamente limpio.

☞ESTABILIDAD

Conservar a 2-8 °C y protegidos de la luz. No congelar.

No utilice después de la fecha de caducidad indicada en la etiqueta de los frascos.

El estándar debe cerrarse inmediatamente y correctamente para evitar contaminación y evaporación.

Estabilidad en el equipo:

La estabilidad es específica para cada equipo. (Referirse al § DATOS DE RENDIMIENTO).

PREPARACIÓN

El reactivo y el estándar están listos para su uso.

DETERIORACIÓN DEL PRODUCTO

- El producto debe ser claro. Turbidez indicaría deterioro.
- No utilice el producto si este presenta signos evidentes de contaminación o deterioro (p. ej partículas).
- Un frasco dañado puede tener un impacto en el rendimiento del producto. No utilice el producto si este tiene signos físicos de deterioro (p. ej, fugas, frasco perforado).

☞MUESTRAS

Muestras requeridas [1]

- Suero
- Plasma (heparina de litio).
- Plasma (fluoruro de sodio / oxalato de potasio (Inhibidor de la glicólisis)).
- El uso de cualquier otro tipo de muestra debe ser validado por el laboratorio.

Advertencias y precauciones

- Las muestras tomadas sin un inhibidor de la glicólisis deben separarse de las células inmediatamente después de la recolección para limitar la pérdida de glucosa (5-7% de disminución por hora en sangre total a temperatura ambiente). [1]
- El método PAP no es adecuado para la medición de glucosa en la orina debido a la gran cantidad de sustancias endógenas interferentes presentes en esta matriz.[1,2]
- Las muestras deben de tomarse de acuerdo con las Buenas Prácticas de Laboratorio y las guías apropiadas establecidas.

Conservación y estabilidad [1,6]

Suero / Plasma (heparina de litio)
- 8 horas a temperatura ambiente
- 3 días a 2-8°C

Plasma (fluoruro de sodio / oxalato de potasio)
- 2 días a temperatura ambiente
- 7 días a 2-8°C

☞VALORES DE REFERENCIA [3]

Suero/plasma	mg/dL	mmol/L
Recien nacidos	30 – 60	1.7 – 3.3
Niños	60 – 100	3.3 – 5.6
Adultos 18-60 años	74 – 106	4.1 – 5.9
Adultos 60-90 años	82 – 115	4.6 – 6.4

Nota : Los valores anteriores son solo indicativos. Se recomienda que cada laboratorio establezca y mantenga sus propios valores de referencia en relación con la población destinataria.

PROCEDIMIENTO

Procedimiento manual

Longitud de onda : 505 nm
Trayectoria óptica : 1 cm
Ratio muestra/reactivo : 1:100
Temperatura: 37 °C
Leer contra blanco reactivo

	CALIBRACIÓN	PRUEBA
Reactivo R	1 000 µL	1 000 µL
Estándar/ Calibrador	10 µL	-
Muestra	-	10 µL

Mezclar y leer las absorbancias (A) después de una incubación de 10 minutos.

Procedimiento automático

Estos reactivos pueden ser utilizados en varios equipos. Para los equipos ELITech Selectra, las aplicaciones validadas están disponibles sobre pedido. Para el software Selectra TouchPro, use la aplicación incluida en el código de barras disponible al final de este inserto.

CÁLCULO

$$\frac{A\ Muestra}{A\ Estándar\ /\ calibrador} \times n \qquad n = \text{concentración del estándar/ calibrador}$$

Factor de conversión: mg/dL x 0.0555 = mmol/L

CALIBRACIÓN

Para las referencias GPSL-0497/0507/0707 : ELICAL 2 o el estándar Glucose Standard 100 mg/dL son trazables al método de referencia DI-EM (Dilución Isotópica - Espectrometría de Masas)

Para las referencias GPSL-0250/0455/0500/0700 : ELICAL 2 es trazable al método de referencia DI-EM (Dilución Isotópica - Espectrometría de Masas).

Frecuencia de calibración : la frecuencia de calibración es específica para cada equipo (referirse al § DATOS DE RENDIMIENTO).

CONTROL DE CALIDAD

Es recomendado que sueros de control tales como ELITROL I y ELITROL II sean usados para monitorear el rendimiento de las pruebas.

Los controles deben realizarse :
- antes que las muestras del paciente sean evaluadas,
- por lo menos una vez al día,
- después de cada calibración,
- y/o en acuerdo con el laboratorio y los requerimientos regulatorios.

Los resultados deben de encontrarse en el rango definido. Si los valores se encuentran fuera del mismo, cada laboratorio deberá tomar las medidas correctivas necesarias.

TRATAMIENTO DE LOS RESIDUOS

Todos los materiales de desecho deben eliminarse de acuerdo con los requisitos regulatorios locales, estatales y federales. (diríjase a la hoja de seguridad (SDS)).

RENDIMIENTO

El rendimiento fue obtenido en un Selectra ProM, siguiendo las recomendaciones técnicas del CLSI, bajo condiciones ambientales controladas.

- Rango analítico

20.0 - 400.0 mg/dL (1.11 - 22.20 mmol/L)

Las muestras que tengan concentraciones mayores deben diluirse 1:5 con una solución de NaCl 9 g/L y volver a analizarse.

Este procedimiento extiende el rango analítico hasta 2 000.0 mg/dL (111.01 mmol/L).

No tome en cuenta resultados fuera del rango analítico extendido.

Para los usuarios del software Selectra TouchPro, la función «diluir» realiza la dilución de las muestras automáticamente. Los resultados toman en cuenta la dilución.

- Límite de detección (LoD), límite de Cuantificación (LoQ)

LoD = 0.2 mg/dL (0.01 mmol/L)
LoQ = 10.0 mg/dL (0.56 mmol/L)

- Precisión

Los datos de imprecisión fueron obtenidos en 2 equipos Selectra ProM durante 20 días (2 corridas por día, pruebas efectuadas en duplicado).

Resultados representativos se presentan a continuación :

		Media		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Nivel 1	80	37.4	2.08	0.7	1.6
Nivel 2	80	113.1	6.28	0.5	0.9
Nivel 3	80	284.0	15.76	0.7	1.3

- Correlación

Un estudio comparativo se llevó a cabo entre el reactivo GLUCOSE PAP SL en el equipo Selectra ProM y un sistema comercial similar en 100 muestras séricas. Las concentraciones de las muestras se encuentran entre 22.2 y 384.9 mg/dL (1.23 - 21.36 mmol/L).

Los resultados son los siguientes :

Coeficiente de correlación: (r) = 1.0000
Regresión linear : y = 0.989x + 1.1 mg/dL (0.06 mmol/L)

☞- Limitaciones/Interferencias

- Estudios fueron llevados a cabo para determinar el nivel de interferencia de diferentes componentes.

Los niveles siguientes de glucosa fueron probados: 36.0 mg/dL, 108.1 mg/dL y 400.0 mg/dL.

Definimos una interferencia no significativa cuando se obtiene una recuperación de ≤±10% con respecto al valor inicial.

Bilirrubina no conjugada : No hay interferencia significativa hasta 6.0 mg/dL (103 µmol/L).
Bilirrubina conjugada : No hay interferencia significativa hasta 5.9 mg/dL (101 µmol/L).
Hemoglobina: No hay interferencia significativa hasta 300 mg/dL.
Triglicéridos: No hay interferencia significativa hasta 920 mg/dL (10.40 mmol/L).
Ácido ascórbico: No hay interferencia significativa hasta 2.0 mg/dL.
Ácido úrico: No hay interferencia significativa hasta 23.0 mg/dL (1 368 µmol/L).
Metil-dopa: No hay interferencia significativa hasta 0,8 mg/dL.
L-Dopa: Induce a resultados falsamente bajos a concentraciones terapéuticas.
Tolazamida : No hay interferencia significativa hasta 40.0 mg/dL.
Acetaminofeno : No hay interferencia significativa hasta 30.0 mg/dL.
No utilizar muestras hemolizadas o ictéricas.

- En casos muy raros, las gammapatías monoclonales (mieloma múltiple), en particular el tipo IgM (macroglobulinemia de Waldenstrom) pueden producir resultados poco confiables.[7]

- Los resultados de dosificaciones pueden ser falsamente bajos cuando la muestra contiene niveles importantes de NAC (*N*-Acetil-cisteína), NAPQI (metabolito del acetaminofén (paracetamol)) o de Metamizol.

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en los artículos publicados por Young.[8-9]

- Estabilidad en el equipo / frecuencia de calibración

Estabilidad en el equipo : 28 días
Frecuencia de calibración : 28 días

Recalibrar cuando los lotes de reactivo cambien, cuando los controles de calidad no se encuentren dentro del rango establecido, y después de operaciones de mantenimiento.

El rendimiento se ha obtenido utilizando el equipo ELITech Selectra ProM. Los resultados pueden variar si se utiliza un instrumento diferente o un procedimiento manual.

El rendimiento obtenido a partir de aplicaciones no validadas por ELITech no se garantiza y deben ser definidas por el usuario.

☞DECLARACIÓN DE INCIDENTES GRAVES

Por favor notifique al fabricante (por medio de su distribuidor) y autoridad competente del Estado miembro de la Unión Europea en donde el usuario o paciente radique, de cualquier incidente grave que se produzca con relación al dispositivo. Para otras jurisdicciones, la declaración de incidentes graves debe realizarse de acuerdo con los requisitos reglamentarios locales, estatales y federales. Reportando incidentes graves usted contribuye a proporcionar más información sobre la seguridad del dispositivo médico de diagnóstico *in vitro*.

☞ASISTENCIA TÉCNICA

Contacte a su distribuidor local o con ELITech Clinical Systems SAS (CCsupport@ elitechgroup.com)

Português – PT

☞UTILIZAÇÃO PREVISTA

ELITech Clinical Systems GLUCOSE PAP SL é um reagente para diagnóstico *in vitro* destinado à determinação quantitativa de glicose em amostras de soro e plasma humanos em analisadores automáticos ou semi-automáticos.

O padrão é destinado à calibração do reagente.

Estes dispositivos de diagnóstico *in vitro* são apenas para uso profissional.

☞SIGNIFICADO CLÍNICO [1-3]

A glicose é a principal fonte de energia para o corpo humano. A glicose é convertida em glicogênio ou em triglicerídeos para serem armazenados. O nível sanguíneo de glicose é regulado principalmente por dois hormônios antagonistas: insulina e glucagon.

Os distúrbios da glicemia aparecem principalmente no diabetes tipo I ou tipo II, bem como no diabetes gestacional. Eles também podem estar associados a vários distúrbios endócrinos, pancreáticos ou hepáticos ou ligados a drogas.

Em condições normais de saúde, a glicose é filtrada e depois reabsorvida pelos rins e, portanto, não está presente na urina. Observam-se concentrações elevadas na urina quando a concentração sanguínea é alta ou em caso de reabsorção tubular prejudicada.

A medição da glicose no sangue é indicada para diabetes, triagem, diagnóstico ou acompanhamento de pacientes. Também é indicado para monitorar pacientes com sintomas de hiperglicemia ou hipoglicemia.

☞LIMITAÇÃO DE USO

Para avaliação do diabetes, as condições de coleta e interpretação das concentrações séricas de glicose devem seguir recomendações locais, como as publicadas pela OMS.[4]

O ensaio quantitativo de glicose sozinho não pode ser usado para diagnosticar uma doença ou uma patologia específica.

Os resultados devem ser interpretados em conjunto com outros resultados de testes de diagnóstico, achados clínicos e histórico médico do paciente.

☞MÉTODO & PRINCÍPIO [5]

Enzimático / PAP - ponto final.

$$Glicose + O_2 \xrightarrow{Oxidase\ de\ glicose} \text{Ácido glicônico} + H_2O_2$$

$$2H_2O_2 + Fenol + 4\text{-}Aminoantipirina \xrightarrow{Peroxidase} Quinoneimina + 4H_2O$$

☞COMPOSIÇÃO

Reagente : R

Tampão de fosfato, pH 7.4		
Fenol	10	mmol/L
4-Aminoantipirina	0.3	mmol/L
Oxidase de glicose	≥ 10 000	U/L
Peroxidase	≥ 700	U/L
Azida de sódio	< 0.1	% (p/p)

Padrão: Std (ref : GPSL-0497/0507/0707)

D-Glucose	100	mg/dL
	5.55	mmol/L

MATERIAIS NECESSÁRIOS MAS NÃO FORNECIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solução salina normal (NaCl 9 g/L).
- Analisador automáticos ou semi-automáticos.
- Equipamento geral de laboratório (por exemplo, pipeta ...).
- Não utilize materiais que não são necessários, tal como indicado acima.

PRECAUÇÕES DE USO E AVISOS

- Consulte a ficha de dados de segurança (SDS) para obter um manuseio adequado.
- O reagente R contém azida de sódio que pode reagir com o chumbo ou cobre das canalizações formando azidas metálicas explosivas. Ao manusear estes reagentes lave as mãos sempre com grandes quantidades de água para evitar a produção de azida.
- Utilize as precauções normais e siga as boas práticas de laboratório.
- Utilizar material de laboratório limpo ou destinado a uma única utilização de modo a evitar qualquer contaminação.

☞ESTABILIDADE

Conservar a 2-8 °C e ao abrigo da luz. Não congelar

Não utilizar após as datas de validade indicadas nos rótulos dos frascos.

O padrão deve ser imediatamente tampado para evitar a contaminação e evaporação.

Estabilidade em equipamentos:

A estabilidade a bordo é específica a cada equipamento (Consultar § DESEMPENHO)

PREPARAÇÃO

O reagente e o padrão estão prontos a usar.

DETERIORAÇÃO DO PRODUTO

- O produto deve ser clara. Qualquer turbidez seria sinal de deterioração do produto.
- Não use o produto se houver evidência visível de contaminação ou dano (por exemplo, partículas).
- Danos ao recipiente de producto podem afetar o desempenho do produto. Não use o produto se houver evidência física de deterioração (por exemplo, vazamentos ou recipiente perfurado).

☞AMOSTRAS

Amostras [1]

- Soro.
- Plasma (heparina de lítio).
- Plasma (fluoreto de sódio / oxalato de potássio (inibidores da glicólise)).
- O uso de qualquer outro tipo de amostra deve ser validado pelo laboratório.

Aviso e precauções

- Nas amostras colhidas sem inibidores da glicólise, as células sanguíneas devem ser removidas rapidamente para evitar a perda de glicose (5% a 7% por hora em sangue total à temperatura ambiente).[1]
- O método PAP não é adequado para a medição de glicose na urina devido à grande quantidade de substâncias endógenas interferentes presentes nessa matriz.[1,2]
- As amostras devem ser coletadas de acordo com as Boas Práticas de Laboratório e com as diretrizes apropriadas que podem estar em vigor.

Armazenamento e estabilidade [1,6]

Soro / Plasma (heparina de lítio)
- 8 horas em temperatura ambiente
- 3 dias a 2-8 °C

Plasma (fluoreto de sódio / oxalato de potássio)
- 2 dias em temperatura ambiente
- 7 dias a 2-8 °C

☞VALORES DE REFERÊNCIAS [3]

Soro / Plasma	mg/dL	mmol/L
Neonatos	30 – 60	1.7 – 3.3
Crianças	60 – 100	3.3 – 5.6
Adultos de 18 a 60 anos	74 – 106	4.1 – 5.9
Adultos 60-90 anos	82 – 115	4.6 – 6.4

Observação: O intervalo citado deve servir apenas como guia. Recomenda-se que cada laboratório verifique esse intervalo ou estabeleça um intervalo de referência para a população pretendida.

PROCEDIMENTO

Procedimento manual

Comprimento de onda : 505 nm
Percurso óptico : 1 cm
Relação Amostra/Reagente : 1:100
Temperatura: 37 °C
Ler comparando com o branco de reagente

	CALIBRAÇÃO	DOSAGEM
Reagente R	1 000 µL	1 000 µL
Padrão/ Calibrador	10 µL	-
Amostra	-	10 µL

Misturar e ler as absorvâncias (A) após 10 minutos.

Procedimento automático

Estes reagentes podem ser utilizados em vários analisadores automáticos. Para os analisadores ELITech Selectra, as aplicações validadas estão disponíveis mediante solicitação. Com o Selectra TouchPro, utilize a aplicação incluída
no código de barras disponível no final deste folheto.

CÁLCULO

$$\frac{(A)\ Amostra}{(A)\ Padrão/\ calibrador} \times n \qquad n = \text{concentração do padrão/ calibrador}$$

Fator de conversão: mg/dL x 0.0555 = mmol/L

CALIBRAÇÃO

Para referências GPSL-0497/0507/0707 : ELICAL 2 ou o padrão Glucose Standard 100 mg/dL são rastreáveis relativamente ao método de referência ID-MS (Diluição Isotópica por Espectrometria de Massa).

Para referências GPSL-0250/0455/0500/0700 : ELICAL 2. o é rastreável relativamente ao método de referência ID-MS (Diluição Isotópica por Espectrometria de Massa).

Frequência de calibração : A frequência de calibração é específica a cada equipamento (consultar § DESEMPENHO).

CONTROLE DE QUALIDADE

Recomenda-se o uso de soros de controle de qualidade, como ELITROL I e ELITROL II, para monitorar o desempenho do ensaio.

Os controles devem ser executados:
- antes de analisar amostras de pacientes,
- pelo menos uma vez por dia,
- após cada calibração,
- e/ou de acordo com os requisitos laboratoriais e regulamentares.

PREPARAÇÃO
O reagente e o padrão estão prontos a usar.

DETERIORAÇÃO DO PRODUTO
- Esses produtos devem ser claros. Qualquer turbidez seria sinal de deterioração do produto.
- Não use o produto se houver evidência visível de contaminação ou dano (por exemplo, partículas).
- Danos ao recipiente de producto podem afetar o desempenho do produto. Não use o producto se houver evidência física de deterioração (por exemplo, vazamentos ou recipiente perfurado).

AMOSTRAS
Amostras [1,6]
- Soro
- Plasma (heparina de lítio).
- Urina
- O uso de qualquer outro tipo de amostra deve ser validado pelo laboratório.

Aviso e precauções [1,2]
- O soro deve ser separado das células o mais rápido possível. [1,2]
- As amostras devem estar isentas de hemólise [1,2]
- Após a coleta, as amostras de urina devem ser acidificadas com ácido clorídrico 6N até um pH <2 para evitar a precipitação de sal de magnésio. [1]

As amostras devem ser coletadas de acordo com as Boas Práticas de Laboratório e com as diretrizes apropriadas que podem estar em vigor.

Armazenamento e estabilidade [6]
Soro/Plasma
- 7 dias a temperatura ambiente
- 7 dias a 2-8°C
- 1 ano a -20°C

Urina (acidificada)
- 3 dias a temperatura ambiente
- 3 dias a 2-8°C
- 1 ano a -20°C

VALORES DE REFERÊNCIAS [7]

Soro/plasma	mg/dL	mmol/L
	1.5 - 2.6	0.63 - 1.05
Urina (24h - coleta)	mg/24h	mmol/24 h
	73 - 122	3.0 - 5.0
	mg/dL*	mmol/L*
	4.9 - 8.1	2.0 - 3.3

* para um volume urinário de 1,5 L em 24 horas

Observação: O intervalo citado deve servir apenas como guia. Recomenda-se que cada laboratório verifique esse intervalo ou estabeleça um intervalo de referência para a população pretendida.

☞PROCEDIMENTO
Procedimento manual

Comprimento de onda : 505 - 625 nm
Percurso óptico : 1 cm
Relação Amostra/Reagente : 1:100
Temperatura: 37 °C
As amostras de urina devem ser diluídas 1:5 com solução de NaCl 9 g/L antes da medição.
Ler comparando com o branco de reagente/ água destilada

	CALIBRAÇÃO	DOSAGEM
Reagente R	2 ml	2 ml
Padrão/Calibrador	20 µl	-
Amostra	-	20 µl

Misturar e ler as absorvâncias (A) após 5 minutos.

Procedimento automático
Estes reagentes podem ser utilizados em vários analisadores automáticos. Para os analisadores ELITech Selectra, as aplicações validadas estão disponíveis mediante solicitação. Com o Selectra TouchPro, utilize a aplicação incluída
no código de barras disponível no final desde folheto.

As amostras de urina devem ser diluídas 1:5 com solução de NaCl 9 g/L antes da medição.
Para usuários do software Selectra TouchPro, a diluição da urina é realizada automaticamente.

Informação de configuração importante :
O Reagente MAGNESIUM XB pode ser levemente contaminado pela CHOLESTEROL SL en Selectra ProM e ProXL.
Para evitar a contaminação nestes equipamentos , programe as seguintes incompatibilidades :

Logiciel	Menu	Parametro
TouchPro	Incompatibilidades de Agulha	incompatibilidade/ CHOLESTEROL - MAGNESIUM
Autres	Incompatibilidade de Agulha	CHOLESTEROL: MAGNESIUM

☞CÁLCULO

$$\frac{\Delta A\ \text{Amostra}}{\Delta A\ \text{Padrão/ calibrador}} \times n \qquad n = \text{concentração do padrão/ calibrador}$$

Para o cálculo da concentração do magnésio na urina, multiplique o resultado pelo fator de diluição (5). Para usuários do software Selectra TouchPro, os resultados levam em consideração o fator de diluição.

Fator de conversão: mg/dL x 0.41 = mmol/L

CALIBRAÇÃO
Para referência MGXB-0600 : ELICAL 2 ou o padrão Magnesium XL são rastreáveis relativamente ao método de referência de absorção atómica.
Para referência MGXB-0250 : ELICAL 2. o é rastreável relativamente ao método de referência de absorção atómica.

Frequência de calibração : A frequência de calibração é específica a cada equipamento (consultar § DESEMPENHO).

CONTROLE DE QUALIDADE
Recomenda-se o uso de soros de controle de qualidade, como ELITROL I e ELITROL II, para monitorar o desempenho do ensaio.
Os controles devem ser executados:
- antes de analisar amostras de pacientes,
- pelo menos uma vez por dia,
- após cada calibração,
- e/ou de acordo com os requisitos laboratoriais e regulamentares.

Os resultados devem estar dentro dos intervalos definidos. Se os valores ficarem fora dos intervalos definidos, cada laboratório deve tomar as medidas corretivas necessárias.

TRATAMENTO DOS RESÍDUOS
O descarte de todo material residual deve estar de acordo com os requisitos regulamentares locais, estaduais e federais (consulte a Ficha de dados de segurança (SDS)).

DESEMPENHO
Os desempenhos foram obtidos no Selectra ProM, seguindo as recomendações técnicas do CLSI, sob condições ambientais controladas.

☞- Precisão de medição
a) Soro / plasma
0.20 - 5.00 mg/dL (0.08 - 2.06 mmol/L)
As amostras com maiores concentrações devem ser diluídas 1:5 com solução de NaCl 9 g/L e analisadas novamente. Este procedimento estende a faixa de medição até 25 mg/dL (10.28 mmol/L).
Não relatar resultados fora do intervalo de medição.

Para utilizadores do Selectra TouchPro, a função de «diluir» realiza a diluição do amostras automaticamente. Os resultados são tomados em consideração na diluição.

b) Urina
1.0 - 20.0 mg/dL (0.41-8.23 mmol/L)
As amostras com maiores concentrações devem ser diluídas 1:5 com solução de NaCl 9 g/L e analisadas novamente. Este procedimento estende a faixa de medição até 100 mg/dL (41.14 mmol/L).
Não relatar resultados fora do intervalo de medição.

Para utilizadores do Selectra TouchPro, a função de «diluir» realiza a diluição do amostras automaticamente. Os resultados são tomados em consideração na diluição.

- Limite de detecção (LoD) e limite de quantificação (LoQ)
a) Soro / plasma
LoD = 0.03 mg/dL (0.01 mmol/L)
LoQ = 0.20 mg/dL (0.08 mmol/L)

b) Urina
LoD = 0.1 mg/dL (0.04 mmol/L)
LoQ = 1.0 mg/dL (0.41 mmol/L)

☞- Precisão
Dados de imprecisão foram obtidos em 2 analisadores Selectra ProM ao longo de 20 dias (2 corridas por dia, testes realizados em duplicata).
Os resultados representativos são apresentados abaixo:
a) Soro / plasma

		Média		Intra-série	Total
	n	mg/dL	mmol/L	CV (%)	
Nível baixo	80	1.55	0.64	1.0	3.5
Nível médio	80	2.51	1.03	1.3	3.7
Nível elevado	80	3.84	1.58	0.7	3.0

b) Urina

		Média		Intra-série	Total
	n	mg/dL	mmol/L	CV (%)	
Nível baixo	80	1.2	0.49	2.9	9.2
Nível médio	80	5.0	2.06	0.7	4.0
Nível elevado	80	16.0	6.58	0.8	3.3

- Correlação
a) Soro / plasma
Foi realizado um estudo comparativo entre o reagente MAGNESIUM XB em um analisador Selectra ProM e um sistema similar disponível comercialmente em 102 amostras de soro humano.
As concentrações da amostra variaram de 0.27 para 4.99 mg/dL (0.11 - 2.05 mmol/L).
Os resultados são os seguintes:
Coeficiente de correlação: (r) = 0.996
Regressão linear: y = 1.041x - 0.01 mg/dL (0.00 mmol/L).

b) Urina
Foi realizado um estudo comparativo entre o reagente MAGNESIUM XB em um analisador Selectra ProM e um sistema similar disponível comercialmente em 80 amostras de urina humana.
As concentrações da amostra variaram de 1.7 para 19.6 mg/dL (0.70 - 8.06 mmol/L)..
Os resultados são os seguintes:
Coeficiente de correlação: (r) = 0.999
Regressão linear: y = 1.011x + 0.1 (0.00 mmol/L).

☞- Limitações/Interferências
a) Soro / plasma
Estudos foram realizados para determinar o nível de interferência de diferentes compostos.
Os seguintes níveis de magnésium foram testados : 1.50 mg /dL e 3.90 mg/dL
Uma interferência não significativa é definida por uma recuperação ≤±10% do valor inicial.
Triglicéridos: Nenhuma interferência significativa até 3000 mg/dL(33.90 mmol/L)
Bilirrubina não conjugada: Nenhuma interferência significativa até 30.0 mg/dL. (513 µmol/L)
Bilirrubina conjugada: Nenhuma interferência significativa até 29.5 mg/dL. (504 µmol/L)
Hemoglobina: Nenhuma interferência significativa até 500 mg/dL
Cálcio: Nenhuma interferência significativa até 20.0 mg/dL. (4.99 mmol/L)
Ácido ascórbico:: Nenhuma interferência significativa até 19.8 mg/dL.
Acetaminofeno: Nenhuma interferência significativa até 30 mg/dL.
Ácido acetilsalicílico: Nenhuma interferência significativa até 200 mg/dL

- Em casos muito raros, as gamopatias monoclonais (mieloma múltiplo), em particular, tipo IgM (macroglobulinemia de Waldenstrom) podem causar resultados não confiáveis.[8]

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young. [9-10].

b) Urina
Estudos foram realizados para determinar o nível de interferência de diferentes compostos.
Os seguintes níveis de magnésio foram testados : 1.2 mg /dL e 15 mg/dL
Uma interferência não significativa é definida por uma recuperação ≤±10% do valor inicial.

Bilirrubina conjugada: : Nenhuma interferência significativa até 29.5 mg/dL (504 µmol/L)
Hemoglobina : Nenhuma interferência significativa até 500 mg/dL.
Cálcio : Nenhuma interferência significativa até 60.0 mg/dL (14.97 mmol/L)
Ácido úrico : Nenhuma interferência significativa até 100 mg/dL (5.95 mmol/L).
Urea : Nenhuma interferência significativa até 5000 mg/dL (832.50 mmol/L).
Ácido ascórbico: Nenhuma interferência significativa até 19.8 mg/dL.
pH : Nenhuma interferência significativa entre 2.5 à 6.0

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young. [9-10].

- Estabilidade a bordo / frequência de calibração
Estabilidade a bordo: 14 dias
Frequência de calibração: 7 dias
Recalibre quando os lotes de reagentes mudarem, quando os resultados do controle de qualidade estiverem fora da faixa estabelecida e após uma operação de manutenção.

Estes desempenhos foram obtidos utilizando o analisador ELITech Selectra ProM. Os resultados podem variar se um instrumento diferente ou um procedimento manual for usado.
Os desempenhos de aplicações não validados pela ELITech não são garantidos e devem ser definidos pelo usuário.

DECLARAÇÃO DE INCIDENTE GRAVE
Notifique o fabricante (através do seu distribuidor) e a autoridade competente do Estado-Membro da união europeia em que o usuário e / ou o paciente está estabelecido, de qualquer incidente grave que tenha ocorrido em relação ao dispositivo.
Para outras jurisdições, a declaração de incidente grave deve estar de acordo com os requisitos regulamentares locais, estaduais e federais.
Ao relatar um incidente grave, você fornece informações que podem contribuir para a segurança de dispositivos médicos *in vitro.*

ASSISTÊNCIA TÉCNICA
Entre em contato com o seu distribuidor local ou com a ELITech Clinical Systems SAS. (CCsupport@elitechgroup.com).

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SYMBOLES/SYMBOLS/ SÍMBOLOS/SÍMBOLOS
- Les symboles utilisés sont décrits dans la norme ISO 15223-1 hormis ceux présentés ci-dessous.
- Symbols used are defined on ISO 15223-1 standard, except those presented below.
- Los símbolos utilizados son descritos en la norma ISO 15223-1 a la excepción de los presentados a continuación.
- Os símbolos utilizados são definidos na norma ISO 15223-1, exceto os apresentados abaixo.

CONT	Contient Content Contiene Conteúdo
R	Réactif Reagent Reactivo Reagente
Std	Standard Standard Estándar Padrão
☞	Modification par rapport à la version précédente Modification from previous version Modificación con respecto a la versión anterior Modificação relativamente à versão anterior
CE	Conformité Européenne European Conformity Conformidad Europea Conformidade Europeia

☞Note/Nota

NOTE IMPORTANTE:
- Uniquement pour la réf.**MGXB-0250**, utilisée avec le logiciel Selectra TouchPro.
- **voir § PROCEDURE:** Risque de contamination

IMPORTANT NOTE:
- Only for ref. **MGXB-0250**,, used with Selectra TouchPro software.
- see § PROCEDURE: Contamination risk

NOTA IMPORTANTE:
- Unicamente para la ref. **MGXB-0250**,, utilizada con el software Selectra TouchPro.
- vea § PROCEDIMIENTO: Riesgo de contaminación

NOTA IMPORTANTE:
- Somente para ref. **MGXB-0250**,, usado com o Selectra TouchPro.
- verificar § PROCEDIMENTO: Risco de contaminação

MGXB

MAGNESIUM XB 0
520 PIT-MGXB

ELITechGroup
EMPOWERING IVD

MAGNESIUM XB

MGXB

MGXB-0250	***R***	*6 x 24 mL*
MGXB-0600	***R***	*2 x 100 mL + **Std** 1 x 5 mL*

CE

PIT-MGXB-4-v2 (10/2020)

Français - FR

USAGE PRÉVU
ELITech Clinical Systems MAGNESIUM XB est un réactif de diagnostic *in vitro*, destiné au dosage quantitatif du magnésium dans les échantillons de sérum, de plasma et d'urine humains sur des automates ou semi-automates.
Le standard est destiné à la calibration du réactif.
Ces dispositifs de diagnostic *in vitro* sont uniquement destinés aux professionnels.

SIGNIFICATION CLINIQUE [1-3]
Le magnésium est le quatrième cation les plus abondant dans le corps humain. Il est le cofacteur de nombreux systèmes enzymatiques dont les enzymes ATP-dépendantes et il joue également un rôle actif dans l'homéostasie minérale osseuse. Moins de 1% du magnésium total du corps humain est véhiculé par le sang dans lequel il se trouve en majorité sous forme d'ion libre, mais aussi lié à des protéines (principalement l'albumine) ou complexé avec divers anions. La magnésémie mesure le magnésium sanguin total mais seule la fraction libre est biologiquement active. Une hypomagnésémie peut être liée à des pertes rénales importantes (prise excessive de diurétiques), des désordres gastro-intestinaux (malabsorption, diarrhées), des maladies endocriniennes, plus rarement à un apport inadéquat. Une hypomagnésémie est souvent associée à une hypokaliémie et/ou une hypocalcémie. Une hypermagnésémie est rare et est presque toujours due à un apport excessif (traitement parentéral, prise excessive de traitements contenant du magnésium) ou à une insuffisance rénale.
Le dosage du magnésium urinaire permet, en présence d'une hypomagnésémie, d'identifier une étiologie rénale.
Dans la pratique clinique, le dosage du magnésium est indiqué pour l'aide au diagnostic des causes de concentrations anormales en calcium et/ou potassium ou de symptômes évoquant une hypo ou une hypermagnésémie, ainsi que pour le suivi de traitements à base de magnésium ou de calcium.

LIMITE D'UTILISATION
Une hypoalbuminémie pouvant induire une pseudo-hypomagnésémie, tout dosage du magnésium sérique doit être analysé en regard de la protidémie et/ou de l'albuminémie.[4]
Le dosage de MAGNESIUM XB ne peut être utilisé seul pour diagnostiquer une maladie ou une pathologie spécifique.
Les résultats doivent toujours être confrontés aux résultats d'autres tests diagnostiques, aux examens cliniques, et à l'historique médical du patient.

MÉTHODE & PRINCIPE [5]
Bleu de Xylidyl - Point Final

Le bleu de Xylidyl contenu dans le réactif se combine avec le magnésium de l'échantillon pour former un complexe rouge-pourpre. L'EGTA sert à complexer le calcium et ainsi l'empêche d'interférer avec le test. L'augmentation d'absorbance à 505-510 nm et la diminution simultanée à 620-630 nm sont proportionnelles à la concentration de magnésium dans l'échantillon

COMPOSITION
Réactif : R

Tampon AMP, pH 11.2		
Bleu de Xylidyl		120 µmol/L
Azide de sodium	<	0,1 % (p/p)

Contient aussi de l'EGTA et des surfactants pour des performances optimales
AMP: 2-Amino-2-methyl-1-propanol

Standard: Std
Magnésium 2.0 mg/dL
823 µmol/L

MATÉRIELS REQUIS MAIS NON FOURNIS
- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solution saline normale (NaCl 9 g/L).
- Automates ou semi-automates.
- Equipement général de laboratoire (ex. pipette).
- Ne pas utiliser de matériel ne figurant pas ci-dessus.

PRÉCAUTIONS D'EMPLOI ET MISES EN GARDE
- Le réactif R contient de l'azide de sodium qui peut réagir avec le plomb ou le cuivre et former des azides métalliques potentiellement explosifs. Lors de l'élimination de ces réactifs toujours rincer abondamment avec de l'eau pour éviter l'accumulation d'azides.
- Respecter les précautions d'usage et les bonnes pratiques de laboratoire.
- Utiliser du matériel de laboratoire propre ou à usage unique afin d'éviter toute contamination.
- Consulter la fiche de données de sécurité (FDS) pour une manipulation appropriée.

STABILITÉ
Stocker à 2-8 °C et à l'abri de la lumière. Ne pas congeler.
Ne pas utiliser après la date d'expiration indiquée sur les étiquettes des flacons.
Le standard doit être immédiatement et correctement refermé afin d'éviter toute contamination ou évaporation.
Stabilité à bord :
La stabilité à bord est spécifique à chaque automate. (Se référer au § PERFORMANCES).

PRÉPARATION
Le réactif et le standard sont prêts à l'emploi.

DÉTÉRIORATION DU PRODUIT
- Ces produits doivent être limpides. Tout trouble serait le signe d'une détérioration du produit.
- Ne pas utiliser le produit s'il y a des signes évidents de contamination ou de détérioration (ex : particules).
- Un flacon endommagé peut avoir un impact sur les performances du produit. Ne pas utiliser le produit si les flacons présentent des signes physiques de détérioration (par exemple, fuite, flacon percé).

ÉCHANTILLONS
Echantillons requis [1,6]
- Sérum
- Plasma (héparine de lithium)
- Urine
- L'utilisation de toute autre type d'échantillon doit être validée par le laboratoire.

Avertissements et précautions [1,2]
- Le sérum doit être séparé des cellules aussi rapidement que possible. [1,2]
- Les échantillons ne doivent pas être hémolysés [1,2]
- Après collecte, les urines doivent être acidifiées avec de l'acide chlorhydrique 6N à un pH < 2 pour empêcher le sel de magnésium de précipiter. [1]

Les échantillons doivent être prélevés selon les Bonnes Pratiques de Laboratoire et les guides appropriés qui sont mis en place.

Stockage et stabilité [6]
Sérum/Plasma
- 7 jours à température ambiante
- 7 jours à 2-8°C
- 1 an à -20°C

Urine (acidifiée)
- 3 jours à température ambiante
- 3 jours à 2-8°C
- 1 an à -20°C

VALEURS DE RÉFÉRENCE [7]

Sérum/plasma	mg/dL	mmol/L
	1.5 - 2.6	0.63 - 1.05
Urine (recueil de 24h)	mg/24h	mmol/24 h
	73 - 122	3.0 - 5.0
	mg/dL*	mmol/L*
	4.9 - 8.1	2.0 - 3.3

* pour un volume urinaire de 1.5 L par 24 heures

Remarque : Les valeurs ci-dessus ne sont données qu'à titre indicatif. Il est recommandé à chaque laboratoire d'établir et de maintenir ses propres valeurs de référence par rapport à la population visée.

☞PROCÉDURE
Procédure manuelle

Longueur d'onde : 505 - 625 nm
Trajet optique : 1 cm
Ratio échantillon/réactif : 1:100
Température: 37 °C
Les échantillons urinaires doivent être dilués au 1/5 dans une solution de NaCl 9 g/L avant la mesure.
Lire contre le blanc réactif/l'eau distillée.

	CALIBRATION	DOSAGE
Réactif R	2 ml	2 ml
Standard/ Calibrant	20 µl	-
Echantillon	-	20 µl

Mélanger et lire les absorbances (A) après 5 minutes d'incubation.

Procédure sur automate
Ces réactifs peuvent être utilisés sur différents automates. Pour les automates ELITech Selectra, les applications validées sont disponibles sur demande. Avec le logiciel Selectra TouchPro, utilisez l'application incluse dans le code barre disponible à la fin de cette notice.

Les échantillons urinaires doivent être dilués au 1/5 dans une solution de NaCl 9 g/L avant la mesure. Pour les utilisateurs du logiciel Selectra TouchPro, la dilution des urines est réalisée automatiquement.

Information importante de programmation:
Le réactif MAGNESIUM XB peut être faiblement contaminé par le réactif CHOLESTEROL SL sur les Selectra ProM et ProXL.
Afin d'éviter une contamination sur ces instruments, programmer les incompatibilités suivantes:

Logiciel	Menu	Paramètre
TouchPro	Incompatibilités Aiguille	incompatibilité/ CHOLESTEROL - MAGNESIUM
Autres	Incompatibilité Aiguille	CHOLESTEROL: MAGNESIUM

☞CALCUL

$$\frac{\Delta A\ \text{Echantillon}}{\Delta A\ \text{Standard/ Calibrant}} \times n \qquad n = \text{concentration du Standard/ calibrant}$$

Pour le calcul de la concentration de magnésium dans les urines, multiplier le résultat par le facteur de dilution (5). Pour les utilisateurs du logiciel Selectra TouchPro, les résultats tiennent compte du facteur de dilution.

Facteur de conversion : mg/dL x 0.41 = mmol/L

CALIBRATION
Pour la référence MGXB-0600 : ELICAL 2 et le standard Magnesium XL sont traçables par rapport à la méthode de référence d'absorption atomique.
Pour la référence MGXB-0250 : ELICAL 2 est traçable par rapport à la méthode de référence d'absorption atomique.
Fréquence de calibration : La fréquence de calibration est spécifique à chaque automate (se référer au § PERFORMANCES).

CONTRÔLE QUALITÉ
Il est recommandé d'utiliser des sérums de contrôle tels que ELITROL I et ELITROL II pour surveiller les performances du dosage.
Ces contrôles doivent être effectués :
- avant que les échantillons de patients soient testés,
- au moins une fois par jour,
- après chaque calibration,
- et/ou en accord avec les requis du laboratoire et des exigences réglementaires.

Les résultats doivent être dans les intervalles définis. Si les valeurs se situent en dehors des plages définies, chaque laboratoire devra prendre les mesures correctives nécessaires.

TRAITEMENT DES DÉCHETS
L'élimination de tous les déchets doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales (veuillez vous référer à la la fiche de données de sécurité (FDS).

PERFORMANCES
Les performances ont été obtenues sur l'automate Selectra ProM, en suivant les recommandations CLSI, dans des conditions environnementales contrôlées.

☞- Domaine de mesure
a) Sérum/Plasma
0.20 - 5.00 mg/dL (0.08 - 2.06 mmol/L)
Les échantillons ayant des concentrations supérieures devront être dilués au 1/5 dans une solution de NaCl 9 g/L et redosés. Cette procédure étend le domaine de mesure jusqu'à 25 mg/dL (10.28 mmol/L).
Ne pas communiquer de résultats en dehors du domaine de mesure étendu.

Pour les utilisateurs du logiciel Selectra TouchPro, la fonction « diluer » réalise la dilution des échantillons automatiquement. Les résultats tiennent compte de la dilution.

b) Urine
1.0 - 20.0 mg/dL (0.41-8.23 mmol/L)
Les échantillons ayant des concentrations supérieures devront être dilués au 1/5 dans une solution de NaCl 9 g/L et redosés. Cette procédure étend le domaine de mesure jusqu'à 100 mg/dL (41.14 mmol/L).
Ne pas communiquer de résultats en dehors du domaine de mesure étendu.
Pour les utilisateurs du logiciel Selectra TouchPro, la fonction « diluer » réalise la dilution des échantillons automatiquement. Les résultats tiennent compte de la dilution.

- Limite de Détection (LoD) et Limite de Quantification (LoQ)
a) Sérum/Plasma
LoD = 0.03 mg/dL (0.01 mmol/L)
LoQ = 0.20 mg/dL (0.08 mmol/L)

b) Urine
LoD = 0.1 mg/dL (0.04 mmol/L)
LoQ = 1.0 mg/dL (0.41 mmol/L)

☞- Précision
Les données d'imprécision ont été obtenues sur 2 automates Selectra ProM sur 20 jours (2 routines par jour, tests effectués en double).
Des résultats représentatifs sont présentés ci-après :

a) Sérum/Plasma

		Moyenne		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Niveau bas	80	1.55	0.64	1.0	3.5
Niveau moyen	80	2.51	1.03	1.3	3.7
Niveau haut	80	3.84	1.58	0.7	3.0

b) Urine

		Moyenne		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Niveau bas	80	1.2	0.49	2.9	9.2
Niveau moyen	80	5.0	2.06	0.7	4.0
Niveau haut	80	16.0	6.58	0.8	3.3

- Corrélation
a) Sérum/Plasma
Une étude comparative a été réalisée entre le réactif MAGNESIUM XB sur un automate Selectra ProM et un système similaire disponible sur le marché sur 102 échantillons sériques.
Les concentrations des échantillons s'échelonnent de 0.27 à 4.99 mg/dL (0.11 - 2.05 mmol/L).
Les résultats sont les suivants :
Coefficient de corrélation: (r) = 0.996
Droite de régression : y = 1.041x - 0.01 mg/dL (0.00 mmol/L).

b) Urine
Une étude comparative a été réalisée entre le réactif MAGNESIUM XB sur un automate Selectra ProM et un système similaire disponible sur le marché sur 80 échantillons urinaires.
Les concentrations des échantillons s'échelonnent de 1.7 à 19.6 mg/dL (0.70 - 8.06 mmol/L).
Les résultats sont les suivants :
Coefficient de corrélation: (r) = 0.999
Droite de régression : y = 1.011x + 0.1 mg/dL (0.00 mmol/L).

☞- Limitations/Interférences
a) Sérum/Plasma
- Des tests ont été réalisés pour déterminer le niveau d'interférence de différents composés.
Les niveaux suivants de magnésium ont été testés: 1.50 mg /dL et 3.90 mg/dL.
L'absence d'interférence significative est définie par un recouvrement ≤±10% de la valeur initiale.
Triglcérides : Aucune interférence significative jusqu'à 3000 mg/dL(33.90 mmol/L)
Bilirubine non-conjuguée : Aucune interférence significative jusqu'à 30.0 mg/dL. (513 µmol/L)
Bilirubine conjuguée : Aucune interférence significative jusqu'à 29.5 mg/dL. (504 µmol/L)
Hémoglobine : Aucune interférence significative jusqu'à 500 mg/dL.
Calcium : Aucune interférence significative jusqu'à 20.0 mg/dL. (4.99 mmol/L)
Acide Ascorbique : Aucune interférence significative jusqu'à 19.8 mg/dL.
Acétaminophène : Aucune interférence significative jusqu'à 30 mg/dL.
Acide Acétylsalicylique : Aucune interférence significative jusqu'à 200 mg/dL.

- Dans des cas très rares, les gammapathies monoclonales (myélome multiple), en particulier de type IgM (Macroglobulinémie de Waldenström) peuvent être à l'origine de résultats peu fiables.[8]

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.[9-10]

b) Urine
- Des tests ont été réalisés pour déterminer le niveau d'interférence de différents composés.
Les niveaux suivants de magnésium ont été testés: 1.2 mg/dL et 15 mg/dL.
L'absence d'interférence significative est définie par un recouvrement ≤±10% de la valeur initiale.
Bilirubine conjuguée : Aucune interférence significative jusqu'à 29.5 mg/dL (504 µmol/L)
Hémoglobine : Aucune interférence significative jusqu'à 500 mg/dL.
Calcium : Aucune interférence significative jusqu'à 60.0 mg/dL (14.97 mmol/L)
Uric Acid : Aucune interférence significative jusqu'à 100 mg/dL (5.95 mmol/L).
Urea: Aucune interférence significative jusqu'à 5000 mg/dL (832.50 mmol/L).
Acide Ascorbique : Aucune interférence significative jusqu'à 19.8 mg/dL.
pH : Aucune interférence significative pour des valeurs de pH comprises entre 2.5 à 6.0

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.[9-10]

- Stabilité à bord / fréquence de calibration
Stabilité à bord : 14 jours
Fréquence de calibration : 7 jours
Une nouvelle calibration doit être effectuée après chaque changement de lot de réactif, lorsque les résultats du ou des contrôles de qualité sont hors de l'intervalle établi, et après une opération de maintenance.

Ces performances ont été définies sur un automate ELITech Selectra ProM. Les résultats peuvent varier si le réactif est utilisé sur un automate différent ou en méthode manuelle.
Les performances obtenues à partir d'applications non validées par ELITech ne peuvent être garanties et doivent être définies par l'utilisateur.

DECLARATION DES INCIDENTS GRAVES
Veuillez notifier au fabricant (par l'intermédiaire de votre distributeur) et à l'autorité compétente de l'Etat membre de l'union européenne dans lequel l'utilisateur et/ou le patient est établi, les cas d'incident grave survenu en lien avec le dispositif.
Pour les autres juridictions, la déclaration d'incident grave doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales.
En signalant les incidents graves, vous contribuez à fournir davantage d'informations sur la sécurité des dispositifs médicaux de diagnostic *in vitro.*

ASSISTANCE TECHNIQUE
Contacter votre distributeur local ou ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

English - EN

INTENDED USE

ELITech Clinical Systems MAGNESIUM XB is an *in vitro* diagnostic reagent intended for the quantitative determination of magnesium in human serum, plasma and urine samples on analyzers or semi-automatic analyzers.
The standard is intended for the calibration of reagent.
These *in vitro* diagnostic devices are for professional use only.

CLINICAL SIGNIFICANCE [1-3]

Magnesium is the fourth most abundant cation in the human body. It is the cofactor for many enzymatic systems including ATP-dependent enzymes and it also plays an active role in bone mineral homeostasis. Less than 1% of the total magnesium of the human body is carried by blood where it is mainly found as free ion, but also protein-bound (mainly albumin) or complexed with various anions. Magnesemia measures total magnesium but only free magnesium is biologically active. Hypomagnesemia can be due to important renal losses (excessive intake of diuretics), gastrointestinal disorders (malabsorption, diarrheas), endocrinal disorders, less often due to inadequate intake. Hypomagnesemia is often associated with hypokalemia and/or hypocalcemia. Hypermagnesemia is rare and is caused almost always by excessive intake (parenteral therapy, excessive intake of magnesium-containing drugs) or renal insufficiency.
The measure of urinary magnesium allows, in presence of magnesium deficiency, to identify a kidney etiology.
In clinical practice, measurement of magnesium is indicated to help diagnose the causes of abnormal calcium and/or potassium levels or symptoms suggesting hypo or hypermagnesemia as well as for monitoring magnesium- and/or calcium-based treatments.

LIMITATION OF USE

Because hypoalbuminemia may trigger pseudo-hypomagnesemia, serum magnesium results must be interpreted in regards of serum total protein and/or albumin levels. [4]
The quantitative assay of MAGNESIUM XB alone can not be used to diagnose a disease or a specific pathology.
The results must be interpreted in conjunction with other diagnostic test results, clinical findings and the patient's medical history.

METHOD & PRINCIPLE [5]

Xylidyl Blue - End Point

Xylidyl blue in the reagent combines with the magnesium from the sample to form a red-purple chelate. EGTA is used to complex calcium and thus prevents it from interfering with the test.
The simultaneous increase in absorbance at 505-510 nm and decrease of the 620-630 nm absorbance are proportional to the magnesium concentration in the sample.

COMPOSITION

Reagent: R
AMP buffer, pH 11.2
Xylidyl Blue 120 µmol/L
Sodium azide < 0.1 % (w/w)
Also contains EGTA and surfactants for optimal performance

AMP: 2-Amino-2-methyl-1-propanol

Standard: Std
Magnesium 2.0 mg/dL
823 µmol/L

MATERIALS REQUIRED BUT NOT PROVIDED

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Normal saline solution (NaCl 9 g/L).
- Analyzers or semi-automatic analyzers.
- General Laboratory equipment (e.g. pipette).
- Do not use materials that are not required as indicated above.

PRECAUTIONS FOR USE AND WARNINGS

- Reagent R contains sodium azide which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of these reagents always flush with copious amounts of water to prevent azide buildup.
- Take normal precautions and adhere to good laboratory practice.
- Use clean or single use laboratory equipment only to avoid contamination.
- Consult Safety Data Sheet (SDS) for a proper handling.

STABILITY

Store at 2-8 °C and protect from light. Do not freeze.
Do not use after expiration dates indicated on the vial labels.
The standard should be immediately and tightly capped to prevent contamination and evaporation.
On board stability :
The on-board stability is specific for each analyzer. (Refer to § PERFORMANCE DATA).

PREPARATION

The reagent and standard are ready to use.

PRODUCT DETERIORATION

- These products should be clear. Cloudiness would indicate deterioration.
- Do not use the product if there is visible evidence of contamination or damage (e.g. particle matter).
- Damage to the product container may impact on product performance. Do not use the product if there is physical evidence of deterioration (e.g. leakages or punctured container).

SAMPLES

Specimen [1,6]
- Serum.
- Plasma (lithium heparin).
- Urine.
- Using any other specimen type should be validated by the laboratory.

Warnings and precautions [1,2]
- Serum must be separated from cells as rapidly as possible. [1,2]
- Samples must be free from hemolysis [1,2]
- After collection, urine specimens should be acidified with hydrochloric acid 6N to a pH < 2 to prevent magnesium salt precipitation. [1]

Samples should be collected in accordance with Good Laboratory Practice and appropriate guidelines that may be in place.

Storage and stability [6]
Serum/plasma
- 7 days at room temperature.
- 7 days at 2-8°C.
- 1 year at -20°C.

Urine (acidified)
- 3 days at room temperature
- 3 days at 2-8°C
- 1 year at -20°C

REFERENCE VALUES [7]

Serum/plasma	mg/dL	mmol/L
	1.5 - 2.6	0.63 - 1.05
Urine (24h - collection)	mg/24h	mmol/24 h
	73 - 122	3.0 - 5.0
	mg/dL*	mmol/L*
	4.9 - 8.1	2.0 - 3.3

* for a urinary volume of 1.5 L per 24 hours

Note : *The quoted range should serve as a guide only. It is recommended that each laboratory verifies this range or establishes a reference interval for the intended population.*

☞PROCEDURE

Manual Procedure
Wavelength : 505 - 625 nm
Optical path : 1 cm
Sample/ Reagent ratio : 1:100
Temperature: 37 °C
Urine samples must be diluted 1:5 with NaCl 9 g/L solution before measurement.
Read against reagent blank/distilled water.

	CALIBRATION	TEST
Reagent R	2 ml	2 ml
Standard/ Calibrator	20 µl	-
Sample	-	20 µl

Mix and read the absorbances (A) after an incubation of 5 minutes.

Automatic Procedure
These reagents may be used in several automatic analyzers. For ELITech Selectra Analyzers, validated applications are available on request. For Selectra TouchPro software, use the application included in the barcode available at the end of this insert.

Urine samples must be diluted 1:5 with NaCl 9 g/L solution before measurement. For users of Selectra TouchPro software, urine dilution is performed automatically.

Important set-up information:
MAGNESIUM XB reagent can be weakly contaminated by CHOLESTEROL SL on Selectra ProM and ProXL.
In order to avoid contamination on these instruments, program the following incompatibilities:

Software	Menu	Parameter
TouchPro	Probe incompatibilities	incompatibility/ CHOLESTEROL - MAGNESIUM
Other	Needle incompatibility	CHOLESTEROL: MAGNESIUM

☞CALCULATION

$$\frac{\Delta A\ \text{Sample}}{\Delta A\ \text{Calibrator/ Standard}} \times n \qquad n = \text{Calibrator/ standard concentration}$$

For the calculation of magnesium concentration in urine, multiply the result by the dilution factor (5). For users of Selectra TouchPro software, the results take the dilution factor into account.

Conversion factor : mg/dL x 0.41 = mmol/L

CALIBRATION

For the reference MAGX-0600 : ELICAL 2 and Magnesium XL standard are traceable to the atomic absorption reference method
For the reference MAGX-0250 : ELICAL 2 is traceable to the atomic absorption reference method.

Calibration frequency : The calibration is specific for each analyzer. (Refer to § PERFORMANCE DATA).

QUALITY CONTROL

It is recommended that quality control sera such as ELITROL I and ELITROL II be used to monitor the performance of the assay.
Controls have to be performed :
- prior to assaying patient samples,
- at least once per day,
- after every calibration,
- and/or in accordance with laboratory and regulatory requirements.

Results should be within the defined ranges. If values fall outside of the defined ranges, each laboratory should take necessary corrective measures.

WASTE MANAGEMENT

Disposal of all waste material should be in accordance with local, state and federal regulatory requirements (please refer to the Safety Data Sheet (SDS)).

PERFORMANCE DATA

Performances were obtained on Selectra ProM, following CLSI technical recommendations, under controlled environmental conditions.

☞- Measuring range
a) Serum/Plasma
0.20 - 5.00 mg/dL (0.08 - 2.06 mmol/L)
Samples having greater concentrations should be diluted 1:5 with NaCl 9 g/L solution and re-assayed. This procedure extends the measuring range up to 25 mg/dL (10.28 mmol/L).
Do not report results outside this extended range.

For users with Selectra TouchPro software, the «dilute» function performs the sample dilution automatically. Results take the dilution into account.

b) Urine
1.0 - 20.0 mg/dL (0.41-8.23 mmol/L)
Samples having greater concentrations should be diluted 1:5 with NaCl 9 g/L solution and re-assayed. This procedure extends the measuring range up to 100 mg/dL (41.14 mmol/L)
Do not report results outside this extended range.

For users with Selectra TouchPro software, the «dilute» function performs the sample dilution automatically. Results take the dilution into account.

Limit of Detection (LoD) and Limit of Quantification (LoQ)
a) Serum/Plasma
LoD = 0.03 mg/dL (0.01 mmol/L)
LoQ = 0.20 mg/dL (0.08 mmol/L)
b) Urine
LoD = 0.1 mg/dL (0.04 mmol/L)
LoQ = 1.0 mg/dL (0.41 mmol/L)

☞- Precision
Imprecision data has been obtained on 2 Selectra Pro analyzers over 20 days (2 runs per day, tests performed in duplicate).
Representative results are presented below.

a) Serum/Plasma

		Mean		Within-run	Total
	n	mg/dL	mmol/L	CV (%)	
Low level	80	1.55	0.64	1.0	3.5
Medium level	80	2.51	1.03	1.3	3.7
High level	80	3.84	1.58	0.7	3.0

b) Urine

		Mean		Within-run	Total
	n	mg/dL	mmol/L	CV (%)	
Low level	80	1.2	0.49	2.9	9.2
Medium level	80	5.0	2.06	0.7	4.0
High level	80	16.0	6.58	0.8	3.3

- Correlation
a) Serum/Plasma
A comparative study has been performed between MAGNESIUM XB reagent on a Selectra ProM analyzer and a similar commercially available system on 102 human serum samples.
The sample concentrations ranged from 0.27 to 4.99 mg/dL (0.11 - 2.05 mmol/L).
The results are as follows :
Correlation coefficient : (r) = 0.996
Linear regression: y = 1.041x - 0.01 mg/dL (0.00 mmol/L).

b) Urine
A comparative study has been performed between MAGNESIUM XB reagent on a Selectra ProM analyzer and a similar commercially available system on 80 human urine samples.
The sample concentrations ranged from 1.7 to 19.6 mg/dL (0.70 - 8.06 mmol/L).
The results are as follows :
Correlation coefficient : (r) = 0.999
Linear regression: y = 1.011x + 0.1 (0.00 mmol/L).

☞- Limitations/Interferences
a) Serum/Plasma
- Studies have been performed to determine the level of interference from different compounds.
The following analyte levels were tested: 1.50 mg/dL and 3.90 mg/dL
No significant interference is defined by a recovery ≤±10% of the initial value.
Triglycerides : No significant interference up to 3000 mg/dL(33.90 mmol/L).
Unconjugated bilirubin : No significant interference up to 30.0 mg/dL. (513 µmol/L)
Conjugated bilirubin : No significant interference up to 29.5 mg/dL. (504 µmol/L)
Hemoglobin : No significant interference up to 500 mg/dL.
Calcium : No significant interference up to 20.0 mg/dL. (4.99 mmol/L)
Ascorbic acid: No significant interference up to 19.8 mg/dL.
Acetaminophen : No significant interference up to 30 mg/dL.
Acetylsalicylic acid : No significant interference up to 200 mg/dL

- In very rare cases, monoclonal gammopathies (multiple myeloma), in particular IgM type (Waldenstrom's macroglobulinemia) can cause unreliable results.[8]

- Many other substances and drugs may interfere. Some of them are listed in reviews published by Young.[9-10]

b) Urine
- Studies have been performed to determine the level of interference from different compounds.
The following magnesium levels were tested: 1.2 mg /dL and 15 mg/dL.

No significant interference is defined by a recovery ≤±10% of the initial value.
Conjugated bilirubin : Aucune interférence significative jusqu'à 29.5 mg/dL (504 µmol/L)
Hemoglobin : No significant interference up to 500 mg/dL.
Calcium : No significant interference up to 60.0 mg/dL (14.97 mmol/L)
Uric Acid : No significant interference up to100 mg/dL (5.95 mmol/L).
Urea : No significant interference up to 5000 mg/dL (832.50 mmol/L).
Ascorbic acid : No significant interference up to 19.8 mg/dL.
pH : No significant interference for pH values ranging between 2.5 à 6.0

- Many other substances and drugs may interfere. Some of them are listed in reviews published by Young.[9-10]

- On board stability/Calibration frequency
On Board Stability: 14 days
Calibration frequency: 7 days
Recalibrate when reagent lots change, when quality control results fall outside the established range and after a maintenance operation.

These performances have been obtained using ELITech Selectra ProM analyzer. Results may vary if a different instrument or a manual procedure is used. The performances of applications not validated by ELITech are not warranted and must be defined by the user.

DECLARATION OF SERIOUS INCIDENT

Please notify the manufacturer (through your distributor) and competent authority of the Member State of the european union in which the user and/or the patient is established, of any serious incident that has occurred in relation to the device. For other jurisdictions, the declaration of serious incident should be in accordance with local, state and federal regulatory requirements.
By reporting a serious incident, you provide information that can contribute to the safety of *in vitro* medical devices.

TECHNICAL ASSISTANCE

Contact your local distributor or ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

Español - ES

USO PREVISTO

ELITech Clinical Systems MAGNESIUM XB es un reactivo de diagnóstico *in vitro* diseñado para la determinación cuantitativa de magnesio en muestras de suero, plasma y orina humanas en equipos automatizados o equipos semiautomáticos.
El estándar está diseñado para la calibración del reactivo.
Estos dispositivos de diagnóstico *in vitro* están destinados unicamente para los profesionales.

SIGNIFICADO CLÍNICO [1-3]

El magnesio es el cuarto catión más abundante en el cuerpo humano. Es el cofactor de muchos sistemas enzimáticos, incluidas las enzimas dependientes de ATP, y también juega un papel activo en la homeostasis mineral ósea. Menos del 1% del magnesio total en el cuerpo humano es transportado por la sangre en la que se encuentra principalmente en forma de un ion libre, pero también está vinculado a proteínas (principalmente albúmina) o forma un complejo con varios aniones. La magnesemia mide el magnesio sanguíneo total, pero solo la fracción libre es biológicamente activa. La hipomagnesemia puede estar relacionada con pérdidas renales significativas (ingesta excesiva de diuréticos), trastornos gastrointestinales (malabsorción, diarrea), enfermedades endocrinas, más raramente con una ingesta inadecuada. La hipomagnesemia a menudo se asocia con hipocalemia y / o hipocalcemia. La hipermagnesemia es rara y casi siempre se debe a una ingesta excesiva (tratamiento parenteral, ingesta excesiva de tratamientos que contienen magnesio) o insuficiencia renal. La dosificación de magnesio en orina permite, en presencia de hipomagnesemia, identificar una etiología renal.
En la práctica clínica, la cuantificación de magnesio es indicada para ayudar en el diagnóstico de las causas de concentraciones anormales de calcio y / o potasio o de síntomas que sugieren hipo o hipermagnesemia, así como para el monitoreo de tratamientos basados en magnesio o calcio

LÍMITE DE UTILIZACIÓN

Debido a que la hipoalbuminemia puede desencadenar una seudohipomagnesemia, los resultados de magnesio sérico deben interpretarse en relación con los niveles séricos de proteína total y / o albúmina. [4]
La cuantificación del MAGNESIUM XB no puede ser utilizado solo para diagnosticar una enfermedad o patología específica.
Los resultados siempre deben compararse con los resultados de otras pruebas de diagnóstico, exámenes clínicos y el historial médico del paciente.

MÉTODO & PRINCIPIO [5]

Bleu de Xylidyl - Punto Final

El azul de xilidilo en el reactivo se combina con el magnesio de la muestra para formar un quelato rojo púrpura. El EGTA se usa para formar complejos de calcio y, por lo tanto, evita que interfiera con la prueba.
El aumento de la absorbancia a 505-510 nm y la disminución simultáneo de la absorbancia 620-630 nm son proporcionales a la concentración de magnesio en la muestra.

COMPOSICIÓN

Reactivo : R
Tampón AMP, pH 11.2
Azul de Xilidilo 120 µmol/L
Azida sódica < 0.1 % (p/p)
También contiene EGTA y tensioactivos para un rendimiento óptimo.

AMP: 2-amino-2-metil-1-propanol

Estándar : Std
Magnesio 2.0 mg/dL
823 µmol/L

MATERIALES REQUERIDOS PERO NO INCLUIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solución salina normal (NaCl 9 g/L).
- Equipos automáticos o semiautomáticos.
- Equipamiento general de laboratorio (p. ej. pipeta).
- No utilice materiales que no se requieren, tal como se indica anteriormente.

PRECAUCIONES DE USO Y ADVERTENCIAS

- El reactivo R contiene azida sódica que puede reaccionar con el plomo o el cobre de la tubería y formar potencialmente azidas metálicas explosivas. Cuando se elimine el reactivo enjuague con agua abundantemente para prevenir la acumulación de azidas.
- Tome las precauciones normales y respete las buenas prácticas de laboratorio.
- Para evitar contaminaciones utilizar equipo nuevo o completamente limpio.
- Consulte la Hoja de Datos de Seguridad (SDS) para un manejo adecuado.

ESTABILIDAD

Conservar a 2-8 °C y protegidos de la luz. No congelar.
No utilice después de la fecha de caducidad indicada en la etiqueta de los frascos.
El estándar debe cerrarse inmediatamente y correctamente para evitar contaminación y evaporación.
Estabilidad en el equipo:
La estabilidad es específica para cada equipo. (Referirse al § DATOS DE RENDIMIENTO).

PREPARACIÓN

El reactivo y el estándar están listos para su uso.

DETERIORACIÓN DEL PRODUCTO

- Los productos deben ser claros. Turbidez indicaría deterioro.
- No utilice el producto si este presenta signos evidentes de contaminación o deterioro (p. ej partículas).
- Un frasco dañado puede tener un impacto en el rendimiento del producto. No utilice el producto si este tiene signos físicos de deterioro (p. ej, fugas, frasco perforado).

MUESTRAS

Muestras requeridas [1,6]
- Suero
- Plasma (heparina de litio).
- Orina.
- El uso de cualquier otro tipo de muestra debe ser validado por el laboratorio.

Advertencias y precauciónes [1,2]
- El suero debe separarse de las células lo más rápido posible. [1,2]
- Las muestras deben estar libres de hemólisis [1,2]
- Después de la recolección, las muestras de orina deben acidificarse con ácido clorhídrico 6N a un pH <2 para evitar la precipitación de sal de magnesio. [1]

Las muestras deben de tomarse de acuerdo con las Buenas Prácticas de Laboratorio y las guías apropiadas establecidas.

Conservación y estabilidad [6]
Suero/Plasma
- 7 días a temperatura ambiente.
- 7 días a 2-8 °C
- 1 año a -20 °C

Orina (acidificada)
- 3 días a temperatura ambiente.
- 3 días a 2-8 °C
- 1 año a -20 °C

VALORES DE REFERENCIA [7]

Suero/plasma	mg/dL	mmol/L
	1.5 - 2.6	0.63 - 1.05
Orina *(recolectada de 24h)*	mg/24h	mmol/24 h
	73 - 122	3.0 - 5.0
	mg/dL*	mmol/L*
	4.9 - 8.1	2.0 - 3.3

* para un volumen de orina de 1.5 L por 24 horas

Nota : *Los valores anteriores son solo indicativos. Se recomienda que cada laboratorio establezca y mantenga sus propios valores de referencia en relación con la población destinataria.*

☞PROCEDIMIENTO

Procedimiento manual
Longitud de onda : 505 - 625 nm
Trayectoria óptica : 1 cm
Ratio muestra/reactivo : 1:100
Temperatura: 37 °C
Las muestras de orina deben diluirse 1:5 con una solución de NaCl 9 g/L antes de la medición
Leer contra blanco reactivo / agua destilada.

	CALIBRACIÓN	PRUEBA
Reactivo R	2 ml	2 ml
Estándar/Calibrador	20 µl	-
Muestra	-	20 µl

Mezcle y lea las absorbancias (A) después de una incubación de 5 minutos.

Procedimiento automático
Estos reactivos pueden ser utilizados en varios equipos. Para los equipos ELITech Selectra, las aplicaciones validadas están disponibles sobre pedido. Para el software Selectra TouchPro, use la aplicación incluida en el código de barras disponible al final de este inserto.

Las muestras de orina deben diluirse 1:5 con una solución de NaCl 9 g/L antes de la medición. Para los usuarios del software Selectra TouchPro, la dilución de orina se realiza automáticamente.

Información importante de programación:
El reactivo MAGNESIUM XB puede ser ligeramente contaminado con el reactivo CHOLESTEROL SL en Selectra ProM y ProXL. Con el fin de evitar contaminaciones en estos analizadores, programe incompatibilidades de la siguiente manera :

Software	Menú	Parámetro
TouchPro	compatibilidades de las sondas	incompatibilidad/ CHOLESTEROL - MAGNESIUM
Otros	Incompatibilidad de aguja	CHOLESTEROL: MAGNESIUM

☞CÁLCULO

$$\frac{\Delta A\ \text{Muestra}}{\Delta A\ \text{Estándar / calibrador}} \times n \qquad n = \text{concentración del estándar/ calibrador}$$

Para el cálculo de la concentración de magnesio en orina, multiplique el resultado por el factor de dilución (5). Para los usuarios del software Selectra TouchPro, los resultados toman en cuenta el factor de dilución.

Factor de conversión: mg/dL x 0.41 = mmol/L

CALIBRACIÓN

Para la referencia MGXB-0600 : ELICAL 2 o el estándar Magnesium XL son trazables al método de referencia absorción atómica
Para la referencia MGXB-0250 : ELICAL 2 es trazable al método de referencia absorción atómica

Frecuencia de calibración : la frecuencia de calibración es específica para cada equipo (referirse al § DATOS DE RENDIMIENTO).

CONTROL DE CALIDAD

Es recomendado que sueros de control tales como ELITROL I y ELITROL II sean usados para monitorear el rendimiento de las pruebas.
Los controles deben realizarse :
- antes que las muestras del paciente sean evaluadas,
- por lo menos una vez al día,
- después de cada calibración,
- y/o en acuerdo con el laboratorio y los requerimientos regulatorios.

Los resultados deben de encontrarse en el rango definido. Si los valores se encuentran fuera del mismo, cada laboratorio deberá tomar las medidas correctivas necesarias.

TRATAMIENTO DE LOS RESIDUOS

Todos los materiales de desecho deben eliminarse de acuerdo con los requisitos regulatorios locales, estatales y federales. (diríjase a la hoja de seguridad (SDS)).

DATOS DE RENDIMIENTO

El rendimiento fue obtenido en un Selectra ProM, siguiendo las recomendaciones técnicas del CLSI, bajo condiciones ambientales controladas.

☞- Rango analítico
a) Suero/Plasma
0.20 - 5.00 mg/dL (0.08 - 2.06 mmol/L)
Muestras con concentraciones mayores deben diluirse 1/5 con una solución NaCl 9 g/L y analizadas nuevamente. Este procedimiento extiende el rango analítico hasta 25 mg/dL (10.28 mmol/L).
No tome en cuenta resultados fuera del rango analítico extendido.

Para los usuarios del software Selectra TouchPro, la función «diluir» realiza la dilución de las muestras automáticamente. Los resultados toman en cuenta la dilución.

b) Orina
1.0 - 20.0 mg/dL (0.41-8.23 mmol/L)
Muestras con concentraciones mayores deben diluirse 1/5 con una solución NaCl 9 g/L y analizadas nuevamente. Este procedimiento extiende el rango analítico hasta 100 mg/dL (41.14 mmol/L).
No tome en cuenta resultados fuera del rango analítico extendido.

Para los usuarios del software Selectra TouchPro, la función «diluir» realiza la dilución de las muestras automáticamente. Los resultados toman en cuenta la dilución.

- Límite de detección (LoD), límite de Cuantificación (LoQ)
a) Suero/Plasma
LoD = 0.03 mg/dL (0.01 mmol/L)
LoQ = 0.20 mg/dL (0.08 mmol/L)
b) Orina
LoD = 0.1 mg/dL (0.04 mmol/L)
LoQ = 1.0 mg/dL (0.41 mmol/L)

☞- Precisión
Los datos de imprecisión fueron obtenidos en 2 equipos Selectra PRO durante 20 días (2 corridas por día, pruebas efectuadas en duplicado).
Resultados representativos se presentan a continuación:

a) Suero/Plasma

		Media		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Nivel bajo	80	1.55	0.64	1.0	3.5
Nivel medio	80	2.51	1.03	1.3	3.7
Nivel alto	80	3.84	1.58	0.7	3.0

b) Orina

		Media		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Nivel bajo	80	1.2	0.49	2.9	9.2
Nivel medio	80	5.0	2.06	0.7	4.0
Nivel alto	80	16.0	6.58	0.8	3.3

- Correlación
a) Suero/Plasma
Un estudio comparativo se llevó a cabo entre el reactivo MAGNESIUM XB en el equipo Selectra ProM y un sistema comercial similar en 102 muestras séricas.
Las concentraciones de las muestras se encuentran entre 0.27 y 4.99 mg/dL (0.11 - 2.05 mmol/L).
Los resultados son los siguientes :
Coeficiente de correlación: (r) = 0.996
Regresión linear : y = 1.041x - 0.01 mg/dL (0.00 mmol/L).

b) Orina
Un estudio comparativo se llevó a cabo entre el reactivo MAGNESIUM XB en el equipo Selectra ProM y un sistema comercial similar en 80 muestras urinarias.
Las concentraciones de las muestras se encuentran entre 1.7 y 19.6 mg/dL (0.70 - 8.06 mmol/L)..
Los resultados son los siguientes :
Coeficiente de correlación: (r) = 0.999
Regresión linear : y = 1.011x + 0.1 (0.00 mmol/L).

☞- Limitaciones/Interferencias
a) Suero/Plasma
- Estudios fueron llevados a cabo para determinar el nivel de interferencia de diferentes componentes.
Los niveles siguientes de magnesio fueron probados: 1.50 mg /dL y 3.90 mg/dL.
Definimos una interferencia no significativa cuando se obtiene una recuperación de ≤±10% con respecto al valor inicial.

Bilirrubina no conjugada: No hay interferencia significativa hasta 30.0 mg/dL (513 µmol/L)
Bilirrubina conjugada: No hay interferencia significativa hasta 29.5 mg/dL (504 µmol/L)
Hemoglobina: No hay interferencia significativa hasta 500 mg/dL
Calcio: No hay interferencia significativa hasta 20.0 mg/dL. (4.99 mmol/L)
Triglicéridos: No hay interferencia significativa hasta 3000 mg/dL(33.90 mmol/L)
Ácido ascórbico: No hay interferencia significativa hasta 19.8 mg/dL
Acetaminofén: No hay interferencia significativa hasta 30 mg/dL
Ácido acetilsalicílico: No hay interferencia significativa hasta 200 mg/dL

- En casos muy raros, las gammapatías monoclonales (mieloma múltiple), en particular el tipo IgM (macroglobulinemia de Waldenstrom) pueden producir resultados poco confiables.[8]

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en los artículos publicados por Young.[9-10]

b) Orina
- Estudios fueron llevados a cabo para determinar el nivel de interferencia de diferentes componentes.
Los niveles siguientes de magnesio fueron probados: 1.2 mg /dL y 15 mg/dL
Definimos una interferencia no significativa cuando se obtiene una recuperación de ≤±10% con respecto al valor inicial.

Bilirrubina conjugada: No hay interferencia significativa hasta 29.5 mg/dL (504 µmol/L)
Hemoglobina: No hay interferencia significativa hasta 500 mg/dL
Calcio: No hay interferencia significativa hasta 60.0 mg/dL (14.97 mmol/L)
Ácido urico: No hay interferencia significativa hasta 100 mg/dL (5.95 mmol/L).
Urea: No hay interferencia significativa hasta 5000 mg/dL (832.50 mmol/L).
Ácido ascórbico: No hay interferencia significativa hasta 19.8 mg/dL
pH: No hay interferencia significativa para valores de pH entre 2.5 y 6.0

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en los artículos publicados por Young.[9-10]

- Estabilidad en el equipo / frecuencia de calibración
Estabilidad en el equipo : 14 días
Frecuencia de calibración : 7 días
Recalibrar cuando los lotes de reactivo cambien, cuando los controles de calidad no se encuentren dentro del rango establecido, y después de operaciones de mantenimiento.

El rendimiento se ha obtenido utilizando el equipo ELITech Selectra ProM. Los resultados pueden variar si se utiliza un instrumento diferente o un procedimiento manual.
El rendimiento obtenido a partir de aplicaciones no validadas por ELITech no se garantiza y deben ser definidas por el usuario.

DECLARACIÓN DE INCIDENTES GRAVES

Por favor notifique al fabricante (por medio de su distribuidor) y autoridad competente del Estado miembro de la Unión Europea en donde el usuario o paciente radique, de cualquier incidente grave que se produzca con relación al dispositivo. Para otras jurisdicciones, la declaración de incidentes graves debe realizarse de acuerdo con los requisitos reglamentarios locales, estatales y federales. Reportando incidentes graves usted contribuye a proporcionar más información sobre la seguridad del dispositivo médico de diagnóstico *in vitro*.

ASISTENCIA TÉCNICA

Contacte a su distribuidor local o con ELITech Clinical Systems SAS (CCsupport@ elitechgroup.com)

Português – PT

UTILIZAÇÃO PREVISTA

ELITech Clinical Systems MAGNESIUM XB é um reagente para diagnóstico *in vitro* destinado à determinação quantitativa do magnésio em amostras de soro, plasma e urina humanas em analisadores automáticos ou semi-automáticos.
O padrão é destinado à calibração do reagente.
Estes dispositivos de diagnóstico *in vitro* são apenas para uso profissional.

SIGNIFICADO CLÍNICO [1-3]

O magnésio é o quarto cátion mais abundante no corpo humano. É o cofator para muitos sistemas enzimáticos, incluindo enzimas dependentes de ATP, e também desempenha um papel ativo na homeostase mineral óssea. Menos de 1% do magnésio total do corpo humano é transportado pelo sangue, onde é encontrado principalmente como íon livre, mas também ligado a proteínas (principalmente albumina) ou complexado com vários ânions. A magnnesemia mede o magnésio total, mas apenas o magnésio livre é biologicamente ativo. A hipomagnesemia pode ser causada por importantes perdas renais (ingestão excessiva de diuréticos), distúrbios gastrointestinais (má absorção, diarréia), distúrbios endócrinos, menos frequentemente devido à ingestão inadequada. A hipomagnesemia é frequentemente associada a hipocalemia e / ou hipocalcemia. A hipermagnesemia é rara e é causada quase sempre por ingestão excessiva (terapia parenteral, ingestão excessiva de medicamentos contendo magnésio) ou insuficiência renal.
A medida de magnésio na urina permite, na presença de deficiência de magnésio, identificar uma etiologia renal.
Na prática clínica, a medição de magnésio é indicada para ajudar a diagnosticar as causas de níveis ou sintomas anormais de cálcio e / ou potássio, sugerindo hipo ou hipermagnesemia, bem como para monitorar tratamentos à base de magnésio e / ou cálcio.

LIMITAÇÃO DE USO

Como a hipoalbuminemia pode desencadear pseudo-hipomagnesemia, os resultados séricos de magnésio devem ser interpretados em relação aos níveis séricos totais de proteína e / ou albumina.[4]
O ensaio quantitativo de MAGNESIUM XB sozinho não pode ser usado para diagnosticar uma doença ou uma patologia específica.
Os resultados devem ser interpretados em conjunto com outros resultados de testes de diagnóstico, achados clínicos e histórico médico do paciente.

MÉTODO & PRINCÍPIO [5]

Xylidyl azul - Punto final

Xylidyl azul no reagente combina com o magnésio da amostra para formar um quelato de vermelhopúrpura. O EGTA é usado para eliminar o cálcio e, assim, impedir que ele interfira no teste. O aumento imultâneo da absorvância a 505-510 nm e a diminuição da absorbância de 620-630 nm são proporcionais à concentração de magnésio na amostra.

COMPOSIÇÃO

Reagente : R
Tampão AMP, pH 11.2
Xylidyl azul 120 µmol/L
Azida de sódio < 0.1 % (p/p)
Também contém EGTA e surfactantes para desempenho ideal

AMP: 2-Amino-2-methyl-1-propanol

Padrão: Std
Magnésio 2.0 mg/dL
823 µmol/L

MATERIAIS NECESSÁRIOS MAS NÃO FORNECIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solução salina normal (NaCl 9 g/L).
- Analisador automáticos ou semi-automáticos.
- Equipamento geral de laboratório (por exemplo, pipeta ...).
- Não utilize materiais que não são necessários, tal como indicado acima.

PRECAUÇÕES DE USO E AVISOS

- O reagente R contém azida de sódio que pode reagir com o chumbo ou cobre das canalizações formando azidas metálicas explosivas. Ao manusear estes reagentes lave as mãos sempre com grandes quantidades de água para evitar a produção de azida.
- Utilize as precauções normais e siga as boas práticas de laboratório.
- Utilizar material de laboratório limpo ou destinado a uma única utilização de modo a evitar qualquer contaminação.
- Consulte a ficha de dados de segurança (SDS) para obter um manuseio adequado.

ESTABILIDADE

Conservar a 2-8 °C e ao abrigo da luz. Não congelar
Não utilizar após as datas de validade indicadas nos rótulos dos frascos.
O padrão deve ser imediatamente tampado para evitar a contaminação e evaporação.
Estabilidade em equipamentos:
A estabilidade a bordo é específica a cada equipamento (Consultar § DESEMPENHO)

☞CALIBRAÇÃO

Para referências URSL-0427/0507 : ELICAL 2 ou o padrão Urea Standard 50 mg/dL são rastreáveis relativamente ao método de referência ID-MS (Diluição Isotópica por Espectrometria de Massa).
Para referências URSL-0250/0455/0420/0500 : ELICAL 2. o é rastreável relativamente ao método de referência ID-MS (Diluição Isotópica por Espectrometria de Massa).

Frequência de calibração : A frequência de calibração é específica a cada equipamento (consultar § DESEMPENHO).

CONTROLE DE QUALIDADE

Recomenda-se o uso de soros de controle de qualidade, como ELITROL I e ELITROL II, para monitorar o desempenho do ensaio.
Os controles devem ser executados:
- antes de analisar amostras de pacientes,
- pelo menos uma vez por dia,
- após cada calibração,
- e/ou de acordo com os requisitos laboratoriais e regulamentares.

Os resultados devem estar dentro dos intervalos definidos. Se os valores ficarem fora dos intervalos definidos, cada laboratório deve tomar as medidas corretivas necessárias.

TRATAMENTO DOS RESÍDUOS

O descarte de todo material residual deve estar de acordo com os requisitos regulamentares locais, estaduais e federais (consulte a Ficha de dados de segurança (SDS)).

DESEMPENHO

Os desempenhos foram obtidos no Selectra ProM, seguindo as recomendações técnicas do CLSI, sob condições ambientais controladas.

- Precisão de medição

a) Soro / plasma

10 - 300 mg/dL (1.67 - 49.95 mmol/L)
As amostras com maiores concentrações devem ser diluídas 1:5 com solução de NaCl 9 g/L e ensaiado novamente. Este procedimento estende a faixa de medição até 1 500 mg/dL (249.75 mmol/L).
Não relatar resultados fora do intervalo de medição.

Para utilizadores do Selectra TouchPro, a função de «diluir» realiza a diluição do amostras automaticamente. Os resultados são tomados em consideração na diluição.

b) Urina

200 - 6 000 mg/dL (33 - 999 mmol/L).
Não relate resultados fora da faixa de medição.

- Limite de detecção (LoD) e limite de quantificação (LoQ)

a) Soro / plasma

LoD = 1.5 mg/dL (0.25 mmol/L)
LoQ = 5.0 mg/dL (0.83 mmol/L)

b) Urina

LoD = 18 mg/dL (3 mmol/L)
LoQ = 200 mg/dL (33 mmol/L)

- Precisão

Dados de imprecisão foram obtidos em 2 analisadores Selectra ProM ao longo de 20 dias (2 corridas por dia, testes realizados em duplicata).
Os resultados representativos são apresentados abaixo :

a) Soro / plasma

		Média		Intra-série	Total
	n	mg/dL	mmol/L	CV (%)	
Nível 1	80	18.0	3.00	1.6	3.2
Nível 2	80	59.0	9.82	1.2	2.2
Nível 3	80	144.6	24.08	1.0	2.1

b) Urina

		Média		Intra-série	Total
	n	mg/dL	mmol/L	CV (%)	
Nível 1	80	482	80	1.7	3.8
Nível 2	80	1165	194	0.6	3.1
Nível 3	80	2587	431	0.4	3.6

- Correlação

a) Soro / plasma

Foi realizado um estudo comparativo entre o reagente UREA UV SL em um analisador Selectra ProM e um sistema similar disponível comercialmente em 98 amostras de soro humano.
As concentrações da amostra variaram de 12.5 para 285.5 mg/dL (2.08 - 47.54 mmol/L).
Os resultados são os seguintes:
Coeficiente de correlação: (r) = 1.000
Regressão linear: y = 0.993x - 0.1 mg/dL (0.02 mmol/L)

☞*b) Urina*

Foi realizado um estudo comparativo entre o reagente UREA UV SL em um analisador Selectra ProM e um sistema similar disponível comercialmente em 53 amostras de urinas humanas.
As concentrações da amostra variaram de 203 para 5 569 mg/dL (34 - 927 mmol/L).
Os resultados são os seguintes:
Coeficiente de correlação: (r) = 0.999
Regressão linear: y = 1.000x + 52 mg/dL (9 mmol/L)

☞- Limitações/Interferências

a) Soro / plasma

Estudos foram realizados para determinar o nível de interferência de diferentes compostos.
Os seguintes níveis do ureia foram testados : 15.0 mg/dL e 60.1 mg/dL
Uma interferência não significativa é definida por uma recuperação ≤±10% do valor inicial.
Bilirubina não conjugada: Nenhuma interferência significativa até 30,0 mg/dL (513 µmol/L).
Bilirrubina conjugada: Nenhuma interferência significativa até 29.5 mg/dL (505 µmol/L).
Turvação: Nenhuma interferência significativa até 614 mg/dL (6.94 mmol/L) equivalente de triglicéridos.
Hemoglobina: Nenhuma interferência significativa até 500 mg/dL.
Ácido ascórbico: Nenhuma interferência significativa até 20.0 mg/dL.
Metildopa : Nenhuma interferência significativa até 1.0 mg/dL.

- Em casos muito raros, as gamopatias monoclonais (mieloma múltiplo), em particular, tipo IgM (macroglobulinemia de Waldenström) podem causar resultados não confiáveis.[5]

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young. [6-7].

b) Urina

Estudos foram realizados para determinar o nível de interferência de diferentes compostos.
Os seguintes níveis do ureia foram testados : 1 500 mg/dL e 3 000 mg/dL.
Uma interferência não significativa é definida por uma recuperação ≤±10% do valor inicial.
Bilirrubina conjugada: Nenhuma interferência significativa até 29.5 mg/dL (505 µmol/L).
Hemoglobina: Nenhuma interferência significativa até 500 mg/dL.
Ácido ascórbico : Nenhuma interferência signifi cativa até 20.0 mg/dL.
Ácido úrico : Nenhuma interferência significativa até 120 mg/dL (7.14 mmol/L).
pH : Nenhuma interferência significativa para valores de pH variando entre 2.5 e 12.0.

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young. [6-7].

- Estabilidade a bordo / frequência de calibração

Estabilidade a bordo: 14 dias
Frequência de calibração: 7 dias
Recalibre quando os lotes de reagentes mudarem, quando os resultados do controle de qualidade estiverem fora da faixa estabelecida e após uma operação de manutenção.

Estes desempenhos foram obtidos utilizando o analisador ELITech Selectra ProM. Os resultados podem variar se um instrumento diferente ou um procedimento manual for usado.
Os desempenhos de aplicações não validados pela ELITech não são garantidos e devem ser definidos pelo usuário.

☞DECLARAÇÃO DE INCIDENTE GRAVE

Notifique o fabricante (através do seu distribuidor) e a autoridade competente do Estado-Membro da união europeia em que o usuário e / ou o paciente está estabelecido, de qualquer incidente grave que tenha ocorrido em relação ao dispositivo.
Para outras jurisdições, a declaração de incidente grave deve estar de acordo com os requisitos regulamentares locais, estaduais e federais.
Ao relatar um incidente grave, você fornece informações que podem contribuir para a segurança de dispositivos médicos *in vitro*.

☞ASSISTÊNCIA TÉCNICA

Entre em contato com o seu distribuidor local ou com a ELITech Clinical Systems SAS. (CCsupport@elitechgroup.com).

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SYMBOLES/SYMBOLS/ SÍMBOLOS/SÍMBOLOS

- Les symboles utilisés sont décrits dans la norme ISO 15223-1 hormis ceux présentés ci-dessous.
- Symbols used are defined on ISO 15223-1 standard, except those presented below.
- Los símbolos utilizados son descritos en la norma ISO 15223-1 a la excepción de los presentados a continuación.
- Os símbolos utilizados são definidos na norma ISO 15223-1, exceto os apresentados abaixo.

CONT	Contient Content Contiene Conteúdo
R1	Réactif R1 Reagent R1 Reactivo R1 Reagente R1
R2	Réactif R2 Reagent R2 Reactivo R2 Reagente R2
Std	Standard Standard Estándar Padrão
☞	Modification par rapport à la version précédente Modification from previous version Modificación con respecto a la versión anterior Modificação relativamente à versão anterior
CE	Conformité Européenne European Conformity Conformidad Europea Conformidade Europeia

Note/Nota

- Uniquement pour les réf. **URSL-0250/0455**, utilisées avec le logiciel Selectra TouchPro.
- Only for ref. **URSL-0250/0455,** used with Selectra TouchPro software.
- Únicamente para las ref. **URSL-0250/0455,** utilizadas con el software Selectra TouchPro.
- Somente para ref. **URSL-0250/0455,** usados com o Selectra TouchPro.

URSL

Urea 0
640 PIT-URSL

ELITechGroup
EMPOWERING IVD

UREA UV SL

URSL

☞

URSL-0427	**R1**	*4 x 50 mL*	+ **R2**	*2 x 26 mL*	+ **Std**	*1 x 5 mL*
URSL-0507	**R1**	*5 x 100 mL*	+ **R2**	*1 x 127 mL*	+ **Std**	*1 x 5 mL*
URSL-0250	**R1**	*8 x 20 mL*	+ **R2**	*8 x 5 mL*		
URSL-0455	**R1**	*4 x 44 mL*	+ **R2**	*4 x 11 mL*		
URSL-0420	**R1**	*4 x 50 mL*	+ **R2**	*2 x 26 mL*		
URSL-0500	**R1**	*5 x 100 mL*	+ **R2**	*1 x 127 mL*		

CE

PIT-URSL-4-v23 (11/2020)

Français - FR

☞USAGE PRÉVU

ELITech Clinical Systems UREA UV SL est un réactif de diagnostic *in vitro*, destiné au dosage quantitatif de l'urée dans les échantillons de sérum, de plasma et d'urine humains sur des automates ou semi-automates.
Le standard est destiné à la calibration du réactif.
Ces dispositifs de diagnostic *in vitro* sont uniquement destinés aux professionnels.

☞SIGNIFICATION CLINIQUE [1-3]

L'urée est le principal produit du catabolisme protéique. Elle provient du foie et est principalement excrétée par les reins.
La concentration en urée dans le sang peut être augmentée par de nombreux facteurs liés soit à des causes pré-rénales (augmentation du catabolisme protéique comme lors d'une hémorragie au niveau du tractus gastro-intestinal, un choc), soit à des causes rénales (maladies rénales aiguës ou chroniques) ou post-rénales (obstruction à l'écoulement urinaire). L'urémie est également augmentée en cas de régime à haute valeur protéique ou de déshydratation. Une diminution de la concentration sérique en urée peut s'observer pendant la grossesse ou avec une alimentation pauvre en protéines.
En pratique le dosage de l'urée dans le sérum est effectué pour aider au diagnostic des pathologies rénales, pour le suivi des traitements de certaines de ces pathologies ainsi que pour le suivi de la fonction rénale en cours de certains traitements pouvant altérer cette fonction. En raison des nombreuses causes non rénales de variation des taux sériques, l'urée est un moins bon marqueur de la fonction rénale que la créatinine.

☞LIMITE D'UTILISATION

Le dosage de l'urée ne peut être utilisé seul pour diagnostiquer une maladie ou une pathologie spécifique.
Les résultats doivent toujours être confrontés aux résultats d'autres tests diagnostiques, aux examens cliniques, et à l'historique médical du patient.

☞MÉTHODE & PRINCIPE [4]

Uréase/GlDH – Cinétique

$$\text{Urée} + 2H_2O \xrightarrow{\text{Uréase}} 2NH_4^+ + CO_3^{2-}$$

$$NH_4^+ + \alpha\text{-Cétoglutarate} + NADH \xrightarrow{\text{GlDH}} \text{L-Glutamate} + NAD^+ + H_2O$$

GlDH = Glutamate déshydrogénase

☞COMPOSITION

Réactif 1 : R1

Tampon buffer, pH 7.60 (37 °C)			
α-Cétoglutarate		9	mmol/L
Uréase	≥	8 100	U/L
GlDH	≥	1 350	U/L
Azide de sodium	<	0.1	% (p/p)

Réactif 2 : R2

NADH		1.3	mmol/L
Azide de sodium	<	0.1	% (p/p)

Standard: Std (Ref : URSL-0427/0507)

Urea	50	mg/dL
	8.33	mmol/L

MATÉRIELS REQUIS MAIS NON FOURNIS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solution saline normale (NaCl 9 g/L).
- Automates ou semi-automates.
- Equipement général de laboratoire (ex. pipette).
- Ne pas utiliser de matériel ne figurant pas ci-dessus.

☞PRÉCAUTIONS D'EMPLOI ET MISES EN GARDE

- Consulter la fiche de données de sécurité (FDS) pour une manipulation appropriée.
- Les réactifs contiennent de l'azide de sodium qui peut réagir avec le plomb ou le cuivre et former des azides métalliques potentiellement explosifs. Lors de l'élimination de ces réactifs toujours rincer abondamment avec de l'eau pour éviter l'accumulation d'azides.
- Respecter les précautions d'usage et les bonnes pratiques de laboratoire.
- Utiliser du matériel de laboratoire propre ou à usage unique afin d'éviter toute contamination.
- Ne pas échanger les flacons réactifs de différents kits.

☞STABILITÉ

Stocker à 2-8 °C et à l'abri de la lumière. Ne pas congeler.
Ne pas utiliser après la date d'expiration indiquée sur les étiquettes des flacons.
Le standard doit être immédiatement et correctement refermé afin d'éviter toute contamination ou évaporation.
Stabilité à bord :
La stabilité à bord est spécifique à chaque automate. (Se référer au § PERFORMANCES).

PRÉPARATION

Le réactif et le standard sont prêts à l'emploi.

DÉTÉRIORATION DU PRODUIT

- Le produit doit être limpide. Tout trouble serait le signe d'une détérioration du produit.
- Ne pas utiliser le produit s'il y a des signes évidents de contamination ou de détérioration (ex : particules).
- Un flacon endommagé peut avoir un impact sur les performances du produit. Ne pas utiliser le produit si les flacons présentent des signes physiques de détérioration (par exemple, fuite, flacon percé).

☞ÉCHANTILLONS

Echantillons requis [3]
- Sérum
- Plasma (héparine de lithium)
- Urine
- L'utilisation de toute autre type d'échantillon doit être validée par le laboratoire.

Avertissements et précautions
- L'utilisation de thymol comme conservateur n'est pas recommandé car il inhibe l'activité de l'uréase. [3]
- Les échantillons doivent être prélevés selon les Bonnes Pratiques de Laboratoire et les guides appropriés qui sont mis en place.

Stockage et stabilité [2,3]
Sérum/Plasma
- 24h à température ambiante
- 1 semaine à 2-8°C
- 3 mois à -20°C

Urine
- 4 jours à 2-8°C en l'absence de contamination bactérienne.

☞VALEURS DE RÉFÉRENCE [2]

Sérum/plasma	mg/dL	mmol/L
Enfants <1 an	8.6 - 40.7	1.4 - 6.8
Enfants 1-18 ans	10.7 - 38.6	1.8 - 6.4
Adultes (18 - 60 ans)	12.9 - 42.9	2.14 - 7.14
Adultes (60 - 90 ans)	17.2 - 49.3	2.86 - 8.21
Adultes (> 90 ans)	21.4 - 66.5	3.57 - 11.07

Urine (recueil de 24h)	g/24h	mol/24 h
Adultes	26 - 43	0.43 - 0.71
	mg/dL*	mmol/L*
	1 700 - 2 900	290 - 470

* pour un volume urinaire de 1.5 L par 24 heures

Remarque : Les valeurs ci-dessus ne sont données qu'à titre indicatif. Il est recommandé à chaque laboratoire d'établir et de maintenir ses propres valeurs de référence par rapport à la population visée.

☞PROCÉDURE

Procédure manuelle

Longueur d'onde :	*340 nm*
Trajet optique :	*1 cm*
Ratio échantillon/réactif :	*1:100*
Température:	*37 °C*

Les échantillons urinaires doivent être dilués au 1/20 dans une solution de NaCl 9 g/L avant la mesure.

Lire contre l'eau distillée.

Réactif de travail (4 volumes de R1 + 1 volume de R2)	1000 µL
Echantillon	10 µL

Mélanger et après 30 secondes d'incubation, lire l'absorbance toutes les 30 secondes pendant 90 secondes. Mesurer la variation d'absorbance par minute (ΔA/min.)

Procédure sur automate
Ces réactifs peuvent être utilisés sur différents automates. Pour les automates ELITech Selectra, les applications validées sont disponibles sur demande. Avec le logiciel Selectra TouchPro, utilisez l'application incluse dans le code barre disponible à la fin de cette notice.

Les échantillons urinaires doivent être dilués au 1/20 dans une solution de NaCl 9 g/L avant la mesure. Pour les utilisateurs du logiciel Selectra TouchPro, la dilution des urines est réalisée automatiquement.

☞CALCUL

$$\frac{\Delta A/\text{min}_{\text{Echantillon}}}{\Delta A/\text{min}_{\text{Calibrant Standard}}} \times n \quad n = \text{concentration du calibrant/Standard}$$

Pour le calcul de la concentration de l'urée dans les urines, multiplier le résultat par le facteur de dilution (20). Pour les utilisateurs du logiciel Selectra TouchPro, les résultats tiennent compte du facteur de dilution.

Facteur de conversion : mg/dL x 0.1665 = mmol/L

☞CALIBRATION

Pour les références URSL-0427/0507 : ELICAL 2 et Urea Standard 50 mg/dL sont traçables par rapport à la méthode de référence ID-MS (Dilution Isotopique - Spectrométrie de Masse).
Pour les références URSL-0250/0455/0420/0500 : ELICAL 2 est traçable par rapport à la méthode de référence ID-MS (Dilution Isotopique - Spectrométrie de Masse).

Fréquence de calibration : La fréquence de calibration est spécifique à chaque automate (se référer au § PERFORMANCES).

CONTRÔLE QUALITÉ

Il est recommandé d'utiliser des sérums de contrôle tels que ELITROL I et ELITROL II pour surveiller les performances du dosage.
Ces contrôles doivent être effectués :
- avant que les échantillons de patients soient testés,
- au moins une fois par jour,
- après chaque calibration,
- et/ou en accord avec les requis du laboratoire et des exigences réglementaires.

Les résultats doivent être dans les intervalles définis. Si les valeurs se situent en dehors des plages définies, chaque laboratoire devra prendre les mesures correctives nécessaires.

TRAITEMENT DES DÉCHETS

L'élimination de tous les déchets doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales (veuillez vous référer à la fiche de données de sécurité (FDS)).

PERFORMANCES

Les performances ont été obtenues sur l'automate Selectra ProM, en suivant les recommandations CLSI, dans des conditions environnementales contrôlées.

- Domaine de mesure

a) Sérum/Plasma

10 - 300 mg/dL (1.67 - 49.95 mmol/L).

Les échantillons ayant des concentrations supérieures devront être dilués au 1/5 dans une solution de NaCl 9 g/L et redosés. Cette procédure étend le domaine de mesure jusqu'à 1 500 mg/dL (249.75 mmol/L).
Ne pas communiquer de résultats en dehors du domaine de mesure étendu.

Pour les utilisateurs du logiciel Selectra TouchPro, la fonction « diluer » réalise la dilution des échantillons automatiquement. Les résultats tiennent compte de la dilution.

b) Urine

200 - 6 000 mg/dL (33 - 999 mmol/L).

Ne pas communiquer de résultats en dehors du domaine de mesure.

- Limite de Détection (LoD) et Limite de Quantification (LoQ)

a) Sérum/Plasma

LoD = 1.5 mg/dL (0.25 mmol/L)
LoQ = 5.0 mg/dL (0.83 mmol/L)

b) Urine

LoD = 18 mg/dL (3 mmol/L)
LoQ = 200 mg/dL (33 mmol/L)

- Précision

Les données d'imprécision ont été obtenues sur 2 automates Selectra ProM sur 20 jours (2 routines par jour, tests effectués en double).
Des résultats représentatifs sont présentés ci dessous :

a) Sérum/Plasma

		Moyenne		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Niveau 1	80	18.0	3.00	1.6	3.2
Niveau 2	80	59.0	9.82	1.2	2.2
Niveau 3	80	144.6	24.08	1.0	2.1

b) Urine

		Moyenne		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Niveau 1	80	482	80	1.7	3.8
Niveau 2	80	1165	194	0.6	3.1
Niveau 3	80	2587	431	0.4	3.6

- Corrélation

a) Sérum/Plasma

Une étude comparative a été réalisée entre le réactif UREA UV SL sur un automate Selectra ProM et un système similaire disponible sur le marché sur 98 échantillons sériques.
Les concentrations des échantillons s'échelonnent de 12.5 à 285.5 mg/dL (2.08 - 47.54 mmol/L).
Les résultats sont les suivants :
Coefficient de corrélation: (r) = 1.000
Droite de régression : y = 0.993x - 0.1 mg/dL (0.02 mmol/L)

☞*b) Urine*

Une étude comparative a été réalisée entre le réactif UREA UV SL sur un automate Selectra ProM et un système similaire disponible sur le marché sur 53 échantillons urinaires.
Les concentrations des échantillons s'échelonnent de 203 à 5 569 mg/dL (34 - 927 mmol/L).
Les résultats sont les suivants :
Coefficient de corrélation: (r) = 0.999
Droite de régression : y = 1.000x + 52 mg/dL (9 mmol/L)

☞- Limitations/Interférences

a) Sérum/Plasma

- Des tests ont été réalisés pour déterminer le niveau d'interférence de différents composés.
Les niveaux suivants d'urée ont été testés: 15.0 mg/dL et 60.1 mg/dL.
L'absence d'interférence significative est définie par un recouvrement ≤±10% de la valeur initiale.
Bilirubine non-conjuguée : Aucune interférence significative jusqu'à 30.0 mg/dL (513 µmol/L).
Bilirubine conjuguée : Aucune interférence significative jusqu'à 29.5 mg/dL (505 µmol/L).
Turbidité: Aucune interférence significative jusqu'à 614 mg/dL (6.94 mmol/L) équivalent en Triglycérides.
Hémoglobine : Aucune interférence significative jusqu'à 500 mg/dL.
Acide ascorbique: Aucune interférence significative jusqu'à 20.0 mg/dL.
MéthylDopa: Aucune interférence significative jusqu'à 1.0 mg/dL.

- Dans des cas très rares, les gammapathies monoclonales (myélome multiple), en particulier de type IgM (Macroglobulinémie de Waldenström) peuvent être à l'origine de résultats peu fiables.[5]

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.[6-7]

b) Urine

- Des tests ont été réalisés pour déterminer le niveau d'interférence de différents composés.
Les niveaux suivants d'urée ont été testés: 1 500 mg/dL et 3 000 mg/dL.
L'absence d'interférence significative est définie par un recouvrement ≤±10% de la valeur initiale.
Bilirubine conjuguée : Aucune interférence significative jusqu'à 29.5 mg/dL (505 µmol/L).
Hémoglobine : Aucune interférence significative jusqu'à 500 mg/dL.
Acide ascorbique: Aucune interférence significative jusqu'à 20.0 mg/dL.
Acide Urique: Aucune interférence significative jusqu'à 120 mg/dL (7.14 mmol/L).
pH: Aucune interférence significative pour des valeurs de pH de 2.5 à 12.0.

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.[6-7]

- Stabilité à bord / fréquence de calibration

Stabilité à bord : 14 jours
Fréquence de calibration : 7 jours
Une nouvelle calibration doit être effectuée après chaque changement de lot de réactif, lorsque les résultats du ou des contrôles de qualité sont hors de l'intervalle établi, et après une opération de maintenance.

Ces performances ont été obtenues sur un automate ELITech Selectra ProM. Les résultats peuvent varier si le réactif est utilisé sur un automate différent ou en méthode manuelle.
Les performances obtenues à partir d'applications non validées par ELITech ne peuvent être garanties et doivent être définies par l'utilisateur.

☞DECLARATION DES INCIDENTS GRAVES

Veuillez notifier au fabricant (par l'intermédiaire de votre distributeur) et à l'autorité compétente de l'Etat membre de l'union européenne dans lequel l'utilisateur et/ou le patient est établi, les cas d'incident grave survenu en lien avec le dispositif.
Pour les autres juridictions, la déclaration d'incident grave doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales.
En signalant les incidents graves, vous contribuez à fournir davantage d'informations sur la sécurité des dispositifs médicaux de diagnostic *in vitro*.

☞ASSISTANCE TECHNIQUE

Contacter votre distributeur local ou ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

English - EN

☞INTENDED USE

ELITech Clinical Systems UREA UV SL is an *in vitro* diagnostic reagent intended for the quantitative determination of urea in human serum, plasma and urine samples on analyzers or semi-automatic analyzers.
The standard is intended for the calibration of the reagent.
These *in vitro* diagnostic devices are for professional use only.

☞CLINICAL SIGNIFICANCE [1-3]

Urea is the major byproduct of protein catabolism. It originates from the liver and is mostly excreted though the kidneys.
Blood urea concentrations can be increased by numerous factors linked to prerenal causes (increased protein catabolism as in hemorrhage into gastrointestinal tract, shock), renal causes (acute or chronic renal diseases) or postrenal causes (obstruct to urine flow). Uremia is also increased by high-protein diet or dehydration. A decreased serum urea concentration can be observed during pregnancy or with a low-protein diet.
In practice, urea measurement in serum is performed to help diagnose kidney diseases, to monitor treatments against these pathologies or to monitor renal function during treatments that may impair this function. Due to many non-renal causes for seric level variation, urea is however a less good marker of kidney function than creatinine.

☞LIMITATION OF USE

The quantitative assay of urea alone can not be used to diagnose a disease or a specific pathology.
The results must be interpreted in conjunction with other diagnostic test results, clinical findings and the patient's medical history.

☞METHOD & PRINCIPLE [4]

Urease/GlDH - Kinetic.

$$Urea + 2H_20 \xrightarrow{Urease} 2NH_4^+ + CO_3^{2-}$$

$$NH_4^+ + \alpha\text{-Ketoglutarate} + NADH \xrightarrow{GlDH} \text{L-Glutamate} + NAD^+ + H_20$$

GlDH = Glutamate dehydrogenase

☞COMPOSITION

Reagent 1 : R1
Tris buffer, pH 7.60 (37 °C)
α-Ketoglutarate 9 mmol/L
Urease ≥ 8100 U/L
GlDH ≥ 1 350 U/L
Sodium azide < 0.1% (w/w)
Reagent 2 : R2
NADH 1.3 mmol/L
Sodium azide < 0.1% (w/w)
Standard: Std (Ref : URSL-0427/0507)
Urea 50 mg/dL
8.33 mmol/L

MATERIALS REQUIRED BUT NOT PROVIDED

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Normal saline solution (NaCl 9 g/L).
- Analyzers or semi-automatic analyzers.
- General Laboratory equipment (e.g. pipette).
- Do not use materials that are not required as indicated above.

☞PRECAUTIONS FOR USE AND WARNINGS

- Consult Safety Data Sheet (SDS) for a proper handling.
-The reagents contain sodium azide which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of these reagents always flush with copious amounts of water to prevent azide buildup.
- Take normal precautions and adhere to good laboratory practice.
- Use clean or single use laboratory equipment only to avoid contamination.
- Do not interchange reagent vials from different kits.

☞STABILITY

Store at 2-8 °C and protect from light. Do not freeze.
Do not use after expiration dates indicated on the vial labels.
The standard should be immediately and tightly capped to prevent contamination and evaporation.
On board stability :
The on-board stability is specific for each analyzer. (Refer to § PERFORMANCE DATA).

PREPARATION

The reagent and standard are ready to use.

PRODUCT DETERIORATION

- The product should be clear. Cloudiness would indicate deterioration.
- Do not use the product if there is visible evidence of contamination or damage (e.g. particle matter).
- Damage to the product container may impact on product performance. Do not use the product if there is physical evidence of deterioration (e.g. leakages or punctured container).

☞SAMPLES

Specimen [3]
- Serum.
- Plasma (lithium heparin).
- Urine.
- Using any other specimen type should be validated by the laboratory.

Warnings and precautions
- Addition of thymol as preservative is not recommended as it inhibits urease activity [3]
- Samples should be collected in accordance with Good Laboratory Practice and appropriate guidelines that may be in place.

Storage and stability [2,3]
Serum/plasma
- 24h at room temperature.
- 1 week at 2-8°C.
- 3 months at -20°C.
Urine
- 4 days at 2-8°C provided bacterial contamination is avoided.

☞REFERENCE VALUES [2]

Serum/plasma	mg/dL	mmol/L
Children <1 year old	8.6 - 40.7	1.4 - 6.8
Children 1-18 years old	10.7 - 38.6	1.8 - 6.4
Adults (18 - 60 years)	12.9 - 42.9	2.14 - 7.14
Adults (60 - 90 years)	17.2 - 49.3	2.86 - 8.21
Adults (>90 years)	21.4 - 66.5	3.57 - 11.07

Urine (24h - collection)	g/24h	mol/24 h
Adults	26 - 43	0.43 - 0.71
	mg/dL*	mmol/L*
	1 700 - 2 900	290 - 470

* for a urinary volume of 1.5 L per 24 hours

Note : *The quoted range should serve as a guide only. It is recommended that each laboratory verifies this range or establishes a reference interval for the intended population.*

☞PROCEDURE

Manual Procedure
Wavelength : 340 nm
Optical path : 1 cm
Sample/ Reagent ratio : 1:100
Temperature: 37 °C
Urine samples must be diluted 1:20 with NaCl 9 g/L solution before measurement.
Read against distilled water.

Working reagent (4 volumes of R1 + 1 volume of R2)	1000 µL
Sample	10 µL

Mix and after 30 seconds incubation, read absorbance at 30 seconds intervals during 90 seconds. Calculate the change of absorbances per minute (ΔA/min).

Automatic Procedure
These reagents may be used on several automatic analyzers. For ELITech Selectra Analyzers, validated applications are available on request. For Selectra TouchPro software, use the application included in the barcode available at the end of this insert.

Urine samples must be diluted 1:20 with NaCl 9 g/L solution before measurement. For users of Selectra TouchPro software, urine dilution is performed automatically.

☞CALCULATION

$$\frac{\Delta A/\text{min. Sample}}{\Delta A/\text{min. Calibrator/Standard}} \times n$$ n = Calibrator/ standard concentration

For the calculation of urea concentration in urine, multiply the result by the dilution factor (20). For users of Selectra TouchPro software, the results take the dilution factor into account.

Conversion factor : mg/dL x 0.1665 = mmol/L

☞CALIBRATION

For the reference URSL-0427/0507 : ELICAL 2 and Urea Standard 50 mg/dL are traceable to ID-MS (Isotope Dilution - Mass Spectrometry) reference method.
For the reference URSL-0250/0455/0420/0500 : ELICAL 2 is traceable to ID-MS (Isotope Dilution - Mass Spectrometry) reference method.

Calibration frequency : The calibration is specific for each analyzer. (Refer to § PERFORMANCE DATA).

QUALITY CONTROL

It is recommended that quality control sera such as ELITROL I and ELITROL II be used to monitor the performance of the assay.
Controls have to be performed :
- prior to assaying patient samples,
- at least once per day,
- after every calibration,
- and/or in accordance with laboratory and regulatory requirements.

Results should be within the defined ranges. If values fall outside of the defined ranges, each laboratory should take necessary corrective measures.

WASTE MANAGEMENT

Disposal of all waste material should be in accordance with local, state and federal regulatory requirements (please refer to the Safety Data Sheet (SDS)).

PERFORMANCES

Performances were obtained on Selectra ProM, following CLSI technical recommendations, under controlled environmental conditions.

- Measuring range
a) Serum/Plasma

10 - 300 mg/dL (1.67 - 49.95 mmol/L)
Samples having greater concentrations should be diluted 1:5 with NaCl 9 g/L solution and re-assayed. This procedure extends the measuring range up to 1 500 mg/dL (249.75 mmol/L).
Do not report results outside this extended range.

For users with Selectra TouchPro software, the «dilute» function performs the sample dilution automatically. Results take the dilution into account.

b) Urine

200 - 6 000 mg/dL (33 - 999 mmol/L)

Do not report results outside the measuring range.

Limit of Detection (LoD) and Limit of Quantification (LoQ)
a) Serum/Plasma

LoD = 1.5 mg/dL (0.25 mmol/L)
LoQ = 5.0 mg/dL (0.83 mmol/L)

b) Urine

LoD = 18 mg/dL (3 mmol/L)
LoQ = 200 mg/dL (33 mmol/L)

- Precision

Imprecision data has been obtained on 2 Selectra ProM analyzers over 20 days (2 runs per day, tests performed in duplicate).

Representative results are presented below :

a) Serum/Plasma

		Mean		Within-run	Total
	n	mg/dL	mmol/L	CV (%)	
Level 1	80	18.0	3.00	1.6	3.2
Level 2	80	59.0	9.82	1.2	2.2
Level 3	80	144.6	24.08	1.0	2.1

b) Urine

		Mean		Within-run	Total
	n	mg/dL	mmol/L	CV (%)	
Level 1	80	482	80	1.7	3.8
Level 2	80	1165	194	0.6	3.1
Level 3	80	2587	431	0.4	3.6

- Correlation
a) Serum/Plasma
A comparative study has been performed between UREA UV SL reagent on a Selectra ProM analyzer and a similar commercially available system on 98 human serum samples.
The sample concentrations ranged from 12.5 to 285.5 mg/dL (2.08 - 47.54 mmol/L).
The results are as follows :
Correlation coefficient : (r) = 1.000
Linear regression: y = 0.993x - 0.1 mg/dL (0.02 mmol/L)

☞*b) Urine*
A comparative study has been performed between UREA UV SL reagent on a Selectra ProM analyzer and a similar commercially available system 53 human urine samples.
The sample concentrations ranged from 203 to 5 569 mg/dL (34 - 927 mmol/L).
The results are as follows :
Correlation coefficient : (r) = 0.999
Linear regression: y = 1.000x + 52 mg/dL (9 mmol/L)

☞- Limitations/Interferences
a) Serum/Plasma
Studies have been performed to determine the level of interference from different compounds.
The following urea levels were tested: 15.0 mg/dL and 60.1 mg/dL.
No significant interference is defined by a recovery ≤±10% of the initial value.
Unconjugated Bilirubin: No significant interference up to 30.0 mg/dL (513 µmol/L).
Conjugated Bilirubin: No significant interference up to 29.5 mg/dL (505 µmol/L).
Turbidity: No significant interference up to 614 mg/dL (6.94 mmol/L) Triglyceride equivalent.
Hemoglobin: No significant interference up 500 mg/dL.
Ascorbic acid: No significant interference up 20.0 mg/dL.
Methyl dopa: No significant interference up 1.0 mg/dL.

- In very rare cases, monoclonal gammopathies (multiple myeloma), in particular IgM type (Waldenstrom's macroglobulinemia) can cause unreliable results.[5]

- Many other substances and drugs may interfere. Some of them are listed in reviews published by Young.[6-7]

b) Urine

- Studies have been performed to determine the level of interference from different compounds.
The following urea levels were tested: 1 500 mg/dL and 3 000 mg/dL.
No significant interference is defined by a recovery ≤±10% of the initial value.
Conjugated Bilirubin: No significant interference up to 29.5 mg/dL (505 µmol/L).
Hemoglobin: No significant interference up 500 mg/dL.
Ascorbic acid: No significant interference up 20.0 mg/dL.
Uric acid: No significant interference up 120 mg/dL (7.14 mmol/L).
pH: No significant interference for pH values ranging between 2.5 and 12.0.

- Many other substances and drugs may interfere. Some of them are listed in reviews published by Young.[6-7]

- On board stability/Calibration frequency
On Board Stability: 14 days
Calibration frequency: 7 days
Recalibrate when reagent lots change, when quality control results fall outside the established range and after a maintenance operation.

These performances have been obtained using ELITech Selectra ProM analyzer. Results may vary if a different instrument or a manual procedure is used. The performances of applications not validated by ELITech are not warranted and must be defined by the user.

☞DECLARATION OF SERIOUS INCIDENT

Please notify the manufacturer (through your distributor) and competent authority of the Member State of the european union in which the user and/or the patient is established, of any serious incident that has occurred in relation to the device. For other jurisdictions, the declaration of serious incident should be in accordance with local, state and federal regulatory requirements. By reporting a serious incident, you provide information that can contribute to the safety of *in vitro* medical devices.

☞TECHNICAL ASSISTANCE

Contact your local distributor or ELITech Clinical Systems SAS (CCsupport@elitechgroup.com).

Español - ES

☞USO PREVISTO

ELITech Clinical Systems UREA UV SL es un reactivo de diagnóstico *in vitro* diseñado para la determinación cuantitativa de la urea en muestras de suero, plasma y orina humanas en equipos automatizados o equipos semiautomáticos.
El estándar está diseñado para la calibración del reactivo.
Estos dispositivos de diagnóstico *in vitro* están destinados unicamente para los profesionales.

☞SIGNIFICADO CLÍNICO [1-3]

La urea es el principal subproducto del catabolismo proteico. Se origina en el hígado y se excreta principalmente a través de los riñones.
Las concentraciones de urea en sangre pueden incrementarse por numerosos factores relacionados con causas prerrenales (aumento del catabolismo de las proteínas como en la hemorragia en el tracto gastrointestinal, shock) o causas renales (enfermedades renales agudas o crónicas) o causas post renales (obstrucción del flujo de orina). La uremia también se incrementa por la dieta alta en proteínas o la deshidratación. Se puede observar una disminución de la concentración sérica de urea durante el embarazo o con una dieta baja en proteínas.
En la práctica, la medición de la urea en suero se realiza para ayudar a diagnosticar enfermedades renales, para controlar los tratamientos contra estas patologías o para controlar la función renal durante los tratamientos que pueden afectar esta función. Debido a muchas causas no renales para la variación del nivel sérico, sin embargo la urea es un marcador menos bueno de la función renal que la creatinina.

☞LÍMITE DE UTILIZACIÓN

La cuantificación de la urea no puede ser utilizado solo para diagnosticar una enfermedad o patología específica.
Los resultados siempre deben compararse con los resultados de otras pruebas de diagnóstico, exámenes clínicos y el historial médico del paciente.

☞MÉTODO & PRINCIPIO [4]

Urease/GlDH – Cinética:

$$Urea + 2H_2O \xrightarrow{Ureasa} 2NH_4^+ + CO_3^{2-}$$

$$NH_4^+ + \alpha\text{-Cetoglutarato} + NADH \xrightarrow{GIDH} \text{L-Glutamato} + NAD^+ + H_2O$$

GIDH = Glutamato deshidrogenasa

☞COMPOSICIÓN

Reactivo 1 : R1
Tampón Tris, pH 7.60 (37 °C)
α-Cetoglutarato 9 mmol/L
Ureasa ≥ 8 100 U/L
GIDH ≥ 1 350 U/L
Azida sódica < 0.1 % (p/p)
Reactivo 2 : R2
NADH 1.3 mmol/L
Azida sódica < 0.1 % (p/p)
Estándar : Std (Ref : URSL-0427/0507)
Urea 50 mg/dL
8.33 mmol/L

MATERIALES REQUERIDOS PERO NO INCLUIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solución salina normal (NaCl 9 g/L).
- Equipos automatizados o equipos semiautomáticos.
- Equipamiento general de laboratorio (p. ej. pipeta).
- No utilice materiales que no se requieren, tal como se indica anteriormente.

☞PRECAUCIONES DE USO Y ADVERTENCIAS

- Consulte la Hoja de Datos de Seguridad (SDS) para un manejo adecuado.
- Los reactivos contienen azida sódica que puede reaccionar con el plomo o el cobre de la tubería y formar potencialmente azidas metálicas explosivas. Cuando se elimine el reactivo enjuague con agua abundantemente para prevenir la acumulación de azidas.
- Tome las precauciones normales y respete las buenas prácticas de laboratorio.
- Para evitar contaminaciones utilizar equipo nuevo o completamente limpio.
- No intercambie los frascos de reactivos de diferentes kits.

☞ESTABILIDAD

Conservar a 2-8 °C y protegidos de la luz. No congelar.
No utilice después de la fecha de caducidad indicada en la etiqueta de los frascos.
El estándar debe cerrarse inmediatamente y correctamente para evitar contaminación y evaporación.
Estabilidad en el equipo:
La estabilidad es específica para cada equipo. (Referirse al § DATOS DE RENDIMIENTO).

PREPARACIÓN

El reactivo y el estándar están listos para su uso.

DETERIORACIÓN DEL PRODUCTO

- El producto debe ser claro. Turbidez indicaría deterioro.
- No utilice el producto si este presenta signos evidentes de contaminación o deterioro (p. ej partículas).
- Un frasco dañado puede tener un impacto en el rendimiento del producto. No utilice el producto si este tiene signos físicos de deterioro (p. ej, fugas, frasco perforado).

☞MUESTRAS

Muestras requeridas [3]
- Suero
- Plasma (heparina de litio).
- Orina.
- El uso de cualquier otro tipo de muestra debe ser validado por el laboratorio.

Advertencias y precauciónes
- No se recomienda la adición de timol como conservador, ya que inhibe la actividad de la ureasa. [3]
- Las muestras deben de tomarse de acuerdo con las Buenas Prácticas de Laboratorio y las guías apropiadas establecidas.

Conservación y estabilidad [2,3]
Suero/Plasma
- 24h a temperatura ambiente.
- 1 semana a 2-8 °C
- 3 meses a -20 °C
Orina
- 4 días a 2-8 °C en ausencia de contaminación bacteriana.

☞VALORES DE REFERENCIA [2]

Suero/plasma	mg/dL	mmol/L
Niños <1 años	8.6 - 40.7	1.4 - 6.8
Niños 1-18 años	10.7 - 38.6	1.8 - 6.4
Adultos (18 - 60 años)	12.9 - 42.9	2.14 - 7.14
Adultos (60 - 90 años)	17.2 - 49.3	2.86 - 8.21
Adultos (> 90 años)	21.4 - 66.5	3.57 - 11.07

Orina (recolectada de 24h)	g/24h	mol/24 h
Adultos	26 - 43	0.43 - 0.71
	mg/dL*	mmol/L*
	1 700 - 2 900	290 - 470

* para un volumen de orina de 1.5 L por 24 horas

Nota : *Los valores anteriores son solo indicativos. Se recomienda que cada laboratorio establezca y mantenga sus propios valores de referencia en relación con la población destinataria.*

☞PROCEDIMIENTO

Procedimiento manual
Longitud de onda : 340 nm
Trayectoria óptica : 1 cm
Ratio muestra/reactivo : 1:100
Temperatura: 37 °C
Las muestras de orina deben diluirse 1:20 con una solución de NaCl 9 g/L antes de la medición
Leer contra agua destilada.

Reactivo de trabajo (4 volúmenes de R1 +1 volumen de R2)	1000 µL
Muestra	10 µL

Mezclar después de incubar 30 segundos, leer la absorbancia a intervalos de 30 segundos durante 90 segundos. Calcule el cambio de absorbancia por minuto (ΔA/min).

Procedimiento automático
Estos reactivos pueden ser utilizados en varios equipos. Para los equipos ELITech Selectra, las aplicaciones validadas están disponibles sobre pedido. Para el software Selectra TouchPro, use la aplicación incluida en el código de barras disponible al final de este inserto.

Las muestras de orina deben diluirse 1:20 con una solución de NaCl 9 g/L antes de la medición. Para los usuarios del software Selectra TouchPro, la dilución de orina se realiza automáticamente.

☞CÁLCULO

$$\frac{\Delta A/\text{min. Muestra}}{\Delta A/\text{min. Estándar/calibrador}} \times n$$ n = concentración del estándar/calibrador

Para el cálculo de la concentración de urea en orina, multiplique el resultado por el factor de dilución (20). Para los usuarios del software Selectra TouchPro, los resultados toman en cuenta el factor de dilución.

Factor de conversión: mg/dL x 0.1665 = mmol/L

☞CALIBRACIÓN

Para las referencias URSL-0427/0507 : ELICAL 2 o el estándar Urea Standard 50 mg/dL son trazables al método de referencia DI-EM (Dilución Isotópica - Espectrometria de Masas)
Para las referencias URSL-0250/0455/0420/0500 : ELICAL 2 es trazable al método de referencia DI-EM (Dilución Isotópica - Espectrometria de Masas).

Frecuencia de calibración : la frecuencia de calibración es específica para cada equipo (referirse al § DATOS DE RENDIMIENTO).

CONTROL DE CALIDAD

Es recomendado que sueros de control tales como ELITROL I y ELITROL II sean usados para monitorear el rendimiento de las pruebas.
Los controles deben realizarse :
- antes que las muestras del paciente sean evaluadas,
- por lo menos una vez al día,
- después de cada calibración,
- y/o en acuerdo con el laboratorio y los requerimientos regulatorios.

Los resultados deben de encontrarse en el rango definido. Si los valores se encuentran fuera del mismo, cada laboratorio deberá tomar las medidas correctivas necesarias.

TRATAMIENTO DE LOS RESIDUOS

Todos los materiales de desecho deben eliminarse de acuerdo con los requisitos regulatorios locales, estatales y federales. (diríjase a la hoja de seguridad (SDS)).

RENDIMIENTO

El rendimiento fue obtenido en un Selectra ProM, siguiendo las recomendaciones técnicas del CLSI, bajo condiciones ambientales controladas.

- Rango analítico
a) Suero/Plasma

10 - 300 mg/dL (1.67 - 49.95 mmol/L)

Las muestras que tengan concentraciones mayores deben diluirse 1:5 con una solución de NaCl 9 g/L y volver a analizarse.
Este procedimiento extiende el rango analítico hasta 1 500 mg/dL (249.75 mmol/L).
No tome en cuenta resultados fuera del rango analítico extendido.

Para los usuarios del software Selectra TouchPro, la función «diluir» realiza la dilución de las muestras automáticamente. Los resultados toman en cuenta la dilución.

b) Orina

200 - 6 000 mg/dL (33 - 999 mmol/L)
No tome en cuenta resultados fuera del rango analítico

- Límite de detección (LoD), límite de Cuantificación (LoQ)
a) Suero/Plasma

LoD = 1.5 mg/dL (0.25 mmol/L)
LoQ = 5.0 mg/dL (0.83 mmol/L)

b) Orina

LoD = 18 mg/dL (3 mmol/L)
LoQ = 200 mg/dL (33 mmol/L)

- Precisión

Los datos de imprecisión fueron obtenidos en 2 equipos Selectra ProM durante 20 días (2 corridas por día, pruebas efectuadas en duplicado).

Resultados representativos se presentan a continuación :

a) Suero/Plasma

		Media		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Nivel 1	80	18.0	3.00	1.6	3.2
Nivel 2	80	59.0	9.82	1.2	2.2
Nivel 3	80	144.6	24.08	1.0	2.1

b) Orina

		Media		Intra-serie	Total
	n	mg/dL	mmol/L	CV (%)	
Nivel 1	80	482	80	1.7	3.8
Nivel 2	80	1165	194	0.6	3.1
Nivel 3	80	2587	431	0.4	3.6

- Correlación
a) Suero/Plasma

Un estudio comparativo se llevó a cabo entre el reactivo UREA UV SL en el equipo Selectra ProM y un sistema comercial similar en 98 muestras séricas.
Las concentraciones de las muestras se encuentran entre 12.5 y 285.5 mg/dL (2.08 - 47.54 mmol/L).
Los resultados son los siguientes :
Coeficiente de correlación: (r) = 1.000
Regresión linear : y = 0.993x - 0.1 mg/dL (0.02 mmol/L)

☞*b) Orina*

Un estudio comparativo se llevó a cabo entre el reactivo UREA UV SL en el equipo Selectra ProM y un sistema comercial similar en 53 muestras de orina.
Las concentraciones de las muestras se encuentran entre 203 y 5 569 mg/dL (34 - 927 mmol/L).
Los resultados son los siguientes :
Coeficiente de correlación: (r) = 0.999
Regresión linear : y = 1.000x + 52 mg/dL (9 mmol/L)

☞- Limitaciones/Interferencias
a) Suero/Plasma

- Estudios fueron llevados a cabo para determinar el nivel de interferencia de diferentes componentes.
Los niveles siguientes de urea fueron probados: 15.0 mg/dL y 60.1 mg/dL.
Definimos una interferencia no significativa cuando se obtiene una recuperación de ≤±10% con respecto al valor inicial.
Bilirrubina no conjugada: No hay interferencia significativa hasta 30.0 mg/dL (513 µmol/L).
Bilirrubina conjugada: No hay interferencia significativa hasta 29.5 mg/dL (505 µmol/L).
Turbidez: No hay interferencia significativa hasta 614 mg/dL (6.94 mmol/L) de triglicéridos equivalente.
Hemoglobina: No hay interferencia significativa hasta 500 mg/dL.
Ácido ascórbico: No hay interferencia significativa hasta 20.0 mg/dL.
Metildopa : No hay interferencia significativa hasta 1.0 mg/dL.

- En casos muy raros, las gammapatías monoclonales (mieloma múltiple), en particular el tipo IgM (macroglobulinemia de Waldenstrom) pueden producir resultados poco confiables.[5]

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en los artículos publicados por Young.[6-7]

b) Orina

- Estudios fueron llevados a cabo para determinar el nivel de interferencia de diferentes componentes.
Los niveles siguientes de urea fueron probados: 1 500 mg/dL y 3 000 mg/dL.
Definimos una interferencia no significativa cuando se obtiene una recuperación de ≤±10% con respecto al valor inicial.
Bilirrubina conjugada: No hay interferencia significativa hasta 29.5 mg/dL (505 µmol/L).
Hemoglobina: No hay interferencia significativa hasta 500 mg/dL.
Ácido ascórbico: No hay interferencia significativa hasta 20.0 mg/dL.
Ácido úrico: No hay interferencia significativa hasta 120 mg/dL (7.14 mmol/L).
pH : No hay interferencia significativa para valores de pH que varían entre 2.5 y 12.0.

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en los artículos publicados por Young.[6-7]

- Estabilidad en el equipo / frecuencia de calibración
Estabilidad en el equipo : 14 días
Frecuencia de calibración : 7 días
Recalibrar cuando los lotes de reactivo cambien, cuando los controles de calidad no se encuentren dentro del rango establecido, y después de operaciones de mantenimiento.

El rendimiento se ha obtenido utilizando el equipo ELITech Selectra ProM. Los resultados pueden variar si se utiliza un instrumento diferente o un procedimiento manual.
El rendimiento obtenido a partir de aplicaciones no validadas por ELITech no se garantiza y deben ser definidas por el usuario.

DECLARACIÓN DE INCIDENTES GRAVES

Por favor notifique al fabricante (por medio de su distribuidor) y autoridad competente del Estado miembro de la Unión Europea en donde el usuario o paciente radique, de cualquier incidente grave que se produzca con relación al dispositivo. Para otras jurisdicciones, la declaración de incidentes graves debe realizarse de acuerdo con los requisitos reglamentarios locales, estatales y federales. Reportando incidentes graves usted contribuye a proporcionar más información sobre la seguridad del dispositivo médico de diagnóstico *in vitro*.

ASISTENCIA TÉCNICA

Contacte a su distribuidor local o con ELITech Clinical Systems SAS (CCsupport@ elitechgroup.com)

Português – PT

☞UTILIZAÇÃO PREVISTA

ELITech Clinical Systems UREA UV SL é um reagente para diagnóstico *in vitro* destinado à determinação quantitativa do ureia em amostras de soro, plasma e urina humanas em analisadores automáticos ou semi-automáticos.
O padrão é destinado à calibração do reagente.
Estes dispositivos de diagnóstico *in vitro* são apenas para uso profissional.

☞SIGNIFICADO CLÍNICO [1-3]

A uréia é o principal subproduto do catabolismo protéico. É originário do fígado e é principalmente excretado pelos rins.
As concentrações de uréia no sangue podem ser aumentadas por vários fatores relacionados a causas pré-renais (aumento do catabolismo protéico, como hemorragia no trato gastrointestinal, choque), causas renais (doenças renais agudas ou crônicas) ou causas pós-renais (obstrução ao fluxo urinário). A uremia também é aumentada pela dieta rica em proteínas ou desidratação. Pode ser observada uma diminuição da concentração sérica de uréia durante a gravidez ou com uma dieta pobre em proteínas.
Na prática, a medição da uréia no soro é realizada para ajudar a diagnosticar doenças renais, monitorar tratamentos contra essas patologias ou monitorar a função renal durante tratamentos que possam prejudicar essa função. Devido a muitas causas não renais para variação do nível sérico, a uréia é, no entanto, um marcador menos bom da função renal do que a creatinina.

☞LIMITAÇÃO DE USO

O ensaio quantitativo do ureia sozinho não pode ser usado para diagnosticar uma doença ou uma patologia específica.
Os resultados devem ser interpretados em conjunto com outros resultados de testes de diagnóstico, achados clínicos e histórico médico do paciente.

☞MÉTODO & PRINCÍPIO [4]

Urease / GlDH - Cinético.

$$Ureia + 2H_20 \xrightarrow{Urease} 2NH_4^+ + CO_3^{2-}$$

$$NH_4^+ + \alpha\text{-cetoglutarato} + NADH \xrightarrow{GIDH} \text{L-Glutamato} + NAD^+ + H_20$$

GlDH = Glutamato desidrogenase

☞COMPOSIÇÃO

Reagente 1: R1
Tampão Tris, pH 7.60 (37 °C)
α-cetoglutarato 9 mmol/L
Urease ≥ 8 100 U/L
GIDH ≥ 1 350 U/L
Azida de sódio < 0.1 % (p/p)
Reagente 2: R2
NAD 1.3 mmol/L
Azida de sódio < 0.1 % (p/p)
Padrão: Std (Ref : URSL-0427/0507)
Ureia 50 mg/dL
8.33 mmol/L

MATERIAIS NECESSÁRIOS MAS NÃO FORNECIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Solução salina normal (NaCl 9 g/L).
- Analisador automáticos ou semi-automáticos.
- Equipamento geral de laboratório (por exemplo, pipeta ...).
- Não utilize materiais que não são necessários, tal como indicado acima.

☞PRECAUÇÕES DE USO E AVISOS

- Consulte a ficha de dados de segurança (SDS) para obter um manuseio adequado.
- Reagentes contém azida de sódio que pode reagir com o chumbo ou cobre das canalizações formando azidas metálicas explosivas. Ao manusear estes reagentes lave as mãos sempre com grandes quantidades de água para evitar a produção de azida.
- Utilize as precauções normais e siga as boas práticas de laboratório.
- Utilizar material de laboratório limpo ou destinado a uma única utilização de modo a evitar qualquer contaminação.
- Não trocar os frascos de reagentes de diferentes kits.

☞ESTABILIDADE

Conservar a 2-8 °C e ao abrigo da luz. Não congelar
Não utilizar após as datas de validade indicadas nos rótulos dos frascos.
O padrão deve ser imediatamente tampado para evitar a contaminação e evaporação.
Estabilidade em equipamentos:
A estabilidade a bordo é específica a cada equipamento (Consultar § DESEMPENHO)

PREPARAÇÃO

O reagente e o padrão estão prontos a usar.

DETERIORAÇÃO DO PRODUTO

- O produto deve ser clara. Qualquer turbidez seria sinal de deterioração do produto.
- Não use o produto se houver evidência visível de contaminação ou dano (por exemplo, partículas).
- Danos ao recipiente de producto podem afetar o desempenho do produto. Não use o producto se houver evidência física de deterioração (por exemplo, vazamentos ou recipiente perfurado).

☞AMOSTRAS

Amostras [3]
- Soro.
- Plasma (heparina de lítio).
- Urina.
- O uso de qualquer outro tipo de amostra deve ser validado pelo laboratório.

Aviso e precauções
- A adição de timol como conservante não é recomendada, pois inibe a atividade da urease.[3]
- As amostras devem ser coletadas de acordo com as Boas Práticas de Laboratório e com as diretrizes apropriadas que podem estar em vigor.

Armazenamento e estabilidade [2,3]
Soro/Plasma
- 24h em temperatura ambiente.
- 1 semana a 2-8 °C.
- 3 meses a -20 °C.
Urina
- 4 dias a 2-8 °C, desde que a contaminação bacteriana seja evitada.

☞VALORES DE REFERÊNCIAS [2]

Soro/plasma	mg/dL	mmol/L
Crianças <1 ano	8.6 - 40.7	1.4 - 6.8
Crianças 1-18 anos	10.7 - 38.6	1.8 - 6.4
Adultos (18 - 60 anos)	12.9 - 42.9	2.14 - 7.14
Adultos (60 - 90 anos)	17.2 - 49.3	2.86 - 8.21
Adultos (>90 anos)	21.4 - 66.5	3.57 - 11.07

Urina (24h - coleta)	g/24h	mol/24 h
Adultos	26 - 43	0.43 - 0.71
	mg/dL*	mmol/L*
	1 700 - 2 900	290 - 470

*para um volume urinário de 1.5 L por 24 horas

Observação: *O intervalo citado deve servir apenas como guia. Recomenda-se que cada laboratório verifique esse intervalo ou estabeleça um intervalo de referência para a população pretendida.*

☞PROCEDIMENTO

Procedimento manual
Comprimento de onda : 340 nm
Percurso óptico : 1 cm
Relação Amostra/Reagente : 1:100
Temperatura: 37 °C
As amostras de urina devem ser diluídas 1:20 com solução de NaCl 9 g/L antes da medição.
Ler comparando com o água destilada

Reagente de trabalho (4 volumes de R1 + 1 volume de R2)	1000 µL
Amostra	10 µL

Misture e após 30 segundos de incubação, leia a absorbância em intervalos de 30 segundos durante 90 segundos. Calcule a mudança de absorbância por minuto (ΔA/min).

Procedimento automático
Estes reagentes podem ser utilizados em vários analisadores automáticos. Para os analisadores ELITech Selectra, as aplicações validadas estão disponíveis mediante solicitação. Com o Selectra TouchPro, utilize a aplicação incluída
no código de barras disponível no final desde folheto.

As amostras de urina devem ser diluídas 1:20 com solução de NaCl 9 g/L antes da medição.
Para usuários do software Selectra TouchPro, a diluição da urina é realizada automaticamente.

☞CÁLCULO

$$\frac{\Delta A/\text{min. Amostra}}{\Delta A/\text{min. Padrão/calibrador}} \times n$$ n = concentração do padrão/calibrador

Para o cálculo da concentração do uréia na urina, multiplique o resultado pelo fator de diluição (20). Para usuários do software Selectra TouchPro, os resultados levam em consideração o fator de diluição

Fator de conversão: mg/dL x 0.1665 = mmol/L

a) Soro, plasma
Turvação: Desvio positivo a partir de 300 mg/dL (3,39 mmol/L) equivalente de triglicéridos.
Hemoglobina: Desvio positivo a partir de 250 mg/dL (2,5 g/L).
Bilirrubina conjugada: Nenhuma interferência significativa até 25 mg/dL (427,6 µmol/L).
Bilirrubina não conjugada: Nenhuma interferência significativa até 36 mg/dL (615,8 µmol/L) em soro normal e desvio positivo a partir de 22,5 mg/dL (384,8 µmol/L) em soro patológico.

- Em casos muito raros, as gamopatias monoclonais (mieloma múltiplo), em particular, tipo IgM (macroglobulinemia de Waldenstrom) podem causar resultados não confiáveis.[8]

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young [9-10].

- Os resultados deste teste só devem ser interpretados em conjunto com outros resultados de testes de diagnóstico, que constem no historial médico e clínico do paciente

b) Urina
☞Hemoglobina: Desvio positivo a partir de 3 g/L.
Bilirrubina conjugada : Nenhuma interferência significativa até 25 mg/dL (427,6 µmol/L).

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young [9-10].

- Os resultados deste teste só devem ser interpretados em conjunto com outros resultados de testes de diagnóstico, que constem no historico médico e clínico do paciente.

- Estabilidade a bordo / frequência de calibração
Estabilidade a bordo: 28 dias
Frequência de calibração: 7 dias
Uma nova calibração deve ser efetuada após cada mudança de lote de reagente, quando os resultados do(s) controle(s) de qualidade estiverem fora do intervalo estabelecido e após uma operação de manutenção.

☞*Estes desempenhos foram obtidos utilizando o analisador ELITech Selectra E. Os resultados podem variar se um instrumento diferente ou um procedimento manual for usado.*
Os desempenhos de aplicações não validados pela ELITech não são garantidos e devem ser definidos pelo usuário.

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☞SYMBOLES/SYMBOLS/ SÍMBOLOS/SÍMBOLOS

- Les symboles utilisés sont décrits dans la norme ISO-15223-1 hormis ceux présentés ci-dessous.
- Symbols used are defined on ISO-15223-1 standard, except those presented below.
- Los símbolos utilizados son descritos en la norma ISO-15223-1 a la excepción de los presentados a continuación.
- Os símbolos utilizados são definidos na norma ISO-15223-1, exceto os apresentados abaixo.

CONT	Contient Content Contiene Conteúdo
R	Réactif Reagent Reactivo Reagente
Std	Standard Standard Estándar Padrão
CE	Conformité Européenne European Conformity Conformidad Europea Conformidade Europeia

NOTE/NOTA

- Uniquement pour la réf. **CHLO-0250,** utilisée avec le logiciel Selectra TouchPro.
- Only for ref. **CHLO-0250,** used with Selectra TouchPro software.
- Únicamente para la ref. **CHLO-0250,** utilizada con el software Selectra TouchPro.
- Somente para ref. **CHLO-0250,** usado com o Selectra TouchPro.

CHLO 0
260 VTL-CHLO

☞: Modification par rapport à la version précédente/Modification from previous version/ Modificación con respecto a la versión anterior/Modificação relativamente à versão anterior

ELITechGroup EMPOWERING IVD

CHLORIDE

☞*Références/References/ Referencias/ Referências:* *Composition du coffret/ Kit composition/ Composición del kit/ Conteúdo da embalagem :*
CHLO-0600 *R 2 x 125 mL + Std 1 x 5 mL*
CHLO-0250 *R 12 x 20 mL*

CE

VTL-CHLO-4-v14 (09/2019)

Français - FR

Code technique : EL

☞USAGE PRÉVU
ELITech Clinical Systems CHLORIDE est un réactif de diagnostic *in vitro*, destiné au dosage quantitatif du chlorure dans les échantillons de sérum, de plasma et d'urine humains.

SIGNIFICATION CLINIQUE [1-3]
Le chlorure est le principal anion présent dans le fluide extracellulaire. Il assure une pression osmotique, un bilan hydrique et un équilibre anion-cation appropriés. Sa concentration est similaire à celle du sodium et subit les mêmes influences.
La détermination de la concentration plasmatique en Cl^- est utile pour le diagnostic différentiel des perturbations acido-basiques et est essentiel pour le calcul du trou anionique. Le dosage dans les urines est utile chez les patients avec une alcalose métabolique persistante ne recevant pas de diurétiques.
Une hypochlorémie est observée chez les individus souffrant de néphrite avec perte de sels couplée à une hyponatrémie, lors d'intoxication au bromure, de syndrôme d'antidiurèse, d'expansion du fluide extracellulaire, d'alcalose métabolique, de sécrétions gastriques persistantes ou de vomissements prolongés.
Une hyperchlorémie apparaît lors de déshydratation, d'acidose tubulaire rénale, d'insuffisance rénale aiguë, d'acidose métabolique, de diabètes insipide ou de prise extrêmement importante de sel.

MÉTHODE [4]
Thiocyanate de mercure. Colorimétrique.
Point final.

PRINCIPE [4]
En présence de nitrate ferrique et de thiocyanate mercurique, les ions chlorures provoquent la formation de thiocyanate ferrique. L'intensité de coloration de ce complexe brun est proportionnelle à la concentration en chlorures :

$$2\ Cl^- + Hg(SCN)_2 \longrightarrow HgCl_2 + 2(SCN)^-$$

$$3\ (SCN)^- + Fe^{3+} \longrightarrow Fe\ (SCN)_3$$

☞COMPOSITION
Réactif : R
Thiocyanate de mercure (II) 1,3 mmol/L
Nitrate ferrique (III) 30 mmol/L
Acide nitrique 29 mmol/L
Standard: Std (Ref : CHLO-0600)
Chlorures 100 mEq/L

☞MATÉRIELS REQUIS MAIS NON FOURNIS
- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Equipement général de laboratoire.
- Ne pas utiliser de matériel ne figurant pas ci-dessus.

☞AVERTISSEMENTS ET PRÉCAUTIONS
- Ces dispositifs (réactif et standard) de diagnostic *in vitro* sont uniquement destinés aux professionnels.
- Le réactif R est classé comme dangereux :

ATTENTION : Provoque une irritation cutanée. Provoque une sévère irritation des yeux. Porter des gants de protection / un équipement de protection des yeux / du visage. EN CAS DE CONTACT AVEC LES YEUX: rincer avec précaution à l'eau pendant plusieurs minutes. Enlever les lentilles de contact si la victime en porte et si elles peuvent être facilement enlevées. Continuer à rincer. Si l'irritation oculaire persiste: consulter un médecin.
- Pour plus d'information, se référer à la fiche de données de sécurité (FDS).
- Le standard doit être immédiatement et correctement refermé afin d'éviter toute contamination ou évaporation.
- Respecter les précautions d'usage et les bonnes pratiques de laboratoire.
- Utiliser du matériel de laboratoire propre ou à usage unique afin d'éviter toute contamination.

☞STABILITÉS
Stocker à 15-25 °C et à l'abri de la lumière. Ne pas congeler.
Ne pas utiliser après la date d'expiration indiquée sur les étiquettes des flacons.
Stabilité à bord :
La stabilité à bord est spécifique à chaque automate. (Se réferer au § PERFORMANCES).

PRÉPARATION
Le réactif et le standard sont prêts à l'emploi.

☞DÉTÉRIORATION DU PRODUIT
- Le produit doit être limpide. Tout trouble serait le signe d'une détérioration du produit.
- Ne pas utiliser le produit s'il y a des signes évidents de détérioration biologique, chimique ou physique.
- Ne pas utiliser le produit si les dommages de l'emballage peuvent avoir un effet sur les performances du produit (fuites, flacon percé).

ÉCHANTILLONS [2,5]
Echantillons requis
- Sérum.
- Plasma recueilli sur héparine.
- Urine de 24h diluée au 1/2 avec de l'eau déminéralisée.
- Ne pas utiliser d'autres échantillons.
☞**Avertissements et précautions**
- Selon les Bonnes Pratiques de Laboratoire, tout prélèvement devrait être réalisé avant l'administration de médicaments.
- Après prélèvement, tous les échantillons doivent être rapidement séparés des cellules afin d'éviter une rupture de l'équilibre ionique et des modifications du métabolisme et du pH.
Stockage et stabilité
Les ions chlorures présents dans les échantillons sont stables au moins 1 semaine à température ambiante, au réfrigérateur ou au congélateur

VALEURS DE RÉFÉRENCE [5]
Sérum, plasma : 98 - 107 mEq/L
Urine, 24h : 110 - 250 mEq/24h

☞*Remarque : Il est recommandé à chaque laboratoire d'établir et de maintenir ses propres valeurs de référence par rapport à la population visée. Les valeurs ci-dessus ne sont données qu'à titre indicatif.*

☞PROCÉDURE
Procédure manuelle
Longueur d'onde : *505 nm*
Trajet optique : *1 cm*
Ratio échantillon/réactif : *1:100*
Température: *37 °C*
Lire contre le blanc réactif.

	CALIBRATION	DOSAGE
Réactif R	1 000 µL	1 000 µL
Calibrant/ Standard	10 µL	-
Echantillon	-	10 µL

Mélanger et lire les absorbances (A) après 5 minutes d'incubation.

Procédure sur automate
Ces réactifs peuvent être utilisés sur différents automates. Pour les automates ELITech Selectra, les applications validées sont disponibles sur demande. Avec le logiciel Selectra TouchPro, utilisez l'application incluse dans le code barre disponible à la fin de cette notice.

CALCUL

$$\frac{A_{\text{Echantillon}}}{A_{\text{Standard/ Calibrant}}} \times n \qquad n = \text{concentration du standard/ calibrant}$$

Facteur de conversion : 1 mEq/L = 1 mmol/L

Pour le dosage du chlorure dans les urines, tenir compte du facteur de dilution.

☞CALIBRATION
Pour la référence CHLO-0600 : Pour la calibration utiliser soit le calibrant multiparamétrique ELICAL 2, soit le standard Chloride 100 mEq/L.
Pour la référence CHLO-0250 : Pour la calibration, utiliser le calibrant multiparamétrique ELICAL 2.

Le standard Chloride 100 mEq/L et le calibrant multiparamétrique ELICAL 2 ssont traçables par rapport au matériau de référence SRM 909c (du National Institute of Standards and Technology).

Fréquence de calibration : La fréquence de calibration est spécifique à chaque automate (se référer au § PERFORMANCES).

☞CONTRÔLE QUALITÉ
Pour vérifier l'exactitude des résultats, les sérums de contrôle ELITROL I et ELITROL II doivent être utilisés. Ces contrôles doivent être effectués et validés avant que les échantillons des patients soient testés. La fréquence de contrôle doit être au moins une fois par jour, après chaque calibration et doit être adaptés aux procédures de contrôle de qualité de chaque laboratoire et les exigences réglementaires.
Les résultats doivent être dans les intervalles définis. Si les valeurs se situent en dehors des plages définies, chaque laboratoire doit prendre des mesures correctives. Les matériaux de contrôle qualité doivent être utilisés conformément aux directives locales.

TRAITEMENT DES DÉCHETS
L'élimination de tous les déchets doit être effectuée conformément aux exigences réglementaires locales, d'état et fédérales.

PERFORMANCES à 37 °C sur ELITech Clinical Systems Selectra E
- Domaine de mesure
a) Sérum/plasma
Le réactif est linéaire de 10 à 130 mEq/L.
b) Urine
Le réactif est linéaire de 10 à 250 mEq/L.

- Limite de Detection [6]
Déterminée selon le protocole recommandé par la SFBC, la limite de détection est égale à 2 mEq/L sur sérum/plasma et urine.

- Précision
a) Sérum/plasma

	N	Reproductibilité intrasérielle		Reproductibilité intersérielle	
		Moyenne (mEq/L)	CV (%)	Moyenne (mEq/L)	CV (%)
Niveau normal	20	97,2	0,9	96,3	1,0
Niveau Pathologique	20	113,2	0,9	111,4	1,3

b) Urine

	N	Reproductibilité intrasérielle		Reproductibilité intersérielle	
		Moyenne (mEq/L)	CV (%)	Moyenne (mEq/L)	CV (%)
Niveau bas	20	30,3	0,5	32,7	2,3
Niveau moyen	20	63,8	0,3	81,8	2,1
Niveau haut	20	151,8	0,3	145,2	2,0

- Corrélation
Sérum et plasma
Une étude comparative a été réalisée entre le réactif Chloride et un autre réactif Chlore du commerce (méthode équivalente) sur 35 échantillons de sérum et plasma.
Les valeurs s'échelonnent de 50,3 à 132,5 mEq/L.
Les paramètres de la droite de régression linéaire sont les suivants:
Coefficient de corrélation : (r) = 0,997
Droite de régression linéaire : y = 0,942 x + 3,3 mEq/L

- Limitations/Interférences [6-7]
- Ne pas communiquer de résultats en dehors du domaine de mesure testé.

- Selon les recommandations de la SFBC, des tests ont été réalisés pour déterminer le niveau d'interférence de différents composés :
a) Sérum/plasma
Turbidité : Biais positif à partir de 300 mg/dL (3,39 mmol/L) équivalent Triglycérides.
Hémoglobine: Biais positif à partir de 250 mg/dL (2,5 g/L).
Bilirubine conjuguée: Aucune interférence significative jusqu'à 25 mg/dL (427,6 µmol/L).
Bilirubine non-conjuguée: Aucune interférence significative jusqu'à 36 mg/dL (615,8 µmol/L) sur sérum normal et biais positif à partir de 22,5 mg/dL (384,8 µmol/L) sur sérum pathologique.

- Dans des cas très rares, les gammapathies monoclonales (myélome multiple), en particulier de type IgM (Macroglobulinémie de Waldenström) peuvent être à l'origine de résultats peu fiables.[8]

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.[9-10]

- Pour le diagnostic, les résultats doivent toujours être confrontés aux résultats d'autres examens et aux données de l'anamnèse du patient.

b) Urine
☞Hémoglobine: Biais positif à partir de 3 g/L.
Bilirubine conjuguée: Aucune interférence significative jusqu'à 25 mg/dL (427,6 µmol/L).

- D'autres substances et médicaments peuvent interférer. Certains d'entre eux sont répertoriés dans les revues publiées par Young.[9-10]

- Pour le diagnostic, les résultats doivent toujours être confrontés aux résultats d'autres examens et aux données de l'anamnèse du patient.

- Stabilité à bord/ Fréquence de calibration
Stabilité à bord : 28 jours
Frequence de calibration : 7 jours
Une nouvelle calibration doit être effectuée après chaque changement de lot de réactif, lorsque les résultats du ou des contrôles de qualité sont hors de l'intervalle établi, et après une opération de maintenance.

☞*Ces performances ont été définies sur un automate ELITech Selectra E. Les résultats peuvent varier si le réactif est utilisé sur un automate différent ou en méthode manuelle.*
Les performances obtenues à partir d'applications non validées par ELITech ne peuvent être garanties et doivent être définies par l'utilisateur.

English - EN

☞INTENDED USE
ELITech Clinical Systems CHLORIDE is an *in vitro* diagnostic reagent intended for the quantitative determination of chloride in human serum, plasma and urine samples.

CLINICAL SIGNIFICANCE [1-3]
Chloride ion is the most abundant anion in the extracellular fluid. It ensures appropriated osmotic pressure, hydrous distribution and anion-cation balance. Its concentration is similar to that of sodium and is influenced by the same factors. Determination of plasma Cl^- concentration is useful in the differential diagnoses of acid-base disturbances and is essential for calculation of the anion gap. Measure in urine is of clinical value with patients with persistent metabolic alkalosis who are not receiving diuretics.
Hypochloremia is observed in individuals with salt-losing nephritis coupled with hyponatremia and in cases such as bromide intoxication, SIADH (Secretion of AntiDiuretic Hormone) expansion of extracellular fluid, metabolic alkalosis or persistent gastric secretion and prolonged vomiting.
Hyperchloremia accompanies dehydration, RTA (Renal Tubular Acidosis), acute renal failure, metabolic acidosis, diabetes insipidus, extremely high intake of salt.

METHOD [4]
Mercuric thiocyanate. Colorimetric.
End point.

PRINCIPLE [4]
In presence of ferric nitrate and mercuric thiocyanate, chloride ions lead to ferric thiocyanate formation. The coloration intensity of this brown complex is proportional to the chloride concentration.

$$2\ Cl^- + Hg(SCN)_2 \longrightarrow HgCl_2 + 2(SCN)^-$$

$$3\ (SCN)^- + Fe^{3+} \longrightarrow Fe\ (SCN)_3$$

☞COMPOSITION
Reagent : R
Mercury (II) thiocyanate 1.3 mmol/L
Ferric (III) nitrate 30 mmol/L
Nitric acid 29 mmol/L
Standard : Std (Ref : CHLO-0600)
Chloride 100 mEq/L

☞MATERIALS REQUIRED BUT NOT PROVIDED
- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- General Laboratory equipment.
- Do not use materials that are not required as indicated above.

☞WARNINGS AND PRECAUTIONS
- These *in vitro* diagnostic devices (reagent and standard) are for professional use only.
- The reagent R is classified as hazardous :

WARNING : Causes skin irritation. Causes serious eye irritation. Wear protective gloves / eye protection / face protection. IF IN EYES : Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists: Get medical advice/attention.
- For more information, refer to the Safety Data Sheet (SDS).
- The standard should be immediately and tightly capped to prevent contamination and evaporation.
- Take normal precautions and adhere to good laboratory practice.
- Use clean or single use laboratory equipment only to avoid contamination.

☞STABILITIES

Store at 15-25 °C and protect from light. Do not freeze.
Do not use after expiration dates indicated on the vial labels.
On board stability :
The on-board stability is specific for each analyzer. (Refer to § PERFORMANCE DATA).

PREPARATION

The reagent and standard are ready to use.

☞PRODUCT DETERIORATION

- The product should be clear. Cloudiness would indicate deterioration.
- Do not use the product if there is visible evidence of biological, chemical or physical deterioration.
- Do not use the product if the damages of packaging might have an effect on the product performances (leakages, pierced vial).

SAMPLES (2,5)

Specimen
- Serum.
- Heparinized plasma.
- 24h-Urine to be diluted 1:2 with demineralized water.
- Do not use other specimens.

☞Warnings and precautions
- According to Good Laboratory Practice, sampling should be performed prior to the administration of drugs.
- After collection, all samples should be promptly separated from cells to avoid shifts in the ionic equilibrium with metabolism and pH changes.

Storage
Chloride ions in the samples are stable at least 1 week at room, refrigerator, or freezer temperatures.

REFERENCE VALUES (5)

Serum, plasma : 98 - 107 mEq/L

Urine, 24h : 110 - 250 mEq/24h

Note : *The quoted range should serve as a guide only. It is recommended that each laboratory verifies this range or establishes a reference interval for the intended population.*

☞PROCEDURE

Manual Procedure
Wavelength : 505 nm
Optical path : 1 cm
Sample/reagent ratio : 1:100
Temperature: 37 °C
Read against reagent blank.

	CALIBRATION	TEST
Reagent R	1 000 µL	1 000 µL
Standard/ Calibrator	10 µL	-
Sample	-	10 µL

Mix and read the absorbances (A) after an incubation of 5 minutes.

Automatic Procedure
These reagents may be used in several automatic analyzers. For ELITech Selectra Analyzers, validated applications are available on request. For Selectra TouchPro software, use the application included in the barcode available at the end of this insert.

CALCULATION

$$\frac{A_{\text{Sample}}}{A_{\text{Standard/Calibrator}}} \times n \qquad n = \text{calibrator/standard concentration}$$

Conversion factor : 1 mEq/L = 1 mmol/L

Take dilution factor into account for calculation of chloride concentration in urine.

CALIBRATION

For reference CHLO-0600 : For calibration, use either multiparametric calibrator ELICAL 2 or Chloride Standard 100 mEq/L.
For reference CHLO-0250 : For calibration , use multiparametric calibrator ELICAL 2.

Chloride Standard 100 mEq/L and multiparametric calibrator ELICAL 2 are traceable to the Standard Reference Material SRM 909c (of the National Institute of Standards and Technology).

Calibration frequency : The calibration is specific for each analyzer. (Refer to § PERFORMANCE DATA).

☞QUALITY CONTROL

To check the accuracy of assays, control sera such as ELITROL I and ELITROL II should be used. These controls must be performed and validated before the patient samples are assayed. The control frequency must be at least once a day, after each calibration and should be adapted to Quality Control procedures of each laboratory and the regulatory requirements. Results should be within the defined ranges. If values fall outside of the defined ranges, each laboratory should take corrective measures. Quality control materials should be used in accordance with local guidelines.

WASTE MANAGEMENT

Disposal of all waste material should be in accordance with local, state and Federal regulatory requirements.

PERFORMANCE DATA at 37 °C on ELITech Clinical Systems Selectra E Analyzers

- Analytical range
a) Serum/Plasma
The reagent is linear from 10 to 130 mEq/L.

b) Urine
The reagent is linear from 10 to 250 mEq/L.

- Detection limit (6)
Determined according to SFBC protocol, the detection limit is equal to 2 mEq/L on serum/plasma and urine.

- Precision
a) Serum/Plasma

	N	Within-run reproducibility		Between-run reproducibility	
		Mean (mEq/L)	CV (%)	Mean (mEql/L)	CV (%)
Normal level	20	97.2	0.9	96.3	1.0
Pathological level	20	113.2	0.9	111.4	1.3

b) Urine

	N	Within-run reproducibility		Between-run reproducibility	
		Mean (mEq/L)	CV (%)	Mean (mEq/L)	CV (%)
Low level	20	30.3	0.5	32.7	2.3
Normal level	20	63.8	0.3	81.8	2.1
High level	20	151.8	0.3	145.2	2.0

- Correlation
Serum and Plasma
A comparative study has been performed between Chloride reagent and another commercial chloride reagent (equivalent method) on 35 human serum/ plasma samples.
The values were between 50.3 and 132.5 mEq/L.
The linear regression parameters are as follows :
Correlation coefficient: (r) = 0.997
Linear regression: y = 0.942 x + 3.3 mEq/L

Limitations/Interferences (6-7)
- Do not report results outside of the usable range.

- According to SFBC recommendations, studies have been performed to determine the level of interference from different compounds :

a) Serum/Plasma
Turbidity : Positive bias from 300 mg/dL (3.39 mmol/L) Triglycerides equivalent.
Hemoglobin: Positive bias from 250 mg/dL (2.5 g/L).
Conjugated bilirubin: No significant interference up to 25 mg/dL (427.6 µmol/L).
Unconjugated bilirubin: No significant interference up to 36 mg/dL (615.8 µmol/L) on normal serum and positif bias from 22.5 mg/dL (384.8 µmol/L) on pathological serum.

- In very rare cases, monoclonal gammopathies (multiple myeloma), in particular IgM type (Waldenstrom's macroglobulinemia) can cause unreliable results.(8)

- Many other substances and drugs may interfere. Some of them are listed in reviews published by Young.(9-10)

- The results of this assay should only be interpreted in conjunction with other diagnostic test results, clinical findings and the patient's medical history.

b) Urine
☞Hemoglobin: Positive bias from 3 g/L.
Conjugated bilirubin: No significant interference up to 25 mg/dL (427.6 µmol/L).

- Many other substances and drugs may interfere. Some of them are listed in reviews published by Young.(9-10)

- The results of this assay should only be interpreted in conjunction with other diagnostic test results, clinical findings and the patient's medical history.

- On board stability/Calibration frequency
On Board Stability: 28 days
Calibration frequency: 7 days
Recalibrate when reagent lots change, when quality control results fall outside the established range, and after a maintenance operation.

☞These performances have been obtained using ELITech Selectra E analyzer. Results may vary if a different instrument or a manual procedure is used.
The performances of applications not validated by ELITech are not warranted and must be defined by the user.

Español - ES

☞USO PREVISTO

ELITech Clinical Systems CHLORIDE es un reactivo de diagnóstico *in vitro* diseñado para la determinación cuantitativa del cloruro en muestras de suero, plasma y orina humanas.

SIGNIFICADO CLÍNICO (1-3)

El cloruro es el principal ión que se halla presente en el líquido extracelular. Asegura la existencia de una presión osmótica, un equilibrio hídrico y un equilibrio anión-catión apropiados. Su concentración es similar a la del sodio y está sujeta a las mismas influencias.
La determinación de la concentración plasmática del Cl^- es útil para establecer el diagnóstico diferencial de los trastornos del equilibrio ácido-básico y resulta esencial para el cálculo del intervalo aniónico. Su determinación en orina es útil en aquellos pacientes con una alcalosis metabólica persistente que no reciben tratamiento diurético.
Se observa hipocloremia en aquellos individuos que padecen una nefritis con pérdida de sal asociada a hiponatremia, en la intoxicación por bromuro, en el síndrome de antidiuresis, en la expansión del líquido extracelular, en la alcalosis metabólica, en casos de secreciones gástricas persistentes o en los vómitos prolongados. La hipercloremia aparece durante la deshidratación, la acidosis tubular renal, la insuficiencia renal aguda, la acidosis metabólica, la diabetes insípida o tras la ingestión de cantidades muy importantes de sal.

MÉTODO (4)

Tiocianato de mercurio. Colorimétrico.
Punto final.

PRINCIPIO (4)

En presencia de nitrato férrico y de tiocianato de mercurio, los iones cloruro provocan la formación de tiocianato férrico. La intensidad del tono marrón de este complejo es proporcional a la concentración de cloruros.

$$2\,Cl^- + Hg(SCN)_2 \longrightarrow HgCl_2 + 2(SCN)^-$$

$$3\,(SCN)^- + Fe^{3+} \longrightarrow Fe\,(SCN)_3$$

☞COMPOSICIÓN

Reactivo: R
Tiocianato de Mercurio (II) 1,3 mmol/L
Nitrato de hierro (III) 30 mmol/L
Ácido nítrico 29 mmol/L
Estándar: Std (Ref : CHLO-0600)
Cloruro 100 mEq/L

☞MATERIALES REQUERIDOS PERO NO INCLUIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Equipamiento general de laboratorio.
- No utilice materiales que no se requieren, tal como se indica anteriormente.

☞ATENCIÓN Y PRECAUCIONES

- Estos dispositivos (reactivo y estándar) de diagnóstico *in vitro* son solo para uso profesional.
- El reactivo R está clasificado como peligroso :

ATENCIÓN : Provoca irritación cutánea. Provoca irritación ocular grave. Llevar guantes de protección / gafas de protección / máscara de protección. EN CASO DE CONTACTO CON LOS OJOS: Enjuagar con agua cuidadosamente durante varios minutos. Quitar las lentes de contacto cuando estén presentes y pueda hacerse con facilidad. Proseguir con el lavado. Si persiste la irritación ocular: Consultar a un médico.
- Para más información, consulte la ficha de datos de seguridad (FDS).
- El estándar debe cerrarse inmediatamente y correctamente para evitar contaminación y evaporación.
- Tome las precauciones normales y respete las buenas prácticas de laboratorio.
- Para evitar contaminaciones utilizar equipo nuevo o completamente limpio.

☞ESTABILIDADES

Conservar a 15-25 °C y protegidos de la luz. No congelar.
No utilice después de la fecha de caducidad indicada en la etiqueta de los frascos.
Estabilidad en el equipo:
La estabilidad es específica para cada equipo. (Referirse al § DATOS DE RENDIMIENTO).

PREPARACIÓN

El reactivo y el estándar están listos para su uso.

☞DETERIORACIÓN DEL PRODUCTO

- El producto debe ser claro. Turbidez indicaría deterioro.
- No utilice el producto si este presenta signos evidentes de deterioración biológica, química o física.
- No utilice el producto si los daños al embalaje pudiesen tener un efecto sobre el rendimiento del producto (fugas, frasco perforado).

MUESTRAS (2,5)

Muestras requeridas
- Suero.
- Plasma heparinizado.
- Orina de 24 h diluida a 1/2 con agua desmineralizada.
- No utilice otras muestras.

☞Advertencias y precauciónes
- De acuerdo con las buenas prácticas de laboratorio, la toma de muestra debe ser llevada a cabo antes de la administración de medicamentos.
- Tras la obtención de la muestra, estas deberán ser separadas rápidamente de las células para evitar la ruptura del equilibrio iónico y las modificaciones del metabolismo y del pH.

Conservación y estabilidad
Los iones cloruro presentes en las muestras son estables durante al menos 1 semana a temperatura ambiente, en el refrigerador o en el congelador.

VALORES DE REFERENCIA (5)

Suero, plasma : 98 - 107 mEq/L

Orina, 24h : 110 - 250 mEq/24h

Nota : Se recomienda que cada laboratorio establezca y mantenga sus propios valores de referencia con respecto a la población destinataria. Los datos aquí proporcionados son únicamente una indicación.

☞PROCEDIMIENTO

Procedimiento manual
Longitud de onda : 505 nm
Trayectoria óptica : 1 cm
Ratio muestra/reactivo : 1:100
Temperatura: 37 °C
Leer contra blanco reactivo.

	CALIBRACIÓN	PRUEBA
Reactivo R	1 000 µL	1 000 µL
Estándar/ Calibrador	10 µL	-
Muestra	-	10 µL

Mezclar y leer las absorbancias (A) después de una incubación de 5 minutos.

Procedimiento automático
Estos reactivos pueden ser utilizados en varios equipos. Para los equipos ELITech Selectra, las aplicaciones validadas están disponibles sobre pedido.
Para el software Selectra TouchPro, use la aplicación incluida en el código de barras disponible al final de este inserto.

CÁLCULO

$$\frac{A_{\text{Muestra}}}{A_{\text{Estándar/Calibrador}}} \times n \qquad n = \text{concentración del estándar/calibrador}$$

Factor de conversión: 1 mEq/L = 1 mmol/L

Para el calculo de la concentracion de cloruro en las orinas, tener en cuenta el factor de dilucion.

CALIBRACIÓN

Para la referencia CHLO-0600 : Para la calibración, utilizar ya sea el calibrador multiparametrico ELICAL 2 o el estándar Chloride Standard 100 mEq/L.
Para la referencia CHLO-0250 : Para la calibración, utilizar el calibrador multiparametrico ELICAL 2.

El estándar Chloride Standard 100 mEq/L y el calibrador multiparametrico ELICAL 2 son trazable al material de referencia SRM 909c (del National Institute of Standards and Technology).

Frecuencia de calibración : la frecuencia de calibración es específica para cada equipo (referirse al § DATOS DE RENDIMIENTO).

☞CONTROL DE CALIDAD

Para asegurar la exactitud de los resultados, sueros de control tales como ELITROL I y ELITROL II deben ser utilizados. Los controles deben ser realizados y validados antes de que las muestras del paciente sean probadas. La frecuencia de control debe ser al menos una vez al día, después de cada calibración y debe ser adaptada a los procedimientos de control de calidad de cada laboratorio y las exigencias regulatorias. Los resultados deben estar dentro del rango analítico definido. Si los valores quedan fuera del rango analítico definido, cada laboratorio debera de tomar las medidas correctivas. Los materiales de control de calidad deben ser usados conforme a las directivas locales.

TRATAMIENTO DE LOS RESIDUOS

Todos los materiales de desecho deben eliminarse de acuerdo con los requisitos reglamentarios locales, estatales y federales.

DATOS DE RENDIMIENTO a 37 °C en equipo ELITech Clinical Systems Selectra E

- Rango analítico
a) Suero, plasma
El reactivo es lineal desde 10 hasta 130 mEq/L.

b) Orina
El reactivo es lineal desde 10 hasta 250 mEq/L.

- Límite de detección (6)
Determinado de acuerdo al protocolo de SFBC, el límite de detección es igual a 2 mEq/L en suero, plasma y orina.

- Precisión
a) Suero, plasma

	N	Reproducibilidad intraserie		Reproducibilidad interserie	
		Media (mEq/L)	CV (%)	Media (mEq/L)	CV (%)
Nivel normal	20	97,2	0,9	96,3	1,0
Nivel Patológico	20	113,2	0,9	111,4	1,3

b) Orina

	N	Reproducibilidad intraserie		Reproducibilidad interserie	
		Media (mEq/L)	CV (%)	Media (mEq/L)	CV (%)
Nivel bajo	20	30,3	0,5	32,7	2,3
Nivel medio	20	63,8	0,3	81,8	2,1
Nivel alto	20	151,8	0,3	145,2	2,0

- Correlación
Suero y plasma
Un estudio comparativo fue llevado a cabo entre el reactivo Chloride y otro reactivo chloride comercial (método equivalente) en 35 muestras de suero y plasma.
Los valores fueron entre 50,3 y 132,5 mEq/L.
Los parámetros de la regresión lineal fueron los siguientes :
Coeficiente de correlación: (r) = 0,997
Regresión lineal: y = 0,942 x + 3,3 mEq/L

Limitaciones/Interferencias(6-7)
- No reporte resultados fuera del rango analítico.

- De acuerdo con las recomendaciones de SFBC, se han realizado algunos estudios para determinar el nivel de interferencia de diferentes componentes:

a) Suero, plasma
Turbidez : Tendencia positiva desde 300 mg/dL (3,39 mmol/L) de triglicéridos equivalente.
Hemoglobina: Tendencia positiva desde 250 mg/dL (2,5 g/L).
Bilirrubina conjugada: No hay interferencia significativa hasta 25 mg/dL (427,6 µmol/L).
Bilirrubina no conjugada: No hay interferencia significativa hasta 36 mg/dL (615,8 µmol/L) sobre suero normal y tendencia positiva desde 22,5 mg/dL (384,8 µmol/L) sobre suero patológico.

- En casos muy raros, las gammapatías monoclonales (mieloma múltiple), en particular el tipo IgM (macroglobulinemia de Waldenstrom) pueden producir resultados poco confiables.(8)

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en los artículos publicados por Young.(9-10)

- Los resultados de este ensayo deben ser interpretados en conjunción con otros resultados de exámenes de diagnóstico, resultados clínicos, así como el historial médico del paciente.

b) Orina
☞Hemoglobina: Tendencia positiva desde (3 g/L).
Bilirrubina conjugada: No hay interferencia significativa hasta 25 mg/dL (427,6 µmol/L).

- Muchas otras substancias y fármacos pueden interferir. Algunos de estos están listados en los artículos publicados por Young.(9-10)

- Los resultados de este ensayo deben ser interpretados en conjunción con otros resultados de exámenes de diagnóstico, resultados clínicos, así como el historial médico del paciente.

- Estabilidad en el equipo / frecuencia de calibración
Estabilidad en el equipo : 28 días
Frecuencia de calibración : 7 días
Se debe ejecutar una nueva calibración si se cambia de lote de reactivo, si los resultados de uno o varios controles de calidad exceden el intervalo establecido después de una operación de mantenimiento.

☞El rendimiento se ha obtenido utilizando el equipo ELITech Selectra E. Los resultados pueden variar si se utiliza un instrumento diferente o un procedimiento manual.
El rendimiento obtenido a partir de aplicaciones no validadas por ELITech no se garantizan y deben ser definidas por el utilizador.

Português – PT

☞UTILIZAÇÃO PREVISTA

ELITech Clinical Systems CHLORIDE é um reagente para diagnóstico *in vitro* destinado à determinação quantitativa de cloreto em amostras de soro, plasma e urina humanas.

SIGNIFICADO CLÍNICO (1-3)

O cloreto é o principal anião presente no fluido extracelular. O mesmo garante uma pressão osmótica, um balanço hídrico e um equilíbrio anião-catião adequados. A sua concentração é semelhante à do sódio e está sujeito às mesmas influências.
A determinação da concentração plasmática em Cl^- é útil para o diagnóstico diferencial de perturbações ácido-básicas e é essencial para o cálculo do hiato aniónico. A dosagem nas urinas é útil nos doentes com uma alcalose metabólica persistente que não estejam a receber diuréticos.
Uma hipocloremia é observada nos indivíduos que sofrem de nefrite com perda de sais associada a uma hiponatremia, em caso de intoxicação com brometo, de síndrome de antidiurese, de expansão do fluido extracelular, de alcalose metabólica, de secreções gástricas persistentes ou de vómitos prolongados.
Uma hipercloremia surge em caso de desidratação, de acidose tubular renal, de insuficiência renal aguda, de acidose metabólica, de diabetes insipidus ou de ingestão extremamente significativa de sal.

MÉTODO (4)

Tiocianato de mercúrio – Colorimétrico
Ponto final.

PRINCÍPIO (4)

Na presença de nitrato férrico ou de tiocianato mercúrico, os iões cloretos provocam a formação de tiocianato férrico. A intensidade de coloração deste complexo castanho é proporcional à concentração em cloretos.

$$2\,Cl^- + Hg(SCN)_2 \longrightarrow HgCl_2 + 2(SCN)^-$$

$$3\,(SCN)^- + Fe^{3+} \longrightarrow Fe(SCN)_3$$

☞COMPOSIÇÃO

Reagente : R
Tiocianato de mercúrio (II) 1,3 mmol/L
Nitrato férrico (III) 30 mmol/L
Ácido nítrico 29 mmol/L
Padrão: Std (Ref : CHLO-0600)
Cloreto 100 mEq/L

☞MATERIAIS NECESSÁRIO MAS NÃO FORNECIDOS

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Equipamento geral de laboratório.
- Não utilize materiais que não são necessários, tal como indicado acima.

☞AVISO E PRECAUÇÕES

- Estes dispositivos de diagnóstico *in vitro* (reagente e padrão) são apenas para uso profissional.
- A reagente R classificado como perigoso :

ATENÇÃO : Provoca irritação cutânea. Provoca irritação ocular grave. Usar luvas de protecção / protecção ocular / protecção facia. SE ENTRAR EM CONTACTO COM OS OLHOS: enxaguar cuidadosamente com água durante vários minutos. Se usar lentes de contacto, retire-as, se tal lhe for possível. Continuar a enxaguar. Caso a irritação ocular persista: consulte um médico.
- Para obter mais informações, consulte la ficha de dados de segurança (FDS).
- O padrão deve ser imediatamente tampado para evitar a contaminação e evaporação.
- Utilize as precauções normais e siga as boas práticas de laboratório.
- Utilizar material de laboratório limpo ou destinado a uma única utilização de modo a evitar qualquer contaminação.

☞ESTABILIDADES

Conservar a 15-25 °C e ao abrigo da luz. Não congelar
Não utilizar após as datas de validade indicadas nos rótulos dos frascos.
Estabilidade em equipamento:
A estabilidade a bordo é específica a cada equipamento (Consultar § DESEMPENHO).

PREPARAÇÃO

O reagente e o padrão estão prontos a usar.

☞DETERIORAÇÃO DO PRODUTO

- O produto deve ser clara. Qualquer turbidez seria sinal de deterioração do produto.
- Não use o produto se houver evidência visível de deterioração física, biológica ou química.
- Não utilizar o produto caso haja danos na embalagem que possam causar algum efeito sobre o desempenho do produto (vazamentos, embalagem perfurada).

AMOSTRAS (2,5)

- Soro.
- Plasma recolhido em heparina.
- Urinas de 24 h a diluir a 1/2 com água desmineralizada.
- Não utilize outros espécimes.

☞Aviso e precauções
- De acordo com as boas praticas de laboratório, a amostragem deve ser executada antes da administração de drogas.
- Após a colheita, todas as amostras devem ser rapidamente separadas das células de modo a evitar uma ruptura do equilíbrio iónico e modificações do metabolismo e do pH.

Armazenamento e estabilidade
Os iões cloretos presentes nas amostras mantêm-se estáveis durante pelo menos 1 semana à temperatura ambiente, no frigorífico ou no congelador.

VALORES DE REFERÊNCIAS (5)

Soro, plasma: 98 - 107 mEq/L

Urina, 24 h: 110 - 250 mEq/24 h

Observação: Recomenda-se que cada laboratório estabeleça e mantenha os seus próprios valores de referência para a população desejada. Os valores anteriores são apenas fornecidos a título indicativo

☞PROCEDIMENTO

Procedimento manual
Comprimento de onda : 505 nm
Percurso óptico : 1 cm
Relação amostra/reagente : 1:100
Temperatura: 37 °C
Ler comparando com o branco de reagente

	CALIBRAÇÃO	DOSAGEM
Reagente R	1 000 µL	1 000 µL
Padrão/ Calibrador	10 µL	-
Amostra	-	10 µL

Misturar e ler as absorvâncias (A) após 5 minutos.

Procedimento automático
Estes reagentes podem ser utilizados em vários analisadores automáticos. Para os analisadores ELITech Selectra, as aplicações validadas estão disponíveis mediante solicitação.
Com o Selectra TouchPro, utilize a aplicação incluída no código de barras disponível no final desde folheto.

CÁLCULO

$$\frac{A_{\text{Amostra}}}{A_{\text{Padrão Calibrador}}} \times n \qquad n = \text{concentração do padrão/calibrador}$$

Fator de conversão: 1 mEq/L = 1 mmol/L

Para a dosagem do cloreto nas urinas, ter em conta o factor de diluição.

☞CALIBRAÇÃO

Para referência CHLO-0600 : Para calibração, use o calibrador multiparamétrico ELICAL 2 ou o padrão Chloride Standard 100 mEq/L.
Para referência CHLO-0250 : Para calibração, use o calibrador multiparamétrico ELICAL 2.

O padrão Chloride Standard 100 mEq/L e o calibrador multiparamétrico ELICAL 2 são rastreáveis ao material de referência SRM 909c (do National Institute of Standards and Technology).

Frequência de calibração : A frequência de calibração é específca a cada equipamento (consultar § DESEMPENHO).

☞CONTROLE DE QUALIDADE

Para verificar a exatidão dos resultados, os soros controle, tal como ELITROL I e ELITROL II devem ser usados. Esses controles devem ser realizados e validados antes das amostras dos pacientes serem testadas. A frequência do controle deve ser efetuada, pelo menos, uma vez por dia, após cada calibração e deve ser adaptada aos procedimentos de controle de qualidade de cada laboratório e aos requisitos regulamentares. Os resultados devem estar dentro dos limites definidos. Se os valores se estiverem fora dos limites definidos, cada laboratório deve tomar as devidas medidas corretivas. Os controles de qualidade devem ser utilizados de acordo com os procedimentos habituais.

TRATAMENTO DOS RESÍDUOS

Todos os resíduos devem ser eliminados de acordo com as exigências locais de regulamentação local, estadual e federal.

DESEMPENHO a 37 °C no ELITech Clinical Systems Selectra E

- Precisão de medição
a) Soro, plasma
O reagente é linear de 10 a 130 mEq/L.

b) Urina
O reagente é linear de 10 a 250 mEq/L.

- Limite de detecção
Determinado de acordo com o protocolo recomendado pela SFBC, o limite de detecção é igual a 2 mEq/L em soro/plasma e urina.

- Precisão
a) Soro, plasma

	N	Reproducibilidad intraserie		Reproducibilidad interserie	
		Media (mEq/L)	CV (%)	Media (mEq/L)	CV (%)
Nivel normal	20	97,2	0,9	96,3	1,0
Nivel Patológico	20	113,2	0,9	111,4	1,3

b) Urina

	N	Reproducibilidad intraserie		Reproducibilidad interserie	
		Media (mEq/L)	CV (%)	Media (mEq/L)	CV (%)
Nivel bajo	20	30,3	0,5	32,7	2,3
Nivel medio	20	63,8	0,3	81,8	2,1
Nivel alto	20	151,8	0,3	145,2	2,0

- Correlação
Soro e plasma
Foi realizado um estudo comparativo entre o reagente Chloride e um outro reagente de Cloro disponível no mercado (método equivalente) em 35 amostras de soro e plasma.
Os valores repartiram-se entre 50,3 e 132,5 mEq/L.
Os parâmetros da linha de regressão linear são os seguintes:
Coeficiente de correlação: (r) = 0,997
Linha de regressão linear: y = 0,942 x + 3,3 mEq/L

- Limitações/Interferências (6-7)
- Não relatam resultados fora do alcance útil.

- Segundo as recomendações da SFBC, foram realizados testes para determinar o nível de interferência de diferentes compostos:

GAMMA-GT PLUS SL

☞Referinţe:	Compoziţia trusei:
GISL-0250	***R1** 8 x 20 mL + **R2** 8 x 5 mL*
GISL-0400	***R1** 2 x 50 mL + **R2** 1 x 26 mL*
GISL-0420	***R1** 4 x 50 mL + **R2** 2 x 26 mL*

CE

VTLRO-GISL-v9 (08/2020)_VTL-GISL-4-v9

☞SCOPUL UTILIZĂRII

ELITech Clinical Systems GAMMA GT PLUS SL este un reactiv de diagnostic *in vitro* destinat determinării cantitative a γ-GT din probele serul uman şi plasmă.

SEMNIFICAŢIE CLINICĂ [1-3]

Gama glutamiltransferaza (γ-GT) este o enzimă legată de membrană prezentă în special în rinichi, pancreas, ficat şi prostată. Această enzimă are un rol important în metabolismul glutationului şi ia parte la transportul aminoacizilor în celule.

Creşterea activităţii γ-GT este mai sensibilă decât fosfataza alcalină (ALP) în timpul unei afecţiuni a ficatului sau a căilor biliare. Cele mai mari creşteri sunt observate în cazurile de obstrucţii biliare intrahepatice sau post-hepatice (ajungând la nivele de 5 până la 30 de ori mai mari decât normalul) , neoplasme primare sau metastazice ale ficatului, bolile pancreatice (pancreatită, cancer…). Gama-glutamiltransferaza (γ-GT) este utilă ca un marker pentru cancerul pancreatic, cancerul de prostată şi hematoame, deoarece nivelele reflectă remiterea şi recurenţa.

Creşteri mai moderate sunt observate în timpul hepatitei infecţioase, cirozei şi steatozei hepatice. Alcool în ingestie cronică, unele medicamente precum antiepilepticele (fenobarbital, fenitoină) pot, de asemenea, creşte rata γ-GT în ser.

METODĂ [4]

Substrat Glupa-C – Standardizare conform metodei IFCC – Enzimatică. Cinetică.

PRINCIPIU [4]

Determinarea cinetică a activităţii γ-glutamiltransferazei (γ-GT).

$$\text{GLUPA-C+ Glicilglicină} \xrightarrow{\gamma\text{-GT}} \text{L-}\gamma\text{-Glutamil-glicilglicină} + \text{5-Amino-2-nitrobenzoat}$$

GLUPA-C: L-γ-Glutamil-3-carboxi-p-nitroanilidă.

Creşterea absorbantei la 405 nm datorită formării de 5-amino-2-nitrobenzoat este proporţională cu activitatea γ-GT.

☞COMPOZIŢIA

Reactiv 1: R1			
Glicilglicină, pH 7,70 (37°C)		138	mmol/L
Azidă de sodiu	<	0,1	%
Reactiv 2: R2			
GLUPA-C		23	mmol/L
Azidă de sodiu	<	0,1	%

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Soluţie salină obişnuită (NaCl 9 g/L).
- Echipamente generale de laborator.
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

☞AVERTISMENTE ŞI PRECAUŢII

- Acest dispozitiv de diagnostic in vitro este destinat numai pentru uz profesional.
- Reactivii R1 şi R2 conţin azidă de sodiu care poate reacţiona cu plumbul sau instalaţiile sanitare din cupru şi poate forma azide metalice explozibile. În cazul aruncării acestor reactivi, spălaţi întotdeauna cu cantităţi mari de apă pentru a preveni formarea de azide.
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.
- Nu interschimbaţi fiolele de reactiv din truse diferite.
- Pentru mai multe informaţii, Fişa de date privind siguranţa (SDS) este disponibilă la cerere pentru utilizatorul profesional.

☞STABILITATEA

A se depozita la 2-8°C şi a se proteja împotriva luminii. A nu se îngheţa.

A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

☞DETERIORAREA PRODUSELOR

- Soluţia de reactivi trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiolă perforată).

PROBE [5]

Specimen

- Ser sau plasmă heparinizată de litiu.
- A nu se utiliza alte specimene.

Avertisment şi precauţii

Conform bunei practici de laborator, prelevarea trebuie efectuată înainte de administrarea de medicamente.

Depozitare şi stabilitate

Serurile sunt stabile timp de 7 zile la 2-8°C şi la temperatura camerei, şi 1 an la -20°C.

VALORI DE REFERINŢĂ [6]

	Bărbaţi	Femei
Ser, plasmă:	10-71 U/L	6-42 U/L

Notă: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems, aplicaţiile sunt disponibile la cerere

Lungime de undă: 405 nm
Temperatură: 37ºC
Citiţi pe reactivul martor.

Reactiv R1	220 µL
Proba	20 µL
Amestecaţi şi aşteptaţi 4 minute şi 43 de secunde.	
Reactiv R2	55 µL

Amestecaţi şi aşteptaţi 50 de secunde incubaţia, măsuraţi schimbarea absorbanţei pe minut (ΔA/min) timp de 159 de secunde.

Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestei inserţii.

CALCUL

$\frac{\Delta A\ \text{Proba}}{\Delta A\ \text{Calibrator}} \times n$ n=concentraţie calibrator

Factor de conversie: U/L x 0,0167 = µkat/L

CALIBRARE

Pentru calibrare, trebuie utilizat calibratorul multiparametric ELICAL 2. Valoarea sa este trasabilă conform metodei IFCC[4].

Frecvenţa de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

CONTROLUL CALITĂŢII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I şi ELITROL II. Aceste controale trebuie efectuate şi validate înainte ca eşantioanele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare, şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform liniilor directoare locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele locale şi legale.

DATE DE PERFORMANŢĂ la 37ºC privind Analizoarele Selectra ProM ale ELITech Clinical Systems

- **☞Interval de măsurare**

Determinat conform protocolului CLSI EP6-A[7], intervalul de măsurare este între 15 şi 1200 U/L (0,25 şi 20,00 µkat/L). care depăşesc 1 200 U/L trebuie să fie diluate 1:10 cu soluţie NaCl 9g/L (salină obişnuită) şi re-evaluate. Utilizarea acestei proceduri extinde intervalul de măsurare până la 12 000 U/L. (200,00 µkat/L).

Pentru utilizatorii Selectra TouchPro, funcţia „diluare" efectuează diluţia automată a eşantionului. Rezultatele iau în considerare diluţia.

Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)

Determinată conform protocolului CLSI EP17-A[8].

LoD= 4,4 U/L (0,07 µkat/L).
LoQ= 11,6 U/L (0,19 µkat/L).

- **Precizie**

Determinată conform protocolului CLSI EP5-A2[9].

		Medie		În interiorul ciclului	Total
	n	U/L	µkat/L	CV (%)	
Nivelul scăzut	80	39,7	0,66	1,7	3,0
Nivelul mediu	80	101,5	1,69	0,5	2,0
Nivelul înalt	80	525,9	8,77	0,2	1,9

- Corelaţie

A fost efectuat un studiu comparativ între reactivul ELITech Clinical Systems şi alt sistem concurent (metoda enzimatică standardizată IFCC) pe 94 de eşantioane de ser uman conform protocolului CLSI EP9-A2[10].

Valorile au fost între 13,0 şi 1169,7 U/L (între 0,22 şi 19,50 µkat/L).

Parametrii regresiilor liniare sunt după cum urmează:

Coeficient de corelaţie: (r)=0,999

Regresie liniară: y=0,900 x + 4,9 U/L (0,08 µkat/L)

- Limitări /interferenţe

- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Nu utilizaţi eşantioane vizibil turbide.
- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2 [11] al CLSI. Recuperarea este în intervalul ±10% din valoarea iniţială a activităţii γ-GT de 100,00 şi 500,00 U/L.

Bilirubină neconjugată: Nicio interferenţă semnificativă până la 30,0 mg/dL (513 µmol/L).

Bilirubină conjugată: Nicio interferenţă semnificativă până la 29,5 mg/dL (504 µmol/L).

Hemoglobină: Nicio interferenţă semnificativă până la 500 mg/dL.

Trigliceride: Nicio interferenţă semnificativă până la 926 mg/dL (10,46 mmol/L).

Glucoză: Nicio interferenţă semnificativă până la 540 mg/dL (29,97 mmol/L).

Acid acetilsalicilic: Nicio interferenţă semnificativă până la 200,00 mg/dL.

Acetaminofen: Nicio interferenţă semnificativă până la 30,0 mg/dL.
Metil-dopa: Nicio interferenţă semnificativă până la 1,0 mg/dL.
Doxaciclină HCl: Nicio interferenţă semnificativă până la 20 mg/dL.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. (12)
-
- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. (13-14)
-
- Rezultatele acestui studiu trebuie interpretate doar în conjuncţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- **Stabilitatea la bord/Frecvenţa calibrării**

Stabilitatea la bord: 14 de zile
Frecvenţa calibrării:14 zile
Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit, şi după o operaţie de întreţinere.

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4. Schumann, G., *et al*., *IFCC Primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37°C. Part 6. Reference procedure for the measurement of catalytic concentration of g-Glutamyltransferase*. Clin. Chem. Lab. Med., (2002), **40**, 734.
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8. *Protocols for Determination of Limits of Detection and Limits of Quantification; Approved Guideline*. CLSI (NCCLS) document EP17-A (2004), **24** (34).
9. *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition.* CLSI (NCCLS) document EP5-A2 (2004), **24** (25).
10. *Method Comparison and Bias estimation Using Patient Samples; Approved Guideline—Second Edition.* CLSI (NCCLS) document EP9-A2 (2002), **22** (19).
11. *Interference Testing in Clinical Chemistry ; Approved Guideline—Second Edition.* CLSI (NCCLS) document EP7-A2 (2005), **25** (27).
12. Berth, M. & Delanghe, J. *Protein precipitation as a possible important pitfall in the clinical chemistry analysis of blood samples containing monoclonal immunoglobulins:* 2 case reports and a review of literature, Acta Clin Belg., (2004), **59**, 263.
13. Young, D. S., Effects of preanalytical variables on clinical laboratory tests, 2nd Ed., AACC Press, (1997).
14. Young, D. S., Effects of drugs on clinical laboratory tests, 4th Ed., AACC Press, (1995).

☞SIMBOLURI

Simbolurile folosite sunt definite conform standardului ISO-15223-1 cu exceptia celor prezentate mai jos.

CONT	Conţinut
R1	Reactiv 1
R2	Reactiv 2
CE	Conformitate europeană

Notă

Doar pentru ref. **GISL-0250,** utilizată cu software-ul TouchPro.

☞

Gamma GT 1
760 VTL-GISL

☞*:Modificare faţă de versiunea precedentă.*

TOTAL PROTEIN PLUS

Referinţe:		**Compoziţia trusei:**
PROB-0250	*12 x 20 mL*	***R*** *12 x 20 mL*
PROB-0600	*2 x 125 mL*	***R*** *2 x 125 mL +* ***Std*** *1 x 5 mL*
PROB-0700	*4 x 250 mL*	***R*** *4 x 250 mL +* ***Std*** *1 x 5 mL*

CE

VTLRO-PROB-v12 (10/2020)_VTL-PROB-4-v12

☞SCOPUL UTILIZĂRII
ELITech Clinical Systems TOTAL PROTEIN PLUS este reactiv de diagnostic *in vitro* destinat determinării cantitative a proteinei totale din probele serul uman și plasmă.

SEMNIFICAŢIE CLINICĂ [1,2]
În plasma umană, albumina este prezentă în procent de 50-60% din proteinele totale: restul fracţiei conţine în special globuline (α1, α2, β şi γ). Majoritatea proteinelor plasmatice sunt sintetizate de ficat, cu excepţia imunoglobulinelor. Creşterea volumului plasmatic (sindromul de reţinere a sării, intoxicaţia cu apă...) sau reducerea sa (deshidratarea legată de vomă, diaree...) induc hipoproteinemie relativă, respectiv hiperproteinemie relativă.
Pentru un volum plasmatic normal, ratele anormale ale proteinelor totale apar doar în cazul bolii care afectează concentraţia albuminei sau imunoglobulinelor.
Astfel, insuficienţa proteică severă (malabsorbţia, maldigestia, insuficienţa dietetică), bolile renale şi hepatice, duc la hiperproteinemie. În cazul în care concentraţia proteinelor totale este mai mică de 4g/dL, pot fi observate edemele. Hiperproteinemia poate fi observată, de exemplu, în cazul hiperimunoglobulinemiei (mielom multiplu, infecţie).

METODĂ [3]
Biuret. Punct final.

PRINCIPIU [3]
Proteinele serice formează un complex colorrat în prezenţa sării de cupru din soluţia alcalină.

$$\text{Proteine} + Cu^{2+} \xrightarrow{\textit{Soluţie alcalină}} \text{Complex colorat}$$

☞COMPOZIŢIA
Reactiv: R

Sulfat de cupru	6 mmol/L
Hidroxid de sodiu	490 mmol/L

Conţine şi ioduri de sodiu şi tartrat de sodiu pentru performanţă optimă.

Standard: Std. (Ref.: PROB-0600/0700)

Albumină	6 g/dL
Azidă de sodiu	< 0.1 %

MATERIALE NECESARE DAR NEFURNIZATE
- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Echipamente generale de laborator.
- Nu utilizaţi materiale care nu sunt necesare, după cum este indicat mai sus.

☞AVERTISMENTE ŞI PRECAUŢII
- Acest dispozitiv de diagnostic in vitro (Reactiv şi Standardul) este destinat numai pentru uz profesional.
- Reactivul R este clasificat ca periculos.

ATENŢIE: Poate fi coroziv pentru metale. Provoacă iritarea pielii. Provoacă o iritare gravă a ochilor. Nociv pentru mediul acvatic cu efecte pe termen lung. Purtaţi mănuşi de protecţie/îmbrăcăminte de protecţie/echipament de protecţie a ochilor/echipament de protecţie a feţei. Evitaţi dispersarea în mediu.
ÎN CAZ DE CONTACT CU OCHII: clătiţi cu atenţie cu apă timp de mai multe minute. Scoateţi lentilele de contact, dacă este cazul şi dacă acest lucru se poate face cu uşurinţă. Continuaţi să clătiţi. Dacă iritarea ochilor persistă: consultaţi medicul. Absorbiţi scurgerile de produs, pentru a nu afecta materialele din apropiere.
- Standardul conţine azidă de sodiu care poate reacţiona cu plumbul sau instalaţiile din cupru pentru a forma potenţiale azide metalice explozive. În momentul eliminării acestui standard, spălaţi întotdeauna cu apă din abundenţă pentru a preveni acumularea de azide.
- Standardul trebuie să fie imediat inchis cu capacul pentru a preveni contaminarea şi evaporarea.
- Pentru mai multe informaţii, consultați Fişa de date privind siguranţa (SDS).
- Luaţi măsurile de precauţie obişnuite şi urmaţi buna practică de laborator.
- Utilizaţi doar echipamente de laborator curate sau de unică folosinţă pentru a evita contaminarea.

☞STABILITATEA
A se depozita la 2-25°C şi a se proteja împotriva luminii. A nu se îngheţa.
A nu se utiliza după datele de expirare indicate pe etichetele fiolelor.
<u>Stabilitatea la bord</u>:
Stabilitatea la bord este specifică pentru fiecare analizor.
(Consultaţi § DATE PRIVIND PERFORMANŢA).

☞PREGĂTIRE
Reactivii şi Standardul sunt gata pentru utilizare.

☞DETERIORAREA PRODUSELOR
- Soluţia de reactiv şi standard trebuie să fie limpede. Aspectul tulbure indică deteriorarea.
- Nu utilizaţi produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizaţi reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanţei produsului (scurgeri, fiolă perforată).

TOTAL PROTEIN PLUS

Referinţe:		Compoziţia trusei:
PROB-0250	*12 x 20 mL*	***R** 12 x 20 mL*
PROB-0600	*2 x 125 mL*	***R** 2 x 125 mL + **Std** 1 x 5 mL*
PROB-0700	*4 x 250 mL*	***R** 4 x 250 mL + **Std** 1 x 5 mL*

PROBE [1,2,4]

Specimen

- Ser
- Plasmă heparinizată cu litiu.
- A nu se utiliza alte specimene.

☞**Avertismente şi precauţii**

- Conform bunei practici de laborator, prelevarea trebuie efectuată înainte de administrarea de medicamente.
- Probele trebuie să fie libere din hemoliză şi lipemie.

Depozitare şi stabilitate

Probele sunt stabile timp de 7 zile la 2-8ºC şi cel puţin 2 luni la -20ºC. Pentru o depozitare mai îndelungată, îngheţaţi eşantioanele la -70ºC.

VALORI DE REFERINŢĂ [1,2,4]

	Pacienţi în ambulatoriu	*Pacienţi în repaus*
Ser:	6,4-8,3 g/dL	6,0-7,8 g/dL
	64-83 g/L	60-78 g/L

Plasmă:

Concentraţiile plasmei sunt mărite de la 0,2 la 0,4 g/dL (de la 2 la 4 g/L), în comparaţie cu concentraţiile serului (fibrinogen).

Notă: *Intervalul menţionat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referinţă pentru populaţia ţintă.*

☞PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems,
aplicaţiile sunt disponibile la cerere

Lungime de undă 546 nm

Temperatură: 37ºC

Citiţi pe reactivul martor.

	MARTOR	CALIBRARE	TEST
Reactiv R	300 µL	300 µL	300 µL
Apă distilată	3 µL		
Calibrator		3 µL	
Eşantion			3 µL

Amestecaţi şi citiţi absorbanţa (A) după o incubaţie de 11 minute şi 30 secunde.

Cu software-ul Selectra TouchPro, utilizaţi aplicaţia inclusă în codul de bare disponibil la finalul acestui insert.

Informaţii importante privind setarea:

Reactivul MAGNESIUM XYLIDYL poate fi slab contaminat cu TOTAL PROTEIN PLUS pe Selectra ProM şi ProXL.

Pentru a evita contaminarea pe aceste instrumente, programaţi următoarele incompatibilităţi:

Software	Meniu	Parametru
TouchPro	Incompatibilităţi sondă	Incompatibilitate/PROTEINA-MAGNEZIU
Altele	Incompatibilitate ace	PROTEINĂ: MAGNEZIU

☞CALCUL

$$\frac{\text{A Proba}}{\text{A Calibrator/Standard}} \times n$$

n = concentraţie calibrator/standard

Factor de conversie: g/dL x 10 = g/L

CALIBRARE

Pentru referinţele PROB-0600/PROB-0700: Pentru calibrare, trebuie utilizat calibratorul multiparametric ELICAL 2 sau Standardul proteină totală 6 g/dL.

Pentru referinţa PROB-0250: Pentru calibrare, utilizaţi calibratorul multiparametric ELICAL 2.

Valorile concentraţiei Standardului de proteina totala de 6 g/dL şi calibratorului multiparametric ELICAL 2 sunt trasabile conform Materialului Standard de Referinţă 909c (al Institutului Naţional de Standarde şi Tehnologie).

Frecvenţa de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultaţi § DATE PRIVIND PERFORMANŢA).

☞CONTROLUL CALITĂŢII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I şi ELITROL II. Aceste controale trebuie efectuate şi validate înainte ca probele pacienţilor să fie testate. Frecvenţa controlului trebuie să fie de cel puţin o dată pe zi, după fiecare calibrare şi trebuie adaptată la procedurile de Controlul Calităţii fiecărui laborator şi cerinţele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsuri corective. Materialele pentru controlul calităţii trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEŞEURILOR

Eliminarea tuturor deşeurilor trebuie să fie în conformitate cu cerinţele de reglementare locale, statale şi federale.

DATE DE PERFORMANŢĂ la 37ºC privind Analizoarele Selectra ProM ale ELITech Clinical Systems

- **Interval de măsurare**

Determinat conform protocolului CLSI EP6-A[5], intervalul de măsurare este între 0,20 şi 12,0 g/dL (de la 2,0 la 120,0 g/L).

- **Limita de detecţie (LoD) şi Limita de cuantificare (LoQ)**

Determinată conform protocolului CLSI EP17-A[6].

LoD= 0,03 g/dL (0,3 g/L).

LoQ= 0,10 g/dL (1,0 g/L).

- **Precizie**

Determinată conform protocolului CLSI EP5-A2[7].

		Medie		**În interiorul ciclului**	**Total**
	n	**g/dL**	**g/L**	**CV (%)**	
Nivel scăzut	80	4,03	40,3	0,4	1,0
Nivel mediu	80	6,62	66,2	0,3	1,6
Nivel înalt	80	9,06	90,6	0,5	1,1

- Corelaţie

A fost efectuat un studiu comparativ între analizorul Selectra ProM ELITech Clinical Systems şi un alt echipament al unui sistem aprobat de FDA (metoda Biuret) pe 100 probe de ser uman, conform protocolului CLSI EP9-A2[8].

Concentraţiile probelor au fost între 0,27 şi 11,25 g/dL (între 2,7 şi 112,5 g/L).

Parametrii regresiilor liniare sunt după cum urmează:

Coeficient de corelaţie: (r)=0,997

Regresie liniară: y=0,993 x + 0,05 g/dL
(0,5 g/L)

- Limitări şi interferenţe

- Nu raportaţi rezultatele în afara intervalului utilizabil.
- Au fost efectuate studii pentru a stabili nivelul interferenţei din diferiţi compuşi conform protocolului CLSI EP7-A2 [9] al CLSL şi recomandările SFBC. Recuperarea este în intervalul ±10% din valoarea iniţială a concentraţiei proteinei totale de 4,00; 6,50 şi 9,00 g/dL.

Bilirubină neconjugată: Nicio interferenţă semnificativă până la 30,0 mg/dL (513 µmol/L).

Bilirubină conjugată: Nicio interferenţă semnificativă până la 29,5 mg/dL (504 µmol/L).

Glucoză: Nicio interferenţă semnificativă până la 507 mg/dL (28,14 mmol/L).

Turbiditate: Nicio interferenţă semnificativă până la 263 mg/dL (2,97 mmol/L) echivalent trigliceride.

Hemoglobină: Nicio interferenţă semnificativă până la 300 mg/dL.

Dextran: Induce rezultate fals ridicate la concentraţii terapeutice.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. [11]

- Multe alte substanţe şi medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. [12,13]

- Rezultatele acestui studiu trebuie interpretate doar în corelaţie cu alte rezultate ale testelor de diagnosticare, constatările clinice şi istoricul medical al pacientului.

- **Stabilitatea la bord/Frecvenţa calibrării**

Stabilitatea la bord: 14 zile

Frecvenţa calibrării:14 zile

Recalibraţi când loturile de reactiv se schimbă, când rezultatele controlului calităţii sunt în afara intervalului stabilit şi după o operaţie de întreţinere.

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13. Young, D.S., Effects of drugs on clinical laboratory tests,4th Ed., AACC Press, (1995).

TOTAL PROTEIN PLUS

Referinţe:		**Compoziţia trusei:**
PROB-0250	*12 x 20 mL*	***R** 12 x 20 mL*
PROB-0600	*2 x 125 mL*	***R** 2 x 125 mL + **Std** 1 x 5 mL*
PROB-0700	*4 x 250 mL*	***R** 4 x 250 mL + **Std** 1 x 5 mL*

CE

☞SIMBOLURI

Simbolurile folosite sunt definite conform standardului ISO-15223-1 cu exceptia celor prezentate mai jos.

CONT	Conţinut
R	Reactiv
Std	Standard
CE	Conformitate europeană
☞	Modificare faţă de versiunea precedentă

NOTĂ IMPORTANTĂ

- Doar pentru ref. **PROB-0250**, utilizată cu software-ul Selectra TouchPro.
- Vezi **§PROCEDURĂ:** Risc de contaminare

Total Protein 0
700 VTL-PROB

MEDICA

Medica Corporation
5 Oak Park Drive
Bedford, Massachusetts 01730
Tel 781 275 4892
Fax 781 275 2731
www.medicacorp.com

Declaration of Conformity CE

Product Name:	Model/Type:
EasyLyte and accessories per attachment	EasyLyte Na/K, Na/K/Cl, Na/K/Li, Na/K/Cl/Li, Na/K/Ca/pH, Na/K/Cl/Ca/Li
EasyElectrolytes and accessories per attachment	EasyElectrolytes Na/K/Cl, Na/K/Li

Manufacturer

Medica Corporation
5 Oak Park Drive, Bedford, Massachusetts, 01730, USA

Representative

EC REP Emergo Europe, Prinsessegracht 20,
2514 AP The Hague, The Netherlands
Tel: +31 70 345 8570
Fax: +31 70 346 7299

Means of Conformity

Medica Corporation declares that the products listed are covered by Annex III of Directive 98/79/EC. These products are self-certified since they are for professional use only and are not listed on Annex II, List A or Annex II, List B of Directive 98/79/EC. In addition, they are in conformity with the Annex I, "Essential Requirements" and provisions of council Directive 98/79/EC for In Vitro Diagnostic Medical Devices, Directive 2011/65/EU Restriction of Hazardous Substance in Electrical and Electronic Equipment, and the corresponding national laws of the Member States.

Place and Date: Bedford, Massachusetts, USA, September 27, 2018

Signature:

Photios Makris

Name: Photios Makris, Ph.D.
Title: VP, Regulatory Affairs

EasyLyte Accessories

Catalog No.	Accessory	EDMA Code
2004	EasyLyte Na/K Analyzer	21 07 11 02
2014	EasyLyte Plus Na/K/Cl Analyzer	21 07 11 02
2015	EasyLyte Lithium Na/K/Li Analyzer	21 07 11 02
2016	EasyLyte Calcium Na/K/Ca/pH Analyzer	21 07 11 02
2021	EasyLyte Na/K/Cl/Li Analyzer	21 07 11 02
2030	EasyLyte EXPAND Analyzer, Na/K/Cl/Ca-Li	21 07 11 02
2070	EasyLyte EasySampler	21 07 11 02
2101	EasyLyte K+ Electrode	11 04 01 06
2102	EasyLyte Na+ Electrode	11 04 01 07
2113	EasyLyte Cl- Electrode	11 04 01 03
2106	EasyLyte Li+ Electrode	11 04 01 04
2150	EasyLyte Ca++ Electrode	11 04 01 02
2151	EasyLyte pH Electrode	11 70 31 02
2152	EasyLyte Disposable Reference Electrode	11 04 04 01
2103	EasyLyte Reference Electrode	11 04 04 01
2258	EasyLyte Membrane Assembly	21 07 11 02
2120	EasyLyte Na/K 800 ml Solutions Pack	11 04 04 02
2121	EasyLyte Na/K/Cl 800mL Solutions Pack	11 04 04 02
2122	EasyLyte Na/K/Li 800mL Solutions Pack	11 04 04 02
2123	EasyLyte Na/K/Ca/pH 800mL Solutions Pack	11 04 04 02
2028	EasyLyte Na/K/Cl/Li 400mL Solution Pack	11 04 04 02
2109	EasyLyte Na/K 400mL Solutions Pack	11 04 04 02
2112	EasyLyte Na/K/Cl 400mL Solutions Pack	11 04 04 02
2115	EasyLyte Na/K/Li 400mL Solutions Pack	11 04 04 02
2114	EasyLyte Na/K/Ca/pH 400mL Solutions Pack	11 04 04 02
2026	EasyLyte Na/K/Cl/Li 800mL Solution Pack	11 04 04 02
2124	EasyLyte Na/K/Cl/Ca-Li 800ml Solutions Pack	11 04 04 02
2814	EasyQC Bi-Level Quality Control Kit	11 50 02 04
2815	EasyQC Tri-Level Quality Control Kit	11 50 02 04
2843	EasyLyte Quality Control Sample Cups (60)	21 07 11 02
2118	Daily Cleaning Solution Kit	11 01 01 27
2598	EasyLyte Daily Cleaner Cup	21 07 11 02
2108	EasyLyte Solutions Valve	21 07 11 02
2107	EasyLyte Sample Probe	21 07 11 02
2257	EasyLyte Sample Detector	21 07 11 02

EasyLyte Accessories, continued

Catalog No.	Accessory	EDMA Code
2104	EasyLyte Tubing Kit	21 07 11 02
2100	EasyLyte Calcium Tubing Kit	21 07 11 02
2492	EasyLyte Internal Filling Solution (125mL)	11 04 04 90
2309	EasyLyte Wash Solution (50mL)	11 04 04 90
2111	EasyLyte Urine Diluent (500mL)	11 04 04 90
2577	EasyLyte Standard Solution, Urine (50mL)	11 04 04 90
2323	EasyLyte Probe Wipers (6)	21 07 11 02
2541	EasyLyte Printer Paper (3 rolls)	21 07 11 02
2595	EasyLyte EasySampler Sample Cups, 500uL (500)	21 07 11 02
2596	EasyLyte Sample Cups 2.0mL (500)	21 07 11 02
10745	Anti-Evaporation Caps (500)	21 07 11 02
2293	EasyLyte Capillary Tubes	21 07 11 02
2590	EasyLyte Capillary Adaptor Kit	21 07 11 02
2292	EasyLyte Capillary Adaptor Cleaning Kit	21 07 11 02
2578	EasyLyte Red Dye Test Solution (50mL)	11 30 01 11
2572	EasyLyte Troubleshooting Kit	21 07 11 02
2571	EasyLyte Troubleshooting Kit (Na/K/Ca/pH and Na/K/Cl/Li)	21 07 11 02
2105	EasyLyte Quarterly Operating Kit	21 07 11 02
2095	EasyLyte Maintenace Kit	21 07 11 02
2076	EasyLyte Sample Tray	21 07 11 02
2074	EasyLyte Sample Cup Retainer Ring	21 07 11 02
7118	Daily Rinse/Cleaning Solution Kit	11 01 01 27
2544	EasyLyte C Series Printer Paper (5 rolls)	21 07 11 02
2934	EasyLyte Barcode Reader Kit	21 07 11 02

EasyElectrolytes Accessories

Catalog No.	Accessory	EDMA Code
4002	EasyElectrolyte Na/K/Cl Analyzer	21 07 11 02
4003	EasyElectrolyte Na/K/Li Analyzer	21 07 11 02
4102	Reagent Module, Na/K/Cl	11 04 04 02
4103	Reagent Module, Na/K/Li	11 04 04 02
7205	EasyElectrolyte/EasyStat Na+ Electrode	11 04 01 07
7206	EasyElectrolyte/EasyStat K+ Electrode	11 04 01 06
4203	EasyElectrolyte Cl- Electrode	11 04 01 03
4204	EasyElectrolyte Li+ Electrode	11 04 01 04
6204	EasyElectrolyte/EasyStat/EasyBloodGas Reference Electrode	11 04 04 01
4207	EasyElectrolyte Spacer Electrode	11 04 01 90
4301	EasyElectrolyte Troubleshooting Kit	21 07 11 02
2118	Daily Cleaning Solution Kit	11 01 01 27
4402	EasyStat/EasyBloodGas/EasyElectrolyte Red Test Dye Solution	11 30 01 11
4403	EasyElectrolyte Urine Diluent	11 04 04 90
2814	Bi-Level Quality Control Kit	11 50 02 04
2815	Tri-Level Quality Control Kit	11 50 02 04
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4522	EasyElectrolyte Daily Cleaner Sample Cups	21 07 11 02
4539	EasyElectrolyte Sensor Module, Li+	21 07 11 02
6537	EasyElectrolyte/EasyStat/EasyBloodGas Serial Cable, 9-pin	21 07 11 02
6520	EasyElectrolyte/EasyStat/EasyBloodGas Barcode Reader Kit	21 07 11 02

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CERTIFICATE OF REGISTRATION

This is to certify that the management system of:

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(FIN F002402)

Main Site: 5 Oak Park Drive, Bedford, Massachusetts, 01730, United States

Additional Site: 3 Oak Park Drive, Bedford, Massachusetts, 01730, United States

has been registered by Intertek, an MDSAP recognized auditing organization, as conforming to the requirements of:

ISO 13485:2016

Brazil: Federal Law n. 6360/76; RDC ANVISA n. 16/2013; RDC ANVISA n. 23/2012; RDC ANVISA n. 67/2009; RDC ANVISA n. 56/2001

Canada: Medical Devices Regulations – Part 1- SOR 98/282

United States: 21 CFR 820, 21 CFR 803, 21 CFR 806, 21 CFR 807 (Subparts A to D)

Japan: MHLW Ministerial Ordinance 169, Article 4 to Article 68; PMD Act

The management system is applicable to:

Design, Development, Manufacture, Service, Installation and Distribution of in-vitro diagnostic medical devices, in-vitro diagnostic test kits, in-vitro diagnostic reagents, in-vitro diagnostic analyzers/software used in diagnosis and management of cancer, immune status, disease status, autoimmune status, cardiac markers, protein metabolism, endocrine disorders, blood analytes, urinalysis, blood gases.

Certificate Number:
0089217

Initial Certification Date:
2019-04-19

Certification Effective Date:
2019-04-19

Certification Expiry Date:
2022-04-18

MDSAP
MEDICAL DEVICE SINGLE AUDIT PROGRAM

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President, Business Assurance

Intertek Testing Services NA, Inc.
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EasyBloodGas™ analyzer
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Training Certificate

This is to certify that

Mr. Sergiu Sorocovici

of ***GBG-MLD S.R.L.***

has completed training for the operation and service of the

EasyBloodGas™ analyzer, **EasyElectrolytes**® analyzer, **EasyLyte**® analyzer and **EasyStat**® analyzer

04/22/2016
DATE

Medica Corporation

David Hagopian
Director of Technical Support

Declaration of Conformity

HL-7-0664DC DOI 2015/08 (1)

In Application of the Council Directive 98/79/EC on the approximation of the laws of the Member States relating to *In Vitro* Diagnostic Medical Devices & CE marking.

Declaration of conformance to applicable sections of Annex I - Essential Requirements and Annex III (EC Declaration of Conformity) imposed by sections 2 to 5. The below listed products are not classified under Annex II Lists A or B. Access to the appropriate technical files will be made available to the appropriate body in the event this is required.

Product Code	**Description**	**GMDN Classification Code**
5267L	Thromboplastin L	55983

I, the undersigned declare that the devices registered against the above GMDN Classification Code conforms to the said Directives.

Full Name: M.J. Stephenson

Title: Managing Director

Signed:

Date: 06 Aug 2015

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United Kingdom

Thromboplastin L

helena
Biosciences Europe

REF 5265HL
REF 5265L
REF 5267L

IVD

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HL-2-3035P 2015/10 (1)

Thromboplastin L
Instructions for use

en

INTENDED PURPOSE

The Thromboplastin L kit is intended for carrying out clot based haemostasis assays.

The first standardised one-stage prothrombin time test was developed by Dr. Armand Quick in 1935. It has now become the basic coagulation screening test for the diagnosis of congential and acquired deficiencies of clotting factors from the extrinsic pathway (factors II, V, VII and X)[1,2]. It is also used for the induction and monitoring of oral anticoagulant therapy[3,4] and can be used to assess the protein synthesis capability of the liver in chronic or acute hepatic disorders.
Thromboplastin L is of rabbit brain origin but resembles human preparations in its low International Sensitivity Index (ISI). The ISI of Thromboplastin L is approximately 1.1 and is calibrated against the WHO international reference preparation[5]. Thromboplastin L is particularly suited to the monitoring of oral anticoagulant therapy and, in conjunction with the appropriate factor deficient plasma, the measurement of factor activity in the extrinsic pathway. Tissue thromboplastin, in the presence of calcium ions, is an activator which initiates the extrinsic pathway of coagulation. When a mixture of tissue thromboplastin and calcium ions is added to normal citrated plasma, the clotting mechanism is activated, leading to a fibrin clot. If a deficiency exists within the extrinsic pathway, the time required for clot formation will be prolonged depending on the severity of the deficiency.

WARNINGS AND PRECAUTIONS

The reagents contained in this kit are for *in vitro* diagnostic use only – DO NOT INGEST. Wear appropriate personal protective equipment when handling all kit components. Refer to the product safety declaration for the link to appropriate hazard and precautionary statements where applicable. Dispose of components in accordance with local regulations.

COMPOSITION

Composition	Content	Description	Preparation
Thromboplastin L	2 x 5 mL (REF 5265HL) 8 x 5 mL (REF 5265L) 10 x 10 mL (REF 5267L)	Liquid Rabbit Brain Thromboplastin containing Calcium Chloride, stabilisers and preservatives.	The liquid, calcified thromboplastin is ready-for-use. No further calcium is required to carry out standard PT Assays. The contents of the vial should be mixed well before use. (5 minutes on roller).
Each kit contains Instructions For Use.			
Each kit contains lot specific reference values insert.			

ITEMS REQUIRED BUT NOT PROVIDED

The below products can be used in conjunction with Thromboplastin L:

REF 5519	ISI Calibrant Plasma Set
REF 5490	INR Reference Set

STORAGE, SHELF-LIFE AND STABILITY

Unopened reagents are stable until the given expiry date when stored under conditions indicated on the vial or kit label.

Thromboplastin L — Opened vials are stable for 2 months at +2 –+8°C, 5 days at +15°C (on-board Sysmex CA-1500) and 6 hours at +37°C (on-board AC-4 including reagent container and cap). A shift-use stability of 7 days (Sysmex CA-1500) can be achieved.
DO NOT FREEZE. Large clumps of particles or changes in expected values may indicate product deterioration.

SAMPLE COLLECTION AND PREPARATION

Plastic or siliconised glass should be used throughout. Blood (9 parts) should be collected into 3.2% or 3.8% sodium citrate anticoagulant (1 part). Separate plasma after centrifugation at 1500 x g for 15 minutes. Plasma should be kept at +18 –+24°C. Testing should be completed within 4 hours of sample collection, or plasma can be stored frozen at -20°C for 2 weeks or -70°C for 6 months. Thaw quickly at +37°C prior to testing. Do not keep at +37°C for more than 5 minutes[6].

PROCEDURE

For accurate INR reporting, it is recommended to determine the laboratory specific ISI of the reagent with the testing system in use. The Helena Biosciences Europe ISI Calibrant Plasma Set (REF 5519) is recommended for this purpose[7,8]. This should be performed for each new reagent batch. The Helena Biosciences Europe INR Reference Set (REF 5490) should be used to check for shifts in the local system ISI which have been noted with changes in laboratory temperature and post instrument servicing, amongst other local variances.

Manual Method

1. Mix sufficient Thromboplastin L to complete the anticipated testing for the day and incubate at +37°C for no more than 4 hours.
2. Pre-warm 0.1 mL of the test plasma at +37°C for 2 minutes.
3. Add 0.2 mL of freshly mixed thromboplastin reagent to the plasma while simultaneously starting a stopwatch.
4. Note the time for clot formation to the nearest 0.1 seconds.

Automated Method

Refer to the appropriate instrument operator manual for detailed instructions or contact Helena Biosciences Europe for instrument specific application guides.

INTERPRETATION OF RESULTS

Results should be reported to the nearest 0.1 seconds and duplicates should agree within 5% of each other. %PT values can be interpolated from the calibration graph (%PT of PT Calibration plasmas versus measured clot time), which should be a straight line when plotted on log-log graph paper.

INR values can be calculated using the following formula: $\mathrm{INR} = (\text{PT Time Patient / Mean Normal PT Time})^{\mathrm{ISI}}$

For clear guidance on the indications for and management of patients on warfarin, please refer to The British Society for Haematology, for their most current edition of 'Guidelines on oral anticoagulation with warfarin'. At time of printing this is the 2011 fourth edition[9].

LIMITATIONS

The use of serial dilutions of a reference plasma for the %PT curve is not recommended as this can lead to discrepancies caused by the low fibrinogen in the reference plasma dilutions which are not reflected in patient samples having predominantly normal fibrinogen levels. Helena Biosciences Europe advise use of the 5504R %PT/Direct INR kit for this purpose.

QUALITY CONTROL

Each laboratory should establish a quality control program. Normal and abnormal control plasmas should be tested prior to each batch of patient samples, to ensure satisfactory instrument and operator performance. If controls do not perform as expected, patient results should be considered invalid.
Helena Biosciences Europe supplies the following controls available for use with this product:

REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA
REF 5490	INR Reference Set

REFERENCE VALUES

Reference values can vary between laboratories depending on the techniques and systems in use. For this reason each laboratory should establish its own reference ranges. This is particularly important for local ISI calibration. Using the Sysmex series of instruments, normal values ranging from 11.50 - 14.60 seconds; 0.930 - 1.160 INR; 79.10 - 112.80 %PT are typical.

PERFORMANCE CHARACTERISTICS

The following performance characteristics have been determined by Helena Biosciences Europe or their representatives using a Sysmex CA-1500 coagulation instrument. Each laboratory should establish its own performance data.

Reproducibility

Sample	Routine Control N		Routine Control A		Routine Control SA	
	SD	*CV (%)*	*SD*	*CV (%)*	*SD*	*CV (%)*
Repeatability	0.07	0.59	0.24	1.09	0.45	1.11
Between-run	0.10	0.83	0.16	0.75	0.49	1.20
Between-day	0.04	0.32	0.06	0.27	0.25	0.62
Within-device / Laboratory	0.12	1.07	0.29	1.35	0.72	1.75

Interferences

Helena Thromboplastin L is insensitive to Heparin levels of up to 2 U/mL. Using a 5% interference threshold, there is no significant interference from Haemoglobin at concentrations up to 10 g/L. Using a 5% interference threshold, there is no significant interference from Bilirubin at concentrations up to 0.5 g/L for Thromboplastin L. Lipid interference testing demonstrates that lipid levels do not directly affect the clot time of the reagent up to 3.75g/L. Lipid concentrations in excess of this prevent clot detection.

Method Comparison

Comparison of clot time in seconds and INR values were determined using Thromboplastin L and Thromboplastin LI on 268 samples. The following correlations were obtained:

Thromboplastin L (Seconds) = 0.9911x + 0.1038	$r^2 = 0.9941$	n = 268
Thromboplastin L (INR) = 0.9853x + 0.0261	$r^2 = 0.9500$	n = 268

BIBLIOGRAPHY

1. Quick AJ (1935) A Study of the Coagulation Defect in Hemophilia and Jaundice, *Am. J. Med. Sci,* **190:** 501.
2. Biggs R (1976) Human Blood Coagulation, Haemostasis and Thrombosis, 2nd Edition, Blackwell Scientific Publications, London.
3. Hirsh J, Poller L, Deykin D, Levine J, Dalen JE (1989) Optimal Therapeutic Range for Oral Anticoagulants, *Chest,* **95:** 5S-11S.
4. Poller L (1986) Laboratory Control of Anticoagulant Therapy, *Sem. Thromb. Haemostasis,* **12:** 13-19.
5. World Health Organisation (1984) Expert Committee on Biological Standards, *Technical Series,* **700:** 19.
6. Clinical and Laboratory Standards Institute (2008) Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Haemostasis Assays: Approved Guideline, 5th edn. CLSI: H21-A5.
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8. Poller L, Triplett DA, Hirsh J, Carroll J, Clarke K (1995) A comparison of lyophilised artificially depleted plasmas and lyophilised plasmas from warfarin treated patients in correcting for coagulometer effects on International Normalised Ratios, *Amer. J. Clin. Pathol,* **103:** 366-371.
9. Keeling D (2011) Guidelines on Oral Anticoagulation with warfarin: Forth Edition, *British Journal of Haematology,* **154(3):** 311-324.

Thromboplastin L
Fiche technique

fr

UTILISATION

Le kit Thromboplastin L est destiné à la réalisation des analyses de l'hémostase basées sur la formation de caillots.

La première méthode de détermination standardisée du temps de prothrombine en une étape a été développée en 1935 par le Dr. Armand Quick. Cette méthode de Quick constitue désormais l'analyse de base de la coagulation servant à diagnostiquer des anomalies des facteurs de coagulation, congénitales ou acquises, à partir de la voie extrinsèque (facteurs II, V, VII et X)[1,2]. Elle sert aussi à l'induction et au monitorage des thérapies avec anticoagulants oraux[3,4] et elle peut être utilisée pour évaluer la capacité de synthèse des protéines du foie chez les patients souffrants de troubles hépatiques chroniques ou aigus.
Le Thromboplastin L provient de cerveaux de lapin mais il ressemble au BCT humain en raison de son indice de sensibilité international (ISI) faible. L'ISI du Thromboplastin L est d'environ 1,1 et est étalonné en comparaison avec la préparation internationale de référence de l'OMS[5]. Le Thromboplastin L convient tout particulièrement au monitorage des thérapies avec anticoagulants oraux et, utilisé conjointement au plasma carencé en un facteur approprié, à la détermination de l'activité du facteur de la voie extrinsèque. La thromboplastine tissulaire, en présence d'ions calcium, est un activateur qui démarre la voie extrinsèque de la coagulation. Quand un mélange de thromboplastine tissulaire et d'ions calcium est ajouté à un plasma citraté normal, le processus de coagulation, qui doit conduire à la production d'un caillot fibreux, s'active. Si la voie extrinsèque présente une anomalie, le temps nécessaire à la formation du caillot est allongé suivant la gravité du trouble de la coagulation.

AVERTISSEMENTS ET PRÉCAUTIONS

Les réactifs du kit sont à usage diagnostique *in vitro* uniquement – NE PAS INGÉRER. Porter un équipement de protection individuelle approprié lors de la manipulation de tous les composants du kit. Consulter la fiche de données de sécurité du produit pour obtenir le lien vers les phrases de risque et les conseils de prudence le cas échéant. Éliminer les composants conformément aux églementations locales.

COMPOSITION

Composant	Contient	Description	Préparation
Thromboplastin L	2 x 5 mL (REF 5265HL) 8 x 5 mL (REF 5265L) 10 x 10 mL (REF 5267L)	Thromboplastine liquide de cerveau de lapin contenant du chlorure de calcium, des stabilisateurs et des conservateurs.	La thromboplastine liquide calcifiée est prête à l'emploi. Aucun calcium supplémentaire n'est nécessaire pour réaliser des déterminations standard du TP. Le contenu du flacon doit être bien mélangé avant utilisation (5 minutes sur un mélangeur à rouleaux).
Chaque kit contient une fiche technique.			
Chaque kit contient valeurs de référence spécifiques du lot.			

MATÉRIEL NÉCESSAIRE NON FOURNI

Les produits ci-dessous peuvent être utilisés en conjonction avec la Thromboplastin L :

REF 5519	ISI Calibrant Plasma Set
REF 5490	INR Reference Set

CONSERVATION, DURÉE DE VIE UTILE ET STABILITÉ

Les flacons de réactif non ouverts sont stables jusqu'à la date de péremption indiquée s'ils sont conservés dans les conditions indiquées sur l'étiquette du kit ou du flacon.

Thromboplastin L — Les flacons ouverts sont stables pendant 2 mois à +2 °C – +8 °C, pendant 5 jours à +15 °C (à bord du Sysmex CA-1500) et pendant 6 heures à +37 °C (à bord de l'AC-4, récipient de réactif et capuchon inclus). Il est possible d'obtenir une stabilité de période de travail de 7 jours (Sysmex CA-1500).
NE PAS CONGELER. La présence de d'amas de particules ou un écart par rapport aux valeurs prévues indique une détérioration du produit.

PRÉLÈVEMENT ET PRÉPARATION DES ÉCHANTILLONS

Utiliser tout au long du prélèvement du plastique ou du verre siliconé. Mélanger 9 volumes de sang et 1 volume de citrate de sodium à 3,2% ou 3,8%. Séparer le plasma après centrifugation à 1500 x g pendant 15 minutes. Conserver le plasma entre +18 –+24°C. L'analyse doit être terminée dans les 4 heures suivant le prélèvement de l'échantillon ; sinon, il est possible de congeler le plasma 2 semaines à -20°C ou 6 mois à -70°C. Décongeler rapidement à +37°C avant de réaliser l'analyse. Ne pas laisser à +37°C plus de 5 minutes[6].

PROCÉDURE

Pour obtenir un RNI (rapport normalisé international) précis, il est recommandé à chaque laboratoire de déterminer l'ISI spécifique du réactif avec le système d'analyse utilisé. Il est conseillé d'utiliser le ISI Calibrant Plasma Set Helena Biosciences Europe (REF 5519) pour cela[7,8]. Cette opération doit être réalisée pour chaque nouveau lot de réactif. Le kit RNI de référence Helena Biosciences Europe (REF 5490) doit être utilisé pour vérifier l'existence d'un décalage de l'ISI du système local déterminé en raison d'une variation de la température du laboratoire, suite à une opération de maintenance réalisée sur l'instrument ou toute autre variable locale.

Méthode Manuelle

1. Mélanger du Thromboplastin L en quantité suffisante pour réaliser les analyses prévues dans la journée et incuber à +37 °C pendant 4 heures au maximum.
2. Préchauffer 0,1 mL de plasma à +37°C pendant 2 minutes.
3. Ajouter 0,2 mL de réactif de thromboplastine fraîchement mélangé au plasma et démarrer à ce moment un chronomètre.
4. Relever le temps de formation du caillot en arrondissant au dixième de seconde.

Méthodes Automatisées

Consulter le manuel d'utilisation de l'instrument approprié pour obtenir des instructions détaillées ou contacter Helena Biosciences Europe pour obtenir des notes d'application spécifiques à l'instrument.

INTERPRÉTATION DES RÉSULTATS

Les résultats doivent être indiqués en arrondissant au dixième de seconde et l'écart maximal entre eux est de 5%. Il est possible d'interpoler les valeurs de %TP à partir de la courbe d'étalonnage (%TP des plasmas d'étalonnage du TP par rapport au temps de coagulation mesuré), qui doit correspondre à une ligne droite quand elle est représentée sur du papier logarithmique.

La formule suivante permet de calculer les valeurs du RNI: $\mathrm{RNI} = (\text{Temps TP patient / Temps TP moyen normal})^{\mathrm{ISI}}$

Pour obtenir des informations claires quant aux indications et à la prise en charge des patients sous warfarine, consulter la British Society for Haematology pour obtenir la dernière édition des Guidelines on oral anticoagulation with warfarin (Recommandations relatives à l'anticoagulothérapie orale avec la warfarine). Au moment de l'impression du présent document, il s'agit de la quatrième édition de 2011[9].

LIMITES

Il est déconseillé de réaliser des dilutions du plasma de référence pour la courbe de %TP, car cela risquerait d'entraîner des divergences dues au faible taux de fibrinogène présent dans les dilutions du plasma de référence, ce qui ne serait pas représentatif des échantillons patients qui ont principalement des taux de fibrinogène normaux. Helena Biosciences Europe conseille l'utilisation du kit 5504R %PT/Direct INR dans ce but.

CONTRÔLE QUALITÉ

Chaque laboratoire doit établir un programme de contrôle qualité. Les plasmas de contrôle, normaux et anormaux, doivent être testés avant chaque lot d'échantillons patients afin de s'assurer que l'instrument et l'opérateur offrent des performances satisfaisantes. Si les contrôles ne donnent pas les résultats prévus, les résultats du patient doivent être considérés comme non valables.
Helena Biosciences Europe distribue les contrôles suivants à utiliser avec ce produit:

REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA
REF 5490	INR Reference Set

VALEURS DE RÉFÉRENCE

Les valeurs de référence peuvent varier d'un laboratoire à l'autre suivant les techniques et les systèmes utilisés. C'est pour cette raison qu'il appartient à chaque laboratoire de déterminer ses propres plages de référence. Ceci est particulièrement important pour l'étalonnage de l'ISI local. Avec les instruments de la série Sysmex, l'intervalle type des valeurs normales est de 11,50 - 14,60 secondes; 0.930 - 1.160 INR; 79.10 - 112.80 %PT .

CARACTÉRISTIQUES DE PERFORMANCES

Helena Biosciences Europe ou ses mandataires ont déterminé les caractéristiques de performance suivantes en utilisant un instrument de coagulation Sysmex CA-1500. Chaque laboratoire doit établir ses propres données de performance.

Reproductibilité

Échantillon	Routine Control N		Routine Control A		Routine Control SA	
	SD	*CV (%)*	*SD*	*CV (%)*	*SD*	*CV (%)*
Répétabilité	0,07	0,59	0,24	1,09	0,45	1,11
Inter-séries	0,10	0,83	0,16	0,75	0,49	1,20
Inter-jours	0,04	0,32	0,06	0,27	0,25	0,62
Intra-dispositif/laboratoire	0,12	1,07	0,29	1,35	0,72	1,75

Interférences

Thromboplastin L (ISI faible) d'Helena ne présente pas d'interférences avec un taux d'héparine jusqu'à 2 U/mL. En utilisant un seuil d'interférence de 5 %, il n'y a pas d'interférences significatives de l'hémoglobine à une concentration jusqu'à 10 g/L. En utilisant un seuil d'interférence de 5 %, il n'y a pas d'interférences significatives de la bilirubine à une concentration jusqu'à 0,5 g/L pour la Thromboplastin L. Une évaluation de l'interférence des lipides montre que les taux de lipides n'affectent pas le temps de coagulation du réactif jusqu'à 3,75 g/L. Une concentration en lipides dépassant cette limite empêche la détection du caillot.

Comparaison de la méthode

Des comparaisons du temps de coagulation en secondes et en valeurs de RNI ont été déterminées en utilisant les produits Thromboplastin L et Thromboplastin LI avec 268 échantillons. Les corrélations suivantes ont été obtenues:

Thromboplastin L (seconde) = 0,9911x + 0,1038	$r^2 = 0{,}9941$	n = 268
Thromboplastin L (INR) = 0,9853x + 0,0261	$r^2 = 0{,}9500$	n = 268

BIBLIOGRAPHIE

1. Quick AJ (1935) A Study of the Coagulation Defect in Hemophilia and Jaundice, *Am. J. Med. Sci,* **190:** 501.
2. Biggs R (1976) Human Blood Coagulation, Haemostasis and Thrombosis, 2nd Edition, Blackwell Scientific Publications, London.
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9. Keeling D (2011) Guidelines on Oral Anticoagulation with warfarin: Forth Edition, *British Journal of Haematology,* **154(3):** 311-324.

Thromboplastin L
Anleitung

de

VERWENDUNGSZWECK

Das Thromboplastin L Kit ist für koagulometrische Gerinnungstests vorgesehen.

Die erste standardisierte Prothrombinzeit als Einstufen-Test wurde 1935 von Dr. Armand Quick entwickelt. Mittlerweile ist er der Standard-Screeningtest in der Gerinnung zur Diagnose eines vererbten oder erworbenen Gerinnungsfaktormangels des extrinsischen Systems (Faktor II, V, VII und X)[1,2]. Er wird auch zur Einstellung und Überwachung von oralen Antikoagulanztherapien[3,4] verwendet und kann bei chronischen und akuten Lebererkrankungen zur Beurteilung der Funktionsfähigkeit der Leber bei der Proteinsynthese herangezogen werden.
Thromboplastin L wird aus Kaninchenhirn gewonnen, ähnelt aber mit seinem niedrigen „International Sensitivity Index" (ISI) humaner Blutgerinnungszeit. Der ISI von Thromboplastin L liegt bei ca. 1,1 und ist gegen WHO „International Reference Preparation" kalibriert[5]. Thromboplastin L ist besonders für die Überwachung oraler Antikoagulanztherapien geeignet und, in Verbindung mit dem entsprechenden Faktor-Mangelplasma, bei der Messung von Faktoraktivitäten im extrinsischen System. Gewebethromboplastin ist in Anwesenheit von Calcium-Ionen ein Aktivator, der das extrinsische Gerinnungssystem auslöst. Gibt man eine Mischung von Gewebethromboplastin und Calcium-Ionen zu normalem Citratplasma, wird die Gerinnungskaskade aktiviert und es bildet sich ein Fibringerinnsel. Besteht innerhalb des extrinsischen Systems ein Mangel, verlängert sich, je nach Schwere dieses Mangels, die Zeit bis zur Ausbildung eines Gerinnsels.

WARNHINWEISE UND VORSICHTSMASSNAHMEN

Die in diesem Kit enthaltenen Reagenzien sind ausschließlich für die Verwendung von *in-vitro*-Diagnosen vorgesehen. NICHT VERSCHLUCKEN. Tragen Sie beim Umgang mit sämtlichen Komponenten des Kits geeignete Schutzausrüstung. Beachten Sie gegebenenfalls die Verweise auf entsprechende Gefahren- und Vorbeugeerklärungen in der Produktsicherheitserklärung. Entsorgen Sie die Komponenten gemäß den örtlichen Vorschriften.

ZUSAMMENSETZUNG

Komponente	Inhalt	Beschreibung	Vorbereitung
Thromboplastin L	2 x 5 mL (REF 5265HL) 8 x 5 mL (REF 5265L) 10 x 10 mL (REF 5267L)	Flüssiges Thromboplastin aus Hasenhirn mit Calciumchlorid, Stabilisatoren und Konservierungsstoffen.	Das flüssige, kalzifizierte Thromboplastin ist einsatzbereit. Für die Durchführung von standardmäßigen PT-Analysen ist kein zusätzliches Calcium erforderlich. Der Inhalt der Ampulle muss vor der Verwendung gut gemischt werden (5 Minuten auf dem Walzenmischer).
Jedes Kit enthält eine Gebrauchsanweisung			
Jedes Kit enthält chargenspezifischen Referenzwerten			

ERFORDERLICHE, ABER NICHT MITGELIEFERTE ARTIKEL

Die folgenden Produkte können in Kombination mit Thromboplastin L verwendet werden:

REF 5519	ISI Calibrant Plasma Set
REF 5490	INR Reference Set

LAGERUNG, HALTBARKEIT UND STABILITÄT

Ungeöffnete Reagenzien sind unter den auf Verpackung oder Fläschchen angegebenen Lagerbedingungen bis zum aufgedruckten Verfallsdatum stabil.

Thromboplastin L — Offene Ampullen sind 2 Monate bei +2 –+8°C, 5 Tage bei +15°C (im Sysmex CA-1500) und 6 Stunden bei +37°C (im AC-4 mit Reagenzbehälter und Deckel) stabil. Eine Stabilität von 7 Tagen im Schichteinsatz (Sysmex CA-1500) kann erreicht werden.
NICHT EINFRIEREN. Große Verklumpungen oder Veränderungen in den Normalwerten können auf eine Verfall des Produkts hinweisen.

PROBENENTNAHME UND VORBEREITUNG

Nur Plastik oder Silikonglas verwenden. Blut (9 Teile) sollte in 3,2% oder 3,8% Natriumcitrat als Antikoagulanz (1 Teil) entnommen werden. 15 Minuten bei 1500 g zentrifugieren und Plasma abpipettieren. Plasma bei +18 –+24°C lagern. Plasma sollte innerhalb von 4 Stunden verarbeitet oder tief gefroren bei -20°C für 2 Wochen oder -70°C für 6 Monat gelagert werden. Vor dem Testen schnell bei +37°C auftauen. Nicht länger als 5 Minuten bei +37°C belassen[6].

VORGEHENSWEISE

Um einen korrekten INR zu erhalten wird empfohlen, den laborspezifischen ISI für das Reagenz mit dem verwendeten Testsystem zu bestimmen. Helena Biosciences Europe empfiehlt zu diesem Zweck das Plasma-Kalibrator-Set REF 5519[7,8]. Das sollte mit jeder neuen Reagenzien-Charge durchgeführt werden. Das Helena Biosciences Europe INR Reference Set (REF 5490) dient zur Überprüfung von Verschiebungen im ISI vor Ort, die unter anderem durch Veränderungen der Labortemperatur und nach Wartungsarbeiten an den Geräten festgestellt worden sind.

Manuelle Methode

1. Mischen Sie eine ausreichende Menge von Thromboplastin L an, um die für den Tag geplanten Tests durchzuführen und inkubieren Sie es nicht länger als 4 Stunden bei +37°C.
2. 0,1 mL des zu testenden Plasmas bei +37°C 2 Minuten vorwärmen.
3. 0,2 mL des frisch zubereiteten Thromboplastin-Reagenz zum Plasma pipettieren, dabei gleichzeitig Stoppuhr drücken.
4. Die Zeit bis zur Gerinnselbildung bis auf 0,1 Sekunden genau stoppen.

Automatisierte Methoden

Siehe die Bedienungsanleitung des entsprechenden Geräts für genaue Anweisungen oder wenden Sie sich an Helena Biosciences Europe für spezielle anwendungstechnische Hinweise.

INTERPRETATION DER ERGEBNISSE

Ergebnisse sollten bis auf 0,1 Sekunden genau gemessen werden und Doppelbestimmungen nicht mehr als 5% abweichen. % TPZ-Werte können ausgehend von der Kalibratorkurve interpoliert werden (% TPZ des TP-Kalibrationsplasmas zu gemessener Gerinnungszeit) und sollten auf doppeltlogarithmischem Millimeterpapier eine gerade Linie ergeben.

INR-Werte können anhand der folgenden Formel berechnet werden: $\mathrm{INR} = (\text{PT Zeit Patient / Mittelwert normale TPZ})^{\mathrm{ISI}}$

Für klare Leitlinien zu den Indikationen für und der Versorgung von Patienten unter Warfarin siehe die aktuelle Ausgabe der "Guidelines on oral anticoagulation with warfarin" der British Society for Haematology. Zum Zeitpunkt der Drucklegung ist das die 4. Ausgabe, 2011[9].

EINSCHRÄNKUNGEN

Die Verwendung einer Serienverdünnung von Referenzplasma ist für die %PT-Kurve nicht zu empfehlen, da das zu Diskrepanzen aufgrund von niedrigem Fibrinogen in den Referenzplasma-Verdünnungen führen kann, das nicht den Patientenproben entspricht, die in der Regel normale Fibrinogen-Werte haben. Helena Biosciences Europe empfiehlt zu diesem Zweck das Set 5504R %PT/Direct INR einzusetzen.

QUALITÄTSKONTROLLE

Jedes Labor muss für eine eigene Qualitätskontrolle sorgen. Vor jeder Testreihe mit Patientenproben müssen normale und pathologische Kontrollplasmen getestet werden, um eine zufrieden stellende Geräteleistung und Bedienung zu gewährleisten. Liegen die Kontrollen außerhalb des Normbereichs, sind die Patientenergebnisse nicht zu verwenden.
In Verbindung mit diesem Produkt bietet Helena Biosciences Europe die folgenden Kontrollen an:

REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA
REF 5490	INR Reference Set

REFERENZWERTE

Referenzwerte können je nach Technik und verwendetem System von Labor zu Labor unterschiedlich sein. Aus diesem Grund sollte jedes Labor seine eigenen Referenzwertbereiche erstellen. Dieses ist besonders für die ISI-Kalibration vor Ort wichtig. Mit der Instrumentenreihe Sysmex liegen die typischen Normwerte zwischen 11,50 - 14,60 Sekunden; 0.930 - 1.160 INR; 79.10 - 112.80 %PT .

LEISTUNGSMERKMALE

Die folgenden Leistungseigenschaften wurden von Helena Biosciences Europe oder in ihrem Auftrag mit einem Sysmex CA-1500 Gerinnungsgerät ermittelt. Jedes Labor muss seine eigenen Werte ermitteln.

Reproduzierbarkeit

Probe	Routine Control N		Routine Control A		Routine Control SA	
	SD	*CV (%)*	*SD*	*CV (%)*	*SD*	*CV (%)*
Wiederholbarkeit	0,07	0,59	0,24	1,09	0,45	1,11
Bei verschiedenen Analysen	0,10	0,83	0,16	0,75	0,49	1,20
An verschiedenen Tagen	0,04	0,32	0,06	0,27	0,25	0,62
Selbes Gerät/Labor	0,12	1,07	0,29	1,35	0,72	1,75

Störungen

Helena Thromboplastin L ist unempfindlich gegenüber Heparinwerten bis zu 2 Einheiten/mL. Mit einer Störschwelle von 5 % gibt es keine besondere Interferenz durch Hämoglobin bei Konzentrationen von bis zu 10 g/l. Mit einer Störschwelle von 5 % gibt es keine besondere Interferenz durch Bilirubin bei Konzentrationen von bis zu 0,5 g/l bei Thromboplastin L. Lipidinterferenztests zeigen, dass die Lipidmenge die Gerinnungszeit des Reagenz bis 3,7 g/l nicht direkt beeinflusst. Höhere Lipidkonzentrationen verhindern die Gerinnungserkennung.

Methodenvergleich

Thromboplastin L und Thromboplastin LI wurden an 268 Proben angewandt. Dabei wurden die Gerinnungszeit in Sekunden verglichen und die INR-Werte bestimmt. Es ergaben sich folgende Korrelationen:

Thromboplastin L (sekunden) = 0,9911x + 0,1038	$r^2 = 0{,}9941$	n = 268
Thromboplastin L (INR) = 0,9853x + 0,0261	$r^2 = 0{,}9500$	n = 268

LITERATURVERZEICHNIS

1. Quick AJ (1935) A Study of the Coagulation Defect in Hemophilia and Jaundice, *Am. J. Med. Sci,* **190:** 501.
2. Biggs R (1976) Human Blood Coagulation, Haemostasis and Thrombosis, 2nd Edition, Blackwell Scientific Publications, London.
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Thromboplastin L
Istruzioni per l'uso

it

SCOPO PREVISTO

III kit Thromboplastin L è concepito per l'esecuzione di dosaggi di emostasi basati sulla presenza di coaguli.

I primo test del tempo di protrombina standardizzato venne messo a punto dal Dr. Armand Quick nel 1935. Attualmente, questo test è diventato il metodo basilare di screening della coagulazione per la diagnosi di deficienze congenite ed acquisite dei fattori di coagulazione dal percorso estrinseco (fattori II, V, VII e X)[1,2]. Questo test viene utilizzato anche per l'induzione e il monitoraggio della terapia anticoagulante orale[3,4] e può essere impiegato per valutare la capacità di sintesi proteica del fegato in disordini epatici cronici o acuti.
Il kit Thromboplastin L è realizzato a partire da cervello di coniglio, ma rassomiglia a BCT umano in termini di basso indice di sensibilità internazionale (ISI). L'ISI del kit Thromboplastin L è approssimativamente pari a 1,1 ed è calibrato rispetto alla preparazione di riferimento internazionale dell'OMS[5]. Il kit Thromboplastin L è particolarmente indicato per il monitoraggio della terapia anticoagulante orale e, in combinazione con plasma carente del fattore appropriato, per la misurazione dell'attività del fattore nel percorso estrinseco. In presenza di ioni di calcio, la tromboplastina tissutale è un attivatore che dà inizio al percorso di coagulazione estrinseco. Quando una miscela di tromboplastina tissutale e di ioni di calcio viene aggiunta a normale plasma citrato, si attiva il meccanismo di coagulazione che porta alla formazione di un coagulo di fibrina. Qualora sussista una deficienza all'interno del percorso estrinseco, il tempo richiesto per la formazione del coagulo risulterà prolungato in funzione della gravità della deficienza.

AVVERTENZE E PRECAUZIONI

I reagenti contenuti in questo kit sono destinati esclusivamente alla diagnostica *in vitro* - NON INGERIRE. Indossare un'adeguata attrezzatura protettiva personale durante la manipolazione di tutti i componenti del kit. Per conoscere i relativi simboli precauzionali e di pericolo, laddove pertinente, fare riferimento alla dichiarazione di sicurezza del prodotto. Smaltire i componenti conformemente alle normative locali vigenti.

COMPOSIZIONE

Componente	Contiene	Descrizione	Preparazione
Thromboplastin L	2 x 5 mL (REF 5265HL) 8 x 5 mL (REF 5265L) 10 x 10 mL (REF 5267L)	Tromboplastina liquida di cervello di coniglio contenente cloruro di calcio, stabilizzatori e conservanti.	La tromboplastina calcica liquida è pronta all'uso. Per eseguire dosaggi PT standard non è necessario altro calcio. Il contenuto della fiala deve essere miscelato accuratamente prima dell'uso (5 minuti su un rullo).

Ogni kit contiene un Istruzioni per l'uso.

Ogni kit contiene un inserto recante i valori di riferimento specifici per il lotto.

MATERIALI NECESSARI, MA NON IN DOTAZIONE

In combinazione con la Thromboplastin L è possibile utilizzare i seguenti prodotti:

REF 5519	ISI Calibrant Plasma Set
REF 5490	INR Reference Set

CONSERVAZIONE, VITA UTILE E STABILITÀ

I reagenti non aperti sono stabili fino alla data di scadenza indicata se conservati nelle condizioni riportate sul flacone o sull'etichetta del kit

Thromboplastin L	Le fiale aperte sono stabili per 2 mesi ad una temperatura compresa tra +2 e +8°C, per 5 giorni a +15°C (Sysmex CA-1500 on-board) e per 6 ore a +37°C (AC-4 on-board compresi il contenitore del reagente e il tappo). È possibile ottenere una stabilità d'uso di 7 giorni (Sysmex CA-1500). NON CONGELARE. Ammassi consistenti di particelle o variazioni nei valori previsti possono essere indice di deterioramento del prodotto.

RACCOLTA E PREPARAZIONE DEI CAMPIONI

Nel corso dell'intera procedura è necessario utilizzare plastica o vetro siliconizzato. Il sangue (9 parti) deve essere raccolto in sodio citrato al 3,2% o al 3,8% come anticoagulante (1 parte). Separare il plasma in seguito a centrifugazione a 1500 x g per 15 minuti. Il plasma deve essere conservato a +18 –+24°C. I test devono essere completati entro 4 ore dalla raccolta dei campioni; in alternativa, il plasma può essere conservato congelato a -20°C per 2 settimane o a -70°C per 6 mese. Decongelare rapidamente a +37°C prima di eseguire i test. Non conservare a +37°C per oltre 5 minuti[6].

PROCEDURA

Per un rilevamento accurato dell'INR si raccomanda di determinare l'ISI specifico del laboratorio per il reagente con il sistema di test in uso. A tale scopo si raccomanda il ISI Calibrant Plasma Set (REF 5519) di Helena Biosciences Europe[7,8]. Questa procedura deve essere eseguita per ogni nuovo lotto di reagente. L'INR Reference Set (REF 5490) di Helena Biosciences Europe deve invece essere utilizzato per rilevare eventuali spostamenti dell'ISI del sistema locale osservati in concomitanza con cambiamenti della temperatura del laboratorio e in seguito a manutenzione dello strumento, tra le altre variazioni locali.

Metodo Manuale

1. Miscelare un quantitativo di Thromboplastin L sufficiente a completare i test previsti per la giornata e incubare a +37°C per un massimo di 4 ore.
2. Preriscaldare 0,1 mL di plasma di prova a +37°C per 2 minuti.
3. Aggiungere al plasma 0,2 mL di reagente a base di tromboplastina appena miscelato, azionando contemporaneamente un cronometro.
4. Annotare il tempo di formazione del coagulo con un'approssimazione a 0,1 secondi.

Metodo Automatico

Fare riferimento al manuale utente dello strumento appropriato per istruzioni dettagliate oppure contattare Helena Biosciences Europe per le note applicative specifiche dello strumento.

INTERPRETAZIONE DEI RISULTATI

I risultati devono essere indicati con un'approssimazione a 0,1 secondi e le ripetizioni devono corrispondere con una tolleranza del 5%. I valori di %PT possono essere interpolati dal grafico di calibrazione (%PT dei plasmi di calibrazione PT vs. tempo di coagulazione rilevato), che, se tracciato su carta a doppia scala logaritmica, deve apparire sotto forma di linea retta.

I valori di INR possono essere calcolati utilizzando la seguente formula: INR = (Tempo di PT Paziente / Tempo di PT normale medio)^{ISI}

Per una guida chiara sulle indicazioni per la gestione dei pazienti con warfarina fare riferimento a The British Society for Haematology per la loro edizione più aggiornata delle 'Linee guida sull'anticoagulazione orale con warfarina'. Al momento della stampa questa è la quarta edizione del 2011[9].

LIMITAZIONI

Si sconsiglia l'impiego di diluizioni seriali di un plasma di riferimento per la curva %PT, che infatti possono dare luogo a discrepanze dovute al basso livello di fibrinogeno nelle diluizioni del plasma di riferimento, che non compaiono invece nei campioni dei pazienti con livelli di fibrinogeno prevalentemente normali. Helena Biosciences Europe consiglia di utilizzare a questo scopo il kit 5504R %PT/Direct INR.

CONTROLLO QUALITÀ

Ogni laboratorio deve definire un programma di controllo qualità. I plasmi di controllo normali e anormali devono essere testati prima di ogni lotto di campioni di pazienti, per garantire un livello prestazionale soddisfacente sia per quanto riguarda lo strumento che per l'operatore. Qualora i controlli non funzionassero come previsto, i risultati relativi ai pazienti dovranno essere considerati non validi.
Helena Biosciences Europe mette a disposizione i seguenti controlli utilizzabili con questo prodotto:

REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA
REF 5490	INR Reference Set

VALORI DI RIFERIMENTO

Per la sicurezza del paziente, è necessario che il sistema sia monitorato continuamente da un operatore qualificato. Per tale motivo ciascun laboratorio dovrà elaborare i propri range di riferimento. Ciò è particolarmente importante per la calibrazione dell'ISI locale. Con l'impiego della gamma di strumenti Symex, i valori normali che variano tra 11,50 - 14,60 secondi; 0.930 - 1.160 INR; 79.10 - 112.80 %PT sono ritenuti tipici.

CARATTERISTICHE PRESTAZIONALI

Le seguenti caratteristiche prestazionali sono state determinate da Helena Biosciences Europe o dai propri rappresentanti con l'utilizzo di uno strumento di coagulazione Sysmex CA-1500. Ciascun laboratorio dovrà pertanto elaborare i propri dati prestazionali.

Riproducibilità

Campione	Routine Control N		Routine Control A		Routine Control SA	
	SD	*CV (%)*	*SD*	*CV (%)*	*SD*	*CV (%)*
Ripetibilità	0,07	0,59	0,24	1,09	0,45	1,11
Tra le serie	0,10	0,83	0,16	0,75	0,49	1,20
Tra giorni	0,04	0,32	0,06	0,27	0,25	0,62
All'interno del dispositivo/laboratorio	0,12	1,07	0,29	1,35	0,72	1,75

Interferenze
La Thromboplastin L Helena non è sensibile ai livelli di eparina di oltre 2 U/mL. Utilizzando una soglia di interferenza del 5%, non risulta esserci alcuna significativa interferenza da parte dell'emoglobina a concentrazioni fino a 10 g/l. Utilizzando una soglia di interferenza del 5%, non risulta esserci alcuna significativa interferenza da parte della bilirubina a concentrazioni fino a 0,5 g/l per la Thromboplastin L. I test per le interferenze dei lipidi dimostrano che i livelli dei lipidi non influenzano direttamente il tempo di coagulazione del reagente fino a 3,75 g/l. Concentrazioni lipidiche superiori a questo valore impediscono il rilevamento del coagulo.

Confronto dei metodi
Si è eseguito un confronto su 268 campioni tra il tempo di coagulazione in secondi e i valori INR utilizzando la tromboplastina L e la tromboplastina LI. Si sono ottenute le seguenti correlazioni:

Thromboplastin L (secondi) = 0,9911x + 0,1038	r^2 = 0,9941	n = 268
Thromboplastin L (INR) = 0,9853x + 0,0261	r^2 = 0,9500	n = 268

BIBLIOGRAFIA

1. Quick AJ (1935) A Study of the Coagulation Defect in Hemophilia and Jaundice, *Am. J. Med. Sci,* **190:** 501.
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6. Clinical and Laboratory Standards Institute (2008) Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Haemostasis Assays: Approved Guideline, 5th edn. CLSI: H21-A5.
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9. Keeling D (2011) Guidelines on Oral Anticoagulation with warfarin: Forth Edition, *British Journal of Haematology,* **154(3):** 311-324.

Thromboplastin L
Instrucciones de uso

es

USO PREVISTO

El uso previsto del kit Thromboplastin L es realizar ensayos de hemostasia basados en la coagulación.

La primera prueba estandarizada de la protrombina en una sola etapa fue desarrollada por el Dr. Armand Quick en 1935. Ahora se ha convertido en la prueba de cribado básico de la coagulación para el diagnóstico de deficiencias congénitas y adquiridas de factores de coagulación de la vía extrínseca (factores II, V, VII y X)[1,2]. Se usa también para la inducción y monitorización del tratamiento anticoagulante oral[3,4] y puede usarse para valorar la capacidad de síntesis de proteínas del hígado en trastornos hepáticos crónicos o agudos.
La Thromboplastin L tiene su origen en cerebro de conejo, pero se parece a la BCT humana en su bajo Índice de Sensibilidad Internacional (ISI). El ISI de Thromboplastin L es de aproximadamente 1,1 y se calibra contra el preparado de referencia internacional de la OMS[5]. La prueba de Thromboplastin L está especialmente adaptada a la monitorización del tratamiento anticoagulante oral y, conjuntamente con el plasma deficiente en el factor oportuno, la medición de la actividad de los factores en la vía extrínseca. La tromboplastina tisular, en presencia de iones calcio, es un activador que inicia la vía extrínseca de la coagulación. Cuando se añade una mezcla de tromboplastina tisular e iones calcio al plasma normal citratado, se activa el mecanismo de coagulación, conduciendo a un coágulo de fibrina. Si se produce una deficiencia dentro de la vía extrínseca, el tiempo necesario para la formación de coágulos se prolongará dependiendo de la intensidad de la deficiencia.

ADVERTENCIAS Y PRECAUCIONES

Los reactivos que contiene este kit son sólo para uso de diagnóstico *in vitro*: NO INGERIR. Lleve el equipo de protección personal adecuado cuando utilice todos los componentes del kit. Consulte la declaración de seguridad del producto para saber más sobre las indicaciones adecuadas de advertencia y riesgo. Desechar los componentes de conformidad con las normativas locales.

COMPOSICIÓN

Componente	Contiene	Descripción	Preparación
Thromboplastin L	2 x 5 mL (REF 5265HL) 8 x 5 mL (REF 5265L) 10 x 10 mL (REF 5267L)	Tromboplastina líquida de cerebro de conejo que contiene cloruro de calcio, estabilizadores y conservantes.	La tromboplastina líquida calcificada está lista para su uso. No es necesario más calcio para realizar pruebas estándar de PT. Los contenidos del vial se deben mezclar bien antes de utilizarlo (5 minutos en el rodillo).

Cada kit contiene instrucciones de uso.

Cada kit contiene valores de referencia específicos insertados del lote.

ARTÍCULOS NECESARIOS NO SUMINISTRADOS

Los siguientes productos se puede utilizar junto con la Thromboplastin L:

REF 5519	ISI Calibrant Plasma Set
REF 5490	INR Reference Set

ALMACENAMIENTO, CADUCIDAD Y ESTABILIDAD

Los reactivos no abiertos son estables hasta la fecha de caducidad indicada cuando se conservan en las condiciones indicadas en el vial o en la etiqueta del kit.

Thromboplastin L	Los viales abiertos permanecen estables durante 2 meses a una temperatura de entre +2 – +8°C, 5 días a una temperatura mayor a +15°C (en el Sysmex CA1500), y 6 horas a una temperatura mayor a +37°C (en el AC-4, incluido el contenedor del reactivo y el tapón). Se puede conseguir estabilidad multiuso de 7 días (Sysmex CA-1500). NO CONGELAR. Los grumos grandes de partículas o los cambios en los valores esperados pueden indicar deterioro del producto.

RECOGIDA Y PREPARACIÓN DE LAS MUESTRAS

Debe usarse siempre plástico o vidrio siliconizado. Debe recogerse sangre (9 partes) en el anticoagulante citrato sódico al 3,2% o al 3,8% (1 parte). Separar el plasma después de la centrifugación a 1500 x g durante 15 minutos. El plasma debe conservarse a +18 –+24°C. Las pruebas deberían terminarse en 4 horas desde la recogida de las muestras o el plasma puede conservarse congelado a -20°C durante 2 semanas o -70°C durante 6 mes. Descongelar rápidamente a +37°C antes de realizar la prueba. No conservar a +37°C durante más de 5 minutos[6].

PROCEDIMIENTO

Para la comunicación exacta del INR, se recomienda determinar la ISI específica del laboratorio del reactivo con el sistema de prueba en uso. Se recomienda el ISI Calibrant Plasma Set de Helena Biosciences Europe (REF 5519) para este fin[7,8]. Esto debe realizarse para cada nuevo lote de reactivos. Debe usarse el Set de Referencia de INR de Helena Biosciences Europe (REF 5490) para comprobar las desviaciones en el ISI del sistema local que se han observado con cambios en la temperatura del laboratorio y el mantenimiento posinstrumental, entre otras variaciones locales.

Método Manual

1. Mezclar la cantidad suficiente de Thromboplastin L para completar la prueba anticipada para el día e incubar a +37°C durante un período de tiempo no superior a 4 horas.
2. Precaliente 0,1 mL del plasma de prueba a +37°C durante 2 minutos.
3. Añada 0,2 mL de reactivo de tromboplastina recién mezclado al plasma mientras pone en marcha simultáneamente un cronómetro.
4. observa el tiempo hasta la formación del coágulo procurando afinar en la décima 0,1 de segundo más próxima.

Método Automatizado

Consulte el manual del usuario del instrumento adecuado para instrucciones detalladas o póngase en contacto con Helena Biosciences Europe para notas de aplicación específicas del instrumento.

INTERPRETACIÓN DE LOS RESULTADOS

Los resultados deben comunicarse en los 0,1 segundos más próximos y las pruebas duplicadas deben estar de acuerdo entre sí dentro del 5%. Los valores de %TP pueden interpolarse a partir del gráfico de calibración (%TP de los plasmas de calibración del TP frente al tiempo de coágulo medido) que debe ser una línea recta cuando se representa en un papel de gráficos log-log.

Los valores de INR pueden calcularse usando la siguiente fórmula: INR = (Tiempo de TP Paciente / Tiempo de TP normal medio)^{ISI}

Si necesita una guía clara de indicaciones y tratamiento de pacientes con warfarina, consulte The British Society for Haematology y su última edición de "Guidelines on oral anticoagulation with warfarin" que, en el momento de impresión de este documento, se encuentra en su cuarta edición de 2011[9].

LIMITACIONES

El uso de diluciones seriadas de un plasma de referencia para la curva de %TP no se recomienda, porque puede llevar a discrepancias producidas por el bajo fibrinógeno en las diluciones del plasma de referencia, que no se reflejan en las muestras de pacientes que tienen fundamentalmente niveles normales de fibrinógeno. Helena Biosciences Europe recomienda utilizar el kit 5504R %PT/INR directa a tal fin.

CONTROL DE CALIDAD

Cada laboratorio debe establecer un programa de control de calidad. Los controles normales y anormales deben estudiarse antes de cada lote de muestras del paciente, para asegurar un funcionamiento adecuado del instrumento y el operador. Si los controles no se realizan como se esperaba, los resultados del paciente deben considerarse inválidos.
Helena Biosciences Europe suministra los siguientes controles disponibles para usar con este producto:

REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA
REF 5490	INR Reference Set

VALORES DE REFERENCIA

Los valores de referencia pueden variar entre los laboratorios dependiendo de las técnicas y sistemas usados. Por esta razón, cada laboratorio debe establecer su propio intervalo normal. Esto es especialmente importante para la calibración local del ISI. Con la serie de instrumentos Sysmex, es frecuente que los valores normales varíen entre 11,50 - 14,60 segundos; 0.930 - 1.160 INR; 79.10 - 112.80 %PT .

CARACTERÍSTICAS FUNCIONALES

Las siguientes características de rendimiento han sido determinadas por Helena Biosciences Europe o sus representantes usando un instrumento de coagulación Sysmex CA-1500. Cada laboratorio debe establecer sus propios datos de rendimiento.

Reproductibilidad

Muestra	Routine Control N		Routine Control A		Routine Control SA	
	SD	*CV (%)*	*SD*	*CV (%)*	*SD*	*CV (%)*
Repetibilidad	0,07	0,59	0,24	1,09	0,45	1,11
Entre series	0,10	0,83	0,16	0,75	0,49	1,20
Entre días	0,04	0,32	0,06	0,27	0,25	0,62
En el dispositivo/laboratorio	0,12	1,07	0,29	1,35	0,72	1,75

Interferencias

Helena Thromboplastin L no detecta niveles de heparina inferiores a 2 U/mL.Con un umbral de interferencia del 5%, no hay interferencias significativas de hemoglobina en concentraciones de hasta 10 g/L. Con un umbral de interferencia del 5%, no hay interferencias significativas de bilirrubina en concentraciones de hasta 0,5 g/L para Thromboplastin L. La interferencia de lípidos demuestra que los niveles de lípidos no afectan directamente al tiempo de coagulación del reactivo hasta 3,75 g/L. Las concentraciones de lípidos superiores evitan detectar la coagulación.

Comparación del método

La comparación del tiempo de coagulación y los valores INR se determinó con tromboplastina L y tromboplastina LI en 268 muestras. Se obtuvieron las siguientes correlaciones:

Thromboplastin L (segundo) = 0,9911x + 0,1038	r^2 = 0,9941	n = 268
Thromboplastin L (INR) = 0,9853x + 0,0261	r^2 = 0,9500	n = 268

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Тест-система "Жидкий тромбопластин"
инструкция

ru

НАЗНАЧЕНИЕ

Комплект Тест-система "Жидкий тромбопластин" предназначен для выполнения анализов гемостаза на основе кровяного сгустка.

Впервые стандартизированный одностадийный тест для определения протромбинового времени был предложен д-ром Армандом Квиком в 1935г. Сейчас он стал основным скрининговым тестом для диагностики врожденного и приобретенного дефицитов факторов свертывания крови по внешнему пути (факторы II, V, VII и X)[1,2]. Он также используется для мониторинга терапии оральными антикоагулянтами[3,4], а также может применяться и для оценки белок синтетической функции печени при ее острых либо хронических заболеваниях.
Реагент приготовлен из экстракта ткани мозга кролика и по значению своего МИЧ (Международного Индекса Чувствительности) сопоставим со Стандартом Тромбопластина Британии (ВСТ – British Comparative Thromboplastin). МИЧ Жидкого тромбопластина примерно равен 1.1 и откалиброван относительно международного референса ВОЗ[5]. Жидкий тромбопластин особенно подходит для мониторинга терапии оральными антикоагулянтами и для измерения активности факторов внешнего пути свертывания(вместе с соответствующей фактор-дефицитной плазмой). Тканевый тромбопластин в присутствии йонов кальция является активатором внешнего пути свертывания крови. При добавлении смеси тканевого тромбопластина с кальцием к нормальной цитратной плазме активируется механизм её свертывания, приводящий к образованию фибринового сгустка. Если у пациента имеет место дефицит факторов внешнего пути, то время, необходимое для образования сгустка будет удлиняться прямо пропорционально степени дефицита факторов.

ПРЕДУПРЕЖДЕНИЯ И МЕРЫ ПРЕДОСТОРОЖНОСТИ

Содержащиеся в данном наборе реагенты предназначены только для *in vitro* диагностики– НЕ ПРИНИМАТЬ ВНУТРЬ! При работе со всеми компонентами набора использовать соответствующие средства индивидуальной защиты. В случае необходимости см. свидетельство о безопасности изделия для ознакомления с соответствующими описаниями опасного воздействия и сведениями о мерах предосторожности. Удаление компонентов в отходы производите в соответствии с местными правилами.

СОСТАВ

Компоненты	Состав набора	Описание	Приготовление реагентов
Жидкий тромбопластин	2 x 5 мл (Кат.№ 5265HL) 8 x 5 мл (Кат.№ 5265L) 10 x 10 мл (Кат.№ 5267L)	Тромбопластин-кальциевая суспензию реагента из экстракта ткани мозга кролика, раствора хлорида кальция и стабилизаторов	Жидкий кальцинированный тромбопластин, готовый для использования. Для проведения теста ПВ дополнительный кальций не требуется. Содержимое флакона перемешать до использования (5 мин. на роллере)

Каждый набор содержит инструкцию по применению.

Вкладыш с указанием рефересных значений к различным анализаторам и методам исследования, характерным для данного лота.

НЕОБХОДИМЫЕ КОМПОНЕНТЫ, НЕ ВКЛЮЧЕННЫЕ В КОМПЛЕКТ ПОСТАВКИ

Продукция ниже, которая может использоваться вместе с Тест-системой «Тромбопластин»:

Кат.№ 5519	Калибратор МИЧ
Кат.№ 5490	Контроль на МНО

ХРАНЕНИЕ, СРОК ГОДНОСТИ И УСТОЙЧИВОСТЬ

Невскрытые флаконы с реагентами хранятся до истечения срока годности в условиях, указанных на этикетке.

Жидкий тромбопластин	Вскрытые флаконы годны к применению в течение 2 месяцев при температуре хранения 2-8°C, 5 дней при 15°C (на борту Sysmex CA-1500) и 6 часов при 37°C (на борту AC-4, используя контейнер для реагентов с крышкой). Стабильность реагента на борту Sysmex CA-1500 - 7 дней. НЕ ЗАМОРАЖИВАТЬ! Признаки ухудшения качества реагента: большое скопление частиц или отличия от ожидаемых значений могут означать ухудшение свойств реактива.

ОТБОР И ПОДГОТОВКА ОБРАЗЦОВ

Для работы следует использовать только пластиковые или силиконированные стеклянные пробирки. Кровь забирается в пробирку с цитратным антикоагулянтом (3,2% или 3,8% цитрат натрия) в соотношении 9 + 1. После центрифугирования при 1500 g, в течение 15 минут (использование других параметров должно проверяться лабораторией), полученную плазму необходимо отделить от форменных элементов крови. Плазму следует хранить при температуре +18 –+24°C. Тестирование должно быть проведено в течение 4 часов после забора образцов, либо плазму можно однократно заморозить и хранить при температуре -20°C в течение 2 недель или при -70°C в течение 6 месяцев. Перед проведением исследования плазму следует быстро разморозить при +37°C. Не держать плазму при +37°C более 5 минут[6].

ПРОЦЕДУРА

Для установления более точного МНО рекомендуется определить специфическое для лаборатории значение МИЧ (так называемый «локальный» МИЧ) для жидкого тромбопластина. Helena Biosciences Europe рекомендует для этих целей применять Калибратор МИЧ (Кат.№ REF 5519)[7,8]. Подобная процедура должна быть проведена для каждой новой партии реагентов. Контроль на МНО (Кат.№ REF 5490) используется для контроля изменения в «локальном» МИЧ, так как его значение может незначительно варьировать в зависимости от используемых приборов, а также изменений температуры в лаборатории и других локальных факторов.

Ручной Метод

1. Взять необходимое количество жидкого тромбопластина, необходимое для проведения тестирования в течение дня и инкубировать при 370С (но не более 4 часов).
2. Прогреть 0,1 мл тестируемой плазмы при +37°C в течение 2 минут.
3. Добавить 0,2 мл свежеприготовленной рабочей смеси реагентов к плазме и немедленно включить таймер.
4. Заметить время, необходимое для образования сгустка с точностью до 0,1сек.

Автоматизированный Метод

Для проведения тестирования на автоматических коагулометрах, необходимо обратиться к руководству пользователя и к соответствующей адаптации, которые доступны у официальных дистрибьюторов и компании Хелена.

ИНТЕРПРЕТАЦИЯ РЕЗУЛЬТАТОВ

Результаты должны быть представлены с точностью до 0,1 сек и разница в повторах не должна превышать 5%. Значение %ПВ можно определить по калибровочному графику (график зависимости %ПВ от измеренного времени), который должен быть строго линейным в билогарифмических координатах при построении графика на миллиметровке с логарифмическим масштабом на обеих осях.

МНО может быть вычислено по формуле: МНО= {ПВ (пациента)/среднее ПВ (норма)}^{МИЧ}

Для более подробной информации по мониторингу пациентов на Варфарине обратитесь к рекомендациям Британского Общества по Гематологии - «Рекомендации по антикоагулянтной терапии варфарином», 4-е издание 2011г. на время печати этого документа[9].

ОГРАНИЧЕНИЯ

Для получения графика зависимости (%ПТ) от времени свертывания не рекомендуется использовать серии разведений референсной плазмы, поскольку это может привести к неточности, вызванной низким содержанием фибриногена в больших разведениях рефересной плазмы, что не соответствует образцам пациентов, имеющих, в основном, нормальный уровень фибриногена. Компания Хелена рекомендует использовать калибратор кат. номер 5504R для %ПВ, и прямого определения МНО.

КОНТРОЛЬ КАЧЕСТВА

Каждая лаборатория должна установить программу контроля качества. Перед измерением каждой партии образцов пациентов необходимо протестировать нормальную и патологическую плазму, чтобы удостовериться в удовлетворительной работе оборудования и оператора. Если контрольные измерения не совпадают с ожидаемыми значениями, то измеренные данные пациентов следует считать недостоверными.
Компания Хелена рекомендует следующие контрольные материалы:

Кат.№ 5186	Контроль качества, норма
Кат.№ 5187	Контроль качества, умеренно выраженная патология
Кат.№ 5183	Контроль качества, высокая патология
Кат.№ 5490	Контроль на МНО

НОРМАЛЬНЫЕ ПОКАЗАТЕЛИ

Референсные значения могут варьировать между лабораториями в зависимости от используемых методов и анализаторов. В связи с этим каждая лаборатория должна определить свою собственную область нормальных значений. Это крайне важно для установки локального МИЧ тромбопластина. Диапазон нормальных значений пациентов 11,50 - 14,60 сек.; 0.930 - 1.160 INR; 79.10 - 112.80 %PT с использованием коагулометров Sysmex.

ЭКСПЛУАТАЦИОННЫЕ ХАРАКТЕРИСТИКИ

Компания Хелена или её дистрибьюторы определили следующие ориентировочные аналитические характеристики. Каждая лаборатория должна определить свои собственные аналитические характеристики. При использовании оптико-механического коагулометра и реагентов Хелена были определены следующие коэффициенты вариации (CV):

Воспроизводимость

Образец	Контроль качества, норма		Контроль качества, умеренно выраженная патология		Контроль качества, высокая патология	
	SD	*CV (%)*	*SD*	*CV (%)*	*SD*	*CV (%)*
Воспроизводимость	0,07	0,59	0,24	1,09	0,45	1,11
в пределах аналитической серии	0,10	0,83	0,16	0,75	0,49	1,20
между разными аналитическими сериями	0,04	0,32	0,06	0,27	0,25	0,62
между партиями/лабораториями	0,12	1,07	0,29	1,35	0,72	1,75

Тест-система "Жидкий тромбопластин" не чувствителен к гепарину в концентрации до 2 Ед/мл. Используя 5% допустимое отклонение, реагент не чувствителен к гемоглобину в концентрации до 10 г/Л. Используя 5% допустимое отклонение, реагент не чувствителен к билирубину в концентрации до 0.5 г/Л. Не обнаружено чувствительности к уровню липидов до 3.75 г/Л оказывающих воздействие на время свёртываемости. Концентрации липидов выше этого уровня предотвратит обнаружение сгустка.

Сравнение со стандартами:
Сравнение значений МНО 268 образцов, определённых с помощью Тест-системы "Тромбопластин" и Тест-системы "Жидкий тромбопластин" дало следующие корреляционные соотношения:

Жидкий Тромбопластин (сек) = 0,9911x + 0,1038	r^2 = 0,9941	n = 268
Жидкий Тромбопластин (МНО) = 0,9853x + 0,0261	r^2 = 0,9500	n = 268

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9. Keeling D (2011) Guidelines on Oral Anticoagulation with warfarin: Forth Edition, *British Journal of Haematology,* **154(3):** 311-324.

Declaration of Conformity

helena
Biosciences Europe

HL-7-0136DC DOI 2015/07 (6)

In Application of the Council Directive 98/79/EC on the approximation of the laws of the Member States relating to *In Vitro* Diagnostic Medical Devices & CE marking.

Declaration of conformance to applicable sections of Annex I - Essential Requirements and Annex III (EC Declaration of Conformity) imposed by sections 2 to 5. The below listed products are not classified under Annex II Lists A or B. Access to the appropriate technical files will be made available to the appropriate body in the event this is required.

Product Code	**Description**	**GMDN Classification Code**
5185	Calibration Plasma	55995

I, the undersigned declare that the devices registered against the above GMDN Classification Code conforms to the said Directives.

Full Name: M.J. Stephenson Title: Managing Director

Signed: Date: 28 Jul 2015

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Calibration Plasma

REF 5185

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HL-2-0424P 2016/01 (14)

Calibration Plasma
Instructions for use

en

INTENDED PURPOSE

The Calibration Plasma kit is intended for use as a calibration material.

Calibration Plasma may be used as a reference plasma when assaying for Factors II, V, VII, VIII, IX, X[1], XI, XII[2], fibrinogen[3], von Willebrand Factor, antigenic and functional Protein C and Protein S (total and free), as well as the chromogenic assays including Antithrombin (AT) III, Protein C, Factor VIII and Plasminogen. Calibration Plasma is used in factor assays and other testing in the same manner as a fresh plasma pool. Factor II, VII, VIII, IX and X values and the chromogenic Factor VIII, AT III and Protein C values are traceable to World Health Organisation standards to ensure the utmost credibility in values stated[4]. The reference plasma should be used to gauge internal factors in each laboratory's system. The reference plasma should not be used to determine normal ranges since normals vary from population to population.

WARNINGS AND PRECAUTIONS

The reagents contained in this kit are for *in vitro* diagnostic use only – DO NOT INGEST. Wear appropriate personal protective equipment when handling all kit components. Refer to the product safety declaration for the link to appropriate hazard and precautionary statements where applicable. Dispose of components in accordance with local regulations.

Blood products have been screened and found negative (unless otherwise stated on the kit box or vial) for the presence of:
Hepatitis B Antigen (HbsAg)
HIV 1 antibody HIV 2 antibody
HCV antibody
However they should be handled with the same precautions as a human patient sample.

COMPOSITION

Component	Content	Description	Preparation
Calibration Plasma	10 x 1 mL	Calibration Plasma is prepared from a frozen pool of citrated plasma from healthy donors and is buffered and lyophilised to ensure stability of all plasma constituents[5].	Reconstitute with 1 mL of distilled or deionised water. Swirl gently. Allow product 20 minutes for complete dissolution.

Each kit contains instructions for use.
Each kit contains a lot specific reference values insert.

ITEMS REQUIRED BUT NOT PROVIDED

Calibration Plasma may be used when performing tests on any mechanical or photo-optical coagulation instrument in conjunction with all suitable, commercial reagents.

STORAGE, SHELF-LIFE AND STABILITY

Unopened vials are stable until the given expiry date when stored under conditions indicated on the vial or kit label. Values for Factor VIII, von Willebrand factor and ristocetin co-factor are stable for 2 hours at +2 – +8°C. All other factors are stable for 4 hours at +2 – +8°C. The unreconstituted Calibration Plasma must appear as a light yellow, dry plug. If any unusual conditions are noted, the customer should notify Helena Biosciences Europe, before using.

SAMPLE COLLECTION AND PREPARATION

Not applicable.

PROCEDURE

Refer to the appropriate instrument Operator Manual for detailed instructions or contact Helena Biosciences Europe for instrument-specific application guides.

INTERPRETATION OF RESULTS

The assayed percent activities of the various coagulation factors should be taken from the "Reference Value" column when Calibration Plasma is used to determine the laboratory's standard curves. Ensure the lot number printed on this assay sheet is the same as that on the vial of Calibration Plasma to be used.

LIMITATIONS

The results obtained with Calibration Plasma depend on several factors strongly associated with instrumentation, types of reagents, deficient substrates and laboratory to laboratory variations[6,7,8]. Each laboratory should establish an expected range for the particular instrument-reagent system.

QUALITY CONTROL

Each laboratory should establish a quality control program. Normal and abnormal control plasmas should be tested prior to each batch of patient samples, to ensure satisfactory instrument and operator performance. If controls do not perform as expected, patient results should be considered invalid.
Helena Biosciences Europe supplies the following controls available for use with this product:
REF 5301 Speciality Assayed Control N
REF 5302 Speciality Assayed Control A

REFERENCE VALUES

Reference values can vary between laboratories depending on the techniques and systems in use. For this reason each laboratory should establish its own normal range.

PERFORMANCE CHARACTERISTICS

The following performance characteristics have been determined by Helena Biosciences Europe or their representatives using an opto-mechanical coagulation instrument. Each laboratory should establish its own performance data.

Reproducibility
Inter-batch precision

Parameter	*n*	*Mean*	*CV (%)*
Fibrinogen (g/L)	5	3.0	3.6
Factor IX (%)	5	124.7	1.9
Protein S (%)	5	98.5	2.8

BIBLIOGRAPHY

1. Babson AL and Flanagen ML (1975) Quantitative One Stage Assays for Factors V and X, *AJCP,* **64:** 817-819.
2. Hardisty RM *et al.* (1962) A One Stage Factor VIII Assay and Its Use on Venous and Capillary Plasma. *Thrombosis et Diathesis Haemorrhagica,* **7:**215-229.
3. Morse EE *et al.* (1971) Automated Fibrinogen Determination, *AJCP,* **55:**671-676.
4. Elodi S *et al* (1978) Some Sources of Error in the One-Stage Assay of Factor VIII, *Haemostasis,* **7:**1-9.
5. Thelin M (1968) Preparation and Standardization of a Stable AHF Plasma, *Thrombosis et Diathesis Haemorrhagica,* **19:**423.
6. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology,* **37:**559-568.
7. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP,* **55:**561-564.
8. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP,* **59:**231-235.

Calibration Plasma
Fiche technique

fr

UTILISATION

Le kit Calibration Plasma est destiné à être utilisé comme produit d'étalonnage.

Le Calibration Plasma peut être utilisé comme plasma de référence lors du dosage des facteurs II, V, VII, VIII, IX, X[1], XI, XII[2], du fibrinogène[3], du facteur von Willebrand, de la protéine C antigénique et fonctionnelle et de la protéine S (total et libre) ainsi que des dosages chromogéniques dont celui de l'antithrombine III, de la protéine C, du facteur VIII et du plasminogène. Le Calibration Plasma sert à doser les facteurs et à réaliser d'autres analyses de la même façon que s'il s'agissait d'un pool de plasma frais. Le taux des facteurs II, VII, VIII, IX et X ainsi que le dosage chromogénique du facteur VIII, de l'AT-III et de la protéine C sont en conformité avec les normes de l'Organisation mondiale de la santé afin de garantir la véracité des valeurs indiquées[4]. Le plasma de référence doit être utilisé pour étalonner les facteurs dans chaque laboratoire. Il ne sert pas déterminer une plage de valeurs normales car celles-ci varient d'une population à l'autre.

AVERTISSEMENTS ET PRÉCAUTIONS

Les réactifs du kit sont à usage diagnostique *in vitro* uniquement – NE PAS INGÉRER. Porter un équipement de protection individuelle approprié lors de la manipulation de tous les composants du kit. Consulter la fiche de données de sécurité du produit pour obtenir le lien vers les phrases de risque et les conseils de prudence le cas échéant. Éliminer les composants conformément aux églementations locales.

Un dépistage des produits sanguins a été réalisé et a donné un résultat négatif (sauf indication contraire sur la boîte du kit ou sur le flacon) quant à la présence de :
Antigène de l'hépatite B (AgHBs)
Anticorps anti-VIH 1
Anticorps anti-VIH 2
Anticorps anti-VHC
Cependant, ils doivent être manipulés avec les mêmes précautions que celles prises pour les échantillons patients humains.

COMPOSITION

Composant	Contient	Description	Préparation
Calibration Plasma	10 x 1 mL	Le Calibration Plasma est préparé à partir d'un pool de plasma citraté congelé provenant de donneurs sains, puis est tamponné et lyophilisé afin de garantir la stabilité de tous les constituants du plasma[5].	Reconstituer en ajoutant 1,0 mL d'eau distillée ou désionisée. Agiter doucement. Attendre 20 minutes que le produit se dissolve complètement.

Chaque kit contient une fiche technique.
Chaque kit contient valeurs de référence spécifiques du lot.

MATÉRIEL NÉCESSAIRE NON FOURNI

Le Calibration Plasma peut être utilisé dans les analyses réalisées sur des instruments de coagulation mécanique ou photo-optique avec les réactifs appropriés vendus dans le commerce.

CONSERVATION, DURÉE DE VIE UTILE ET STABILITÉ

Les flacons non ouverts sont stables jusqu'à la date de péremption indiquée s'ils sont conservés dans les conditions indiquées sur l'étiquette du kit ou du flacon. Les valeurs du facteur VIII, du facteur von Willebrand et du cofacteur de la ristocétine sont stables 2 heures entre +2 – +8°C. Tous les autres facteurs sont stables 4 heures entre +2 – +8°C. Le Calibration Plasma non reconstitué est un lyophilisat sec de couleur jaune clair. S'il présente des caractéristiques inhabituelles, le client doit prévenir Helena Biosciences Europe avant de l'utiliser.

PRÉLÈVEMENT ET PRÉPARATION DES ÉCHANTILLONS

Non applicable.

PROCÉDURE

Consulter le manuel d'utilisation de l'instrument approprié pour obtenir des instructions détaillées ou contacter Helena Biosciences Europe pour obtenir des notes d'application spécifiques à l'instrument.

INTERPRÉTATION DES RÉSULTATS

Les pourcentages d'activité dosée des différents facteurs de coagulation doivent être pris dans la colonne « Valeur de référence » lorsque le Calibration Plasma est utilisé pour déterminer les courbes d'étalonnage du laboratoire. S'assurer que le numéro de lot imprimé sur cette fiche de dosage coïncide avec celui du flacon de Calibration Plasma à utiliser.

LIMITES

Les résultats obtenus avec le Calibration Plasma dépendent de plusieurs facteurs fortement corrélés avec l'instrument, les types de réactifs, les substrats carencés et les variations inter-laboratoires[6,7,8]. Le laboratoire doit déterminer une plage prévue pour chaque système instrument-réactif.

CONTRÔLE QUALITÉ

Chaque laboratoire doit établir un programme de contrôle qualité. Les plasmas de contrôle, normaux et anormaux, doivent être testés avant chaque lot d'échantillons patients afin de s'assurer que l'instrument et l'opérateur offrent des performances satisfaisantes. Si les contrôles ne donnent pas les résultats prévus, les résultats du patient doivent être considérés comme non valables.
Helena Biosciences Europe distribue les contrôles suivants à utiliser avec ce produit:
REF 5301 Speciality Assayed Control N
REF 5302 Speciality Assayed Control A

VALEURS DE RÉFÉRENCE

Les valeurs de référence peuvent varier d'un laboratoire à l'autre suivant les techniques et les systèmes utilisés. C'est pour cette raison qu'il appartient à chaque laboratoire de déterminer sa propre plage normale.

CARACTÉRISTIQUES DE PERFORMANCES

Helena Biosciences Europe ou ses mandataires ont déterminé les caractéristiques de performance suivantes en utilisant un instrument de coagulation opto-mécanique.

Reproductibilite
Précision inter-lots

Paramètre	*n*	*Moyenne*	*CV (%)*
Fibrinogène (g/L)	5	3.0	3.6
Facteur IX (%)	5	124.7	1.9
Protéine S (%)	5	98.5	2.8

BIBLIOGRAPHIE

1. Babson AL and Flanagen ML (1975) Quantitative One Stage Assays for Factors V and X, *AJCP,* **64:** 817-819.
2. Hardisty RM *et al.* (1962) A One Stage Factor VIII Assay and Its Use on Venous and Capillary Plasma. *Thrombosis et Diathesis Haemorrhagica,* **7:**215-229.
3. Morse EE *et al.* (1971) Automated Fibrinogen Determination, *AJCP,* **55:**671-676.
4. Elodi S *et al* (1978) Some Sources of Error in the One-Stage Assay of Factor VIII, *Haemostasis,* **7:**1-9.
5. Thelin M (1968) Preparation and Standardization of a Stable AHF Plasma, *Thrombosis et Diathesis Haemorrhagica,* **19:**423.
6. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology,* **37:**559-568.
7. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP,* **55:**561-564.
8. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP,* **59:**231-235.

Calibration Plasma
Anleitung

de

VERWENDUNGSZWECK

Das Calibration Plasma-Kit ist für die Kalibration vorgesehen.

Calibration Plasma kann als Referenzplasma bei der Untersuchung auf Faktor II, V, VII, VIII, IX, X[1], XI, XII[2], Fibrinogen[3], von Willebrand Faktor, Antigen und Funktion von Protein C und Protein S (gesamt und frei), sowie für Chromogen-Tests einschließlich Antithrombin III, Protein C, Faktor VIII und Plasminogen verwendet werden. Calibration Plasma wird für Faktor-Bestimmungen und andere Tests wie frisches Pool-Plasma verwendet. Faktor II, VII, VIII, IX und X Werte und die chromogenen Faktor VIII, AT-III und Protein C Werte sind entsprechend den Standards der World Health Organisation nachweisbar, um den angegebenen Werten die größtmögliche Plausibilität zu verleihen[4]. Das Referenzplasma sollte dazu verwendet werden, um die internen Faktoren für das jeweilige Laborsystem einzustellen. Es sollte weiterhin dazu verwendet werden, Normalbereiche festzulegen, da sie von der jeweiligen Population abhängig sind.

WARNHINWEISE UND VORSICHTSMASSNAHMEN

Die in diesem Kit enthaltenen Reagenzien sind ausschließlich für die Verwendung von *in-vitro*-Diagnosen vorgesehen. NICHT VERSCHLUCKEN. Tragen Sie beim Umgang mit sämtlichen Komponenten des Kits geeignete Schutzausrüstung. Beachten Sie gegebenenfalls die Verweise auf entsprechende Gefahren- und Vorbeugeerklärungen in der Produktsicherheitserklärung. Entsorgen Sie die Komponenten gemäß den örtlichen Vorschriften.

Die Blutprodukte wurden untersucht und sind für folgende Gene ohne Befund (soweit nicht anderweitig auf der Verpackung oder den Ampullen angegeben):
Hepatitis-B-Antikörper (HbsAg)
HIV-Antikörper 1
HIV-Antikörper 2
HCV-Antikörper
Sie sind jedoch mit den gleichen Vorkehrungen zu behandeln wie Proben von menschlichen Patienten.

ZUSAMMENSETZUNG

Komponente	Inhalt	Beschreibung	Vorbereitung
Calibration Plasma	10 x 1 mL	Calibration Plasma wird aus einem tief gefrorenen Pool Citratplasma von gesunden Spendern hergestellt und ist zur Gewährleistung der Stabilität aller Plasmabestandteile gepuffert und lyophilisiert[5].	Mit 1,0 mL destilliertem oder entionisiertem Wasser rekonstituieren. Leicht schwenken. Produkt 20 Minuten vollständig auflösen lassen.

Jedes Kit enthält eine Gebrauchsanweisung.
Jedes Kit enthält chargenspezifischen Referenzwerten.

ERFORDERLICHE, ABER NICHT MITGELIEFERTE ARTIKEL

Calibration Plasma kann in Verbindung mit allen entsprechenden kommerziellen Reagenzien bei der Durchführung von Tests an mechanischen oder lichtoptischen Koagulometern verwendet werden.

LAGERUNG, HALTBARKEIT UND STABILITÄT

Ungeöffnete Fläschchen sind unter den auf Verpackung oder Fläschchen angegebenen Lagerbedingungen bis zum aufgedruckten Verfallsdatum stabil. Werte für Faktor VIII, von Willebrand Faktor und Ristocetin Co-Faktor sind bei +2 – +8°C Stunden stabil. Alle weiteren Faktoren sind bei +2 – +8°C Stunden stabil. Nicht rekonstituiertes Calibration Plasma muss als hellgelber, trockner Pfropf erscheinen. Bei einem ungewöhnlichen Erscheinungsbild sollte der Kunde vor Gebrauch Helena Biosciences Europe davon in Kenntnis setzen.

PROBENENTNAHME UND VORBEREITUNG

Entfällt.

VORGEHENSWEISE

Siehe die Bedienungsanleitung des entsprechenden Geräts für genaue Anweisungen oder wenden Sie sich an Helena Biosciences Europe für spezielle anwendungstechnische Hinweise.

INTERPRETATION DER ERGEBNISSE

Die getesteten, prozentualen Aktivitäten der verschiedenen Gerinnungsfaktoren sollten aus der Tabelle „Referenzwerte" für die Erstellung einer laboreigenen Standardkurve mit Calibration Plasma entnommen werden. Darauf achten, dass die Chargen-Nummer auf dem Beipackzettel mit der auf dem verwendeten Calibration Plasma-Fläschchen übereinstimmt.

EINSCHRÄNKUNGEN

Die mit Calibration Plasma erzielten Resultate hängen von mehreren Faktoren ab, die stark mit dem Gerät, den verwendeten Reagenzien, mangelnden Substraten und Unterschieden zwischen den Labors in Verbindung stehen[6,7,8]. Jedes Labor sollte daher für jedes Geräte-Reagenzien-System einen eigenen Normalwertebereich erstellen.

QUALITÄTSKONTROLLE

Jedes Labor muss für eine eigene Qualitätskontrolle sorgen. Normale und pathologische Kontrollplasmen müssen vor jeder Testreihe mit Patientenproben getestet werden, um eine zufrieden stellende Geräteleistung und Bedienung zu gewährleisten. Liegen die Kontrollen außerhalb des Normbereichs, sind die Patientenergebnisse nicht zu verwenden.
In Verbindung mit diesem Produkt bietet Helena Biosciences Europe die folgenden Kontrollen an:
REF 5301 Speciality Assayed Control N
REF 5302 Speciality Assayed Control A

REFERENZWERTE

Referenzwerte können je nach Technik und verwendetem System von Labor zu Labor unterschiedlich sein. Aus diesem Grund sollte jedes Labor seinen eigenen Normalwertbereich erstellen.

LEISTUNGSMERKMALE

Die folgenden Leistungseigenschaften wurden von Helena Biosciences Europe oder in ihrem Auftrag mit einem optomechanischen Gerinnungsgerät ermittelt.

Reproduzierbarkeit
Inter-batch-Präzision

Parameter	*n*	*Mittelwert*	*CV (%)*
Fibrinogen (g/L)	5	3.0	3.6
Faktor IX (%)	5	124.7	1.9
Protein S (%)	5	98.5	2.8

LITERATURVERZEICHNIS

1. Babson AL and Flanagen ML (1975) Quantitative One Stage Assays for Factors V and X, *AJCP,* **64:** 817-819.
2. Hardisty RM *et al.* (1962) A One Stage Factor VIII Assay and Its Use on Venous and Capillary Plasma. *Thrombosis et Diathesis Haemorrhagica,* **7:**215-229.
3. Morse EE *et al.* (1971) Automated Fibrinogen Determination, *AJCP,* **55:**671-676.
4. Elodi S *et al* (1978) Some Sources of Error in the One-Stage Assay of Factor VIII, *Haemostasis,* **7:**1-9.
5. Thelin M (1968) Preparation and Standardization of a Stable AHF Plasma, *Thrombosis et Diathesis Haemorrhagica,* **19:**423.
6. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology,* **37:**559-568.
7. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP,* **55:**561-564.
8. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP,* **59:**231-235.

Calibration Plasma
Istruzioni per l'uso

it

SCOPO PREVISTO

Il kit Calibration Plasma è concepito per l'uso come materiale di calibrazione.

Il Calibration Plasma può essere utilizzato come plasma di riferimento per il dosaggio dei fattori II, V, VII, VIII, IX, X[1], XI e XII[2], del fibrinogeno[3], del fattore di von Willebrand, della proteina C e della proteina S (totale e libera) antigeniche e funzionali, nonché per i dosaggi cromogenici, compresi l'antitrombina III, la proteina C, il fattore VIII e il plasminogeno. Il Calibration Plasma viene utilizzato nei dosaggi dei fattori e in altri test seguendo la stessa procedura adottata per un pool di plasma fresco. I valori dei fattori II, VII, VIII, IX e X e i valori cromogenici del fattore VIII, dell'AT-III e della proteina C sono riconducibili agli standard dell'Organizzazione Mondiale della Sanità, a garanzia della massima attendibilità dei valori dichiarati[4]. Il plasma di riferimento deve essere utilizzato per valutare i fattori interni adottati nel sistema di ogni singolo laboratorio. Il plasma di riferimento non deve essere utilizzato per determinare i range normali, in quanto i valori normali variano da una popolazione all'altra.

AVVERTENZE E PRECAUZIONI

I reagenti contenuti in questo kit sono destinati esclusivamente alla diagnostica *in vitro* - NON INGERIRE. Indossare un'adeguata attrezzatura protettiva personale durante la manipolazione di tutti i componenti del kit. Per conoscere i relativi simboli precauzionali e di pericolo, laddove pertinente, fare riferimento alla dichiarazione di sicurezza del prodotto. Smaltire i componenti conformemente alle normative locali vigenti.

I prodotti ematici sono stati sottoposti a screening e trovati negativi (salvo diversa indicazione sulla confezione del kit o sulla fiala) per la presenza di:
Antigene dell'epatite B (HbsAg)
Anticorpo HIV 1
Anticorpo HIV 2
Anticorpo HCV
Questi prodotti devono tuttavia essere manipolati con le stesse misure precauzionali adottate per un campione paziente umano.

COMPOSIZIONE

Componente	Contiene	Descrizione	Preparazione
Calibration Plasma	10 x 1 mL	Il Calibration Plasma viene preparato utilizzando un pool congelato di plasma citrato proveniente da donatori sani e quindi viene tamponato e liofilizzato, per garantire la stabilità di tutti i costituenti plasmatici[5].	Ricostituire con 1,0 mL di acqua distillata o deionizzata. Agitare delicatamente. Attendere 20 minuti per consentire al prodotto di sciogliersi completamente.

Ogni kit contiene un Istruzioni per l'uso.

Ogni kit contiene un inserto recante i valori di riferimento specifici per il lotto.

MATERIALI NECESSARI, MA NON IN DOTAZIONE

Il Calibration Plasma può essere utilizzato durante l'esecuzione di test su qualsiasi strumento di coagulazione meccanico o foto-ottico in combinazione con tutti i reagenti idonei disponibili in commercio.

CONSERVAZIONE, VITA UTILE E STABILITÀ

I flaconi non aperti sono stabili fino alla data di scadenza indicata se conservati nelle condizioni riportate sul flacone o sull'etichetta del kit. I valori relativi al fattore VIII, al fattore di von Willebrand e al cofattore ristocetina sono stabili per 2 ore a +2 –+8°C. Tutti gli altri fattori sono stabili per 4 ore a +2 –+8°C. Il Calibration Plasma non ricostituito deve apparire come un tappo asciutto di colore giallo pallido. Qualora si osservassero condizioni insolite, si raccomanda al cliente di notificarle a Helena Biosciences Europe prima dell'uso.

RACCOLTA E PREPARAZIONE DEI CAMPIONI

Non applicabile.

PROCEDURA

Fare riferimento al manuale utente dello strumento appropriato per istruzioni dettagliate oppure contattare Helena Biosciences Europe per le note applicative specifiche dello strumento.

INTERPRETAZIONE DEI RISULTATI

Quando si utilizza il Calibration Plasma per delineare le curve standard di laboratorio, le percentuali di attività determinate per i vari fattori di coagulazione devono essere ricavate dalla colonna "Valore di riferimento". Assicurarsi che il numero di lotto stampato sul foglio del dosaggio corrisponda a quello riportato sul flacone di Calibration Plasma da utilizzare.

LIMITAZIONI

I risultati ottenuti con il Calibration Plasma dipendono da innumerevoli fattori, strettamente legati alla strumentazione, ai tipi di reagenti, a substrati carenti e alle variazioni dovute ai singoli laboratori[6,7,8]. Ogni laboratorio dovrà definire un range di previsione per il sistema strumento-reagente specificamente utilizzato.

CONTROLLO QUALITÀ

Ogni laboratorio deve definire un programma di controllo qualità. I plasmi di controllo normali e anormali devono essere testati prima di ogni lotto di campioni di pazienti, per garantire un livello prestazionale soddisfacente sia per quanto riguarda lo strumento che per l'operatore. Qualora i controlli non funzionassero come previsto, i risultati relativi ai pazienti dovranno essere considerati non validi.

Helena Biosciences Europe mette a disposizione i seguenti controlli utilizzabili con questo prodotto:
REF 5301 Speciality Assayed Control N
REF 5302 Speciality Assayed Control A

VALORI DI RIFERIMENTO

I valori di riferimento possono variare da un laboratorio all'altro in funzione delle tecniche e dei sistemi in uso. Per tale motivo ciascun laboratorio dovrà elaborare un proprio range normale.

CARATTERISTICHE PRESTAZIONALI

Le seguenti caratteristiche prestazionali sono state determinate da Helena Biosciences Europe o dai propri rappresentanti con l'utilizzo di uno strumento di coagulazione opto-meccanico.

Riproducibilità

Precisione tra i lotti

Parametro	*n*	*Media*	*CV (%)*
Fibrinogeno (g/L)	5	3.0	3.6
Fattore IX (%)	5	124.7	1.9
Proteina S (%)	5	98.5	2.8

BIBLIOGRAFIA

1. Babson AL and Flanagen ML (1975) Quantitative One Stage Assays for Factors V and X, *AJCP*, **64:** 817-819.
2. Hardisty RM *et al.* (1962) A One Stage Factor VIII Assay and Its Use on Venous and Capillary Plasma. *Thrombosis et Diathesis Haemorrhagica*, **7:**215-229.
3. Morse EE *et al.* (1971) Automated Fibrinogen Determination, *AJCP*, **55:**671-676.
4. Elodi S *et al* (1978) Some Sources of Error in the One-Stage Assay of Factor VIII, *Haemostasis*, **7:**1-9.
5. Thelin M (1968) Preparation and Standardization of a Stable AHF Plasma, *Thrombosis et Diathesis Haemorrhagica*, **19:**423.
6. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology*, **37:**559-568.
7. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP*, **55:**561-564.
8. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP*, **59:**231-235.

Calibration Plasma
Instrucciones de uso

es

USO PREVISTO

El uso previsto del kit Calibration Plasma es como material de calibración.

El Calibration Plasma puede usarse como plasma de referencia cuando se valoran los factores II, V, VII, VIII, IX, X[1], XI, XII[2], fibrinógeno[3], factor de von Willebrand, proteína C antigénica y funcional y proteína S (total y libre), así como las valoraciones cromógenas como antitrombina III, proteína C, factor VIII y plasminógeno. Calibration Plasma se usa en valoraciones de factores y en otras pruebas de la misma forma que una reserva de plasma fresco. Los valores de los factores II, VII, VIII, IX y X y los valores cromogénicos de factor VIII, AT-III y proteína C se pueden referenciar a los estándares de Organización Mundial de la Salud para asegurar la máxima credibilidad en los valores indicados[4]. Debe usarse el plasma de referencia para calibrar factores internos en el sistema de cada laboratorio. No debe usarse el plasma de referencia para determinar los intervalos normales, porque los normales varían de una población a otra.

ADVERTENCIAS Y PRECAUCIONES

Los reactivos que contiene este kit son sólo para uso de diagnóstico *in vitro*: NO INGERIR. Lleve el equipo de protección personal adecuado cuando utilice todos los componentes del kit. Consulte la declaración de seguridad del producto para saber más sobre las indicaciones adecuadas de advertencia y riesgo. Desechar los componentes de conformidad con las normativas locales.

La sangre se ha sometido a pruebas que han resultado negativas (a menos que se indique lo contrario en la caja del kit o en el vial) de la presencia de:

Antígeno de la hepatitis B (HbsAg)

Anticuerpos del VIH 1

Anticuerpos del VIH 2

Anticuerpos del VHC

Sin embargo, deben manipularse con las mismas precauciones que una muestra de un paciente.

COMPOSICIÓN

Componente	Contiene	Descripción	Preparación
Calibration Plasma	10 x 1 mL	El Calibration Plasma se elabora a partir de una reserva congelada de plasma citratado de donantes sanos y está tamponado y liofilizado para asegurar la estabilidad de todos los constituyentes del plasma[5].	Reconstituya con 1,0 mL de agua destilada o desionizada. Agite suavemente. Espere 20 minutos para que el producto se disuelva completamente.

Cada kit contiene instrucciones de uso.

Cada kit contiene valores de referencia específicos insertados del lote.

ARTÍCULOS NECESARIOS NO SUMINISTRADOS

El Calibration Plasma puede usarse cuando se realizan pruebas con cualquier instrumento de coagulación mecánica o foto-óptica junto con todos los reactivos adecuados, comerciales.

ALMACENAMIENTO, CADUCIDAD Y ESTABILIDAD

Los viales no abiertos son estables hasta la fecha de caducidad indicada cuando se conservan en las condiciones indicadas en la etiqueta del vial o el kit. Los valores para el factor VIII, el factor de von Willebrand factor y el cofactor de ristocetina son estables durante 2 horas a +2 –+8°C. Todos los demás factores son estables durante 4 horas a +2 –+8°C. El Calibration Plasma no reconstituido debe aparecer como un taco seco, de color amarillo claro. Si se nota alguna condición inusual, el usuario debe notificárselo a Helena Biosciences Europe antes de usarlo.

RECOGIDA Y PREPARACIÓN DE LAS MUESTRAS

No aplicable.

PROCEDIMIENTO

Consulte el manual del usuario del instrumento adecuado para instrucciones detalladas o póngase en contacto con Helena Biosciences Europe para notas de aplicación específicas del instrumento.

INTERPRETACIÓN DE LOS RESULTADOS

Las actividades porcentuales valoradas de los diversos factores de coagulación deben tomarse de la columna "Valor de Referencia" cuando se usa el Calibration Plasma para determinar las curvas estándar de laboratorio. Compruebe que el número de lote impreso en esta hoja de valoración es el mismo que en el vial de Calibration Plasma a usar.

LIMITACIONES

Los resultados obtenidos con Calibration Plasma dependen de varios factores fuertemente asociados a la instrumentación, los tipos de reactivos, sustratos deficientes y variaciones entre laboratorios[6,7,8]. Cada laboratorio debe establecer un intervalo esperado para el sistema instrumento-reactivo concreto.

CONTROL DE CALIDAD

Cada laboratorio debe establecer un programa de control de calidad. Los plasmas de control normales y anormales deben estudiarse antes de cada lote de muestras del paciente, para asegurar un funcionamiento adecuado del instrumento y el operador. Si los controles no se realizan como se esperaba, los resultados del paciente deben considerarse inválidos.

Helena Biosciences Europe suministra los siguientes controles disponibles para usar con este producto:
REF 5301 Speciality Assayed Control N
REF 5302 Speciality Assayed Control A

VALORES DE REFERENCIA

Los valores de referencia pueden variar entre los laboratorios dependiendo de las técnicas y los sistemas usados. Por esta razón, cada laboratorio debe establecer su propio intervalo normal.

CARACTERÍSTICAS FUNCIONALES

Las siguientes características de rendimiento han sido determinadas por Helena Biosciences Europe o sus representantes usando un instrumento de coagulación opto-mecánico.

Reproductibilidad

Precisión inter-lote

Parámetro	*n*	*Media*	*CV (%)*
Fibrinógeno (g/L)	5	3.0	3.6
Factor IX (%)	5	124.7	1.9
Proteína S (%)	5	98.5	2.8

BIBLIOGRAFÍA

1. Babson AL and Flanagen ML (1975) Quantitative One Stage Assays for Factors V and X, *AJCP*, **64:** 817-819.
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8. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP*, **59:**231-235.

УНИВЕРСАЛЬНЫЙ КАЛИБРАТОР
инструкция

ru

НАЗНАЧЕНИЕ

Комплект «Универсальный калибратор» предназначен для использования в качестве материала для калибровки.

«Универсальный калибратор» может использоваться как референсная плазма, для определения факторов II, V, VII, VIII, IX, X[1], XI, XII[2], фибриногена[3], фактора Виллебрандта, антигена и функциональной активности Протеина С и Протеина S (общего и свободного), так же «Универсальный калибратор» можно использовать и для хромогенных тестов, включая Антитромбин III, Протеин С, фактор VIII и Плазминоген. «Универсальный калибратор» используется при калибровке тестов для определения II, VII, VIII, IX и X факторов, а также при калибровке хромогенных тестов: VIII фактора, Антитромбина - III и Протеина С. Уровень значений сопоставим с рекомендациями ВОЗ[4]. Использование референсной плазмы нивелирует влияние внешних факторов на результаты анализа. Референсная плазма не должна использоваться для определения нормального диапазона значений, так как значения нормы варьируют в зависимости от биологических особенностей популяции практически здоровых людей.

ПРЕДУПРЕЖДЕНИЯ И МЕРЫ ПРЕДОСТОРОЖНОСТИ

Содержащиеся в данном наборе реагенты предназначены только для *in vitro* диагностики– НЕ ПРИНИМАТЬ ВНУТРЬ! При работе со всеми компонентами набора использовать соответствующие средства индивидуальной защиты. В случае необходимости см. свидетельство о безопасности изделия для ознакомления с соответствующими описаниями опасного воздействия и сведениями о мерах предосторожности. Удаление компонентов в отходы производите в соответствии с местными правилами.

Препараты крови были подвергнуты скринингу и показали отрицательный результат (если на коробке, в которую упакован комплект или на пробирке не указано иное) на:
Антиген к гепатиту В (HbsAg)
Антитела к ВИЧ 1
Антитела к ВИЧ 2
Антитела к вирусу гепатита С (HCV)
Тем не менее с ними следует обращаться, соблюдая те же меры предосторожности, что и при обращении с образцом, полученным от человека.

СОСТАВ

Компоненты	Состав набора	Описание	Приготовление реагентов
Плазма калибратор	10 x 1 мл	приготовлен из объединенной цитратной плазмы, полученной от практически здоровых доноров. Плазма заморожена и лиофилизирована, чтобы гарантировать стабильность всех плазменных элементов[5].	Разведите соответствующую контрольную плазму добавлением во флакон 1.0 мл дистиллированной или деионизированной воды. Осторожно перемешайте и оставьте при комнатной температуре в течение 20 минут. Перед использованием флакон с разведенной плазмой переворачивайте (без встряхивания).

Каждый набор содержит инструкцию по применению.

Паспорт с референсными значениями.

НЕОБХОДИМЫЕ КОМПОНЕНТЫ, НЕ ВКЛЮЧЕННЫЕ В КОМПЛЕКТ ПОСТАВКИ

Контрольные плазмы могут быть использованы с анализаторами, имеющими различный метод детекции (механический, оптический и т.д.) в сочетании с реагентами различных производителей.

ХРАНЕНИЕ, СРОК ГОДНОСТИ И УСТОЙЧИВОСТЬ

Невскрытые флаконы с лиофилизированной плазмой хранятся до истечения срока годности в условиях, указанных на этикетке. Разведенная плазма в закрытом флаконе может храниться при +2 –+8°C в течение 4 часов. Значения для VIII фактора, фактор Виллебрандта и КоФактор ристоцетина устойчивы в течение 2 часов при +2 –+8°C. Неразведенный калибратор должен выглядеть, как светло-желтый сухой плотный лиофилизат. При появлении необычных признаков продукта, до использования обратитесь в компанию Хелена.

ОТБОР И ПОДГОТОВКА ОБРАЗЦОВ

Не относится.

ПРОЦЕДУРА

«Универсальный калибратор» может использоваться, для выполнения тестов на любом механическом или оптическом коагулометре в наборе с любыми подходящими реактивами. Адаптации реагентов к различным приборам доступны по запросу у официальных дистрибьюторов и компании Хелена.

ИНТЕРПРЕТАЦИЯ РЕЗУЛЬТАТОВ

Значение процента активности различных факторов свертывания должна быть взята из колонки "референсные значения", когда вы используете «Универсальный калибратор», чтобы определить стандартные лабораторные кривые. Убедитесь, что номер партии, напечатанный в паспорте, совпадает с номером указанным на используемом Вами флаконе калибратора.

ОГРАНИЧЕНИЯ

Референсные значения могут варьировать между лабораториями в зависимости от используемых реагентов, методов, коагулометров и других факторов[6,7,8]. По этой причине каждая лаборатория должна установить свои собственные нормативные параметры метода.

КОНТРОЛЬ КАЧЕСТВА

Каждая лаборатория должна установить программу контроля качества. Перед измерением каждой партии образцов пациентов необходимо протестировать нормальную и патологическую плазму, чтобы удостовериться в удовлетворительной работе оборудования и оператора. Если контрольные измерения не совпадают с ожидаемыми значениями, то измеренные данные пациентов следует считать недостоверными. Компания Хелена рекомендует следующие контрольные материалы:
Кат. № 5301 Контроль качества специальные тесты, норма
Кат. № 5302 Контроль качества специальные тесты, патология

НОРМАЛЬНЫЕ ПОКАЗАТЕЛИ

Референсные значения могут варьировать между лабораториями в зависимости от используемых методов и коагулометров. По этой причине каждая лаборатория должна установить свои собственные значения.

ЭКСПЛУАТАЦИОННЫЕ ХАРАКТЕРИСТИКИ

Компания Хелена или её дистрибьюторы определили следующие ориентировочные аналитические характеристики. Каждая лаборатория должна определить свои собственные аналитические характеристики.
При использовании оптико-механического коагулометра и реагентов Хелена были определены следующие коэффициенты вариации (CV):

Воспроизводимость

в пределах аналитической серии

Тест	*n*	*Среднее*	*CV (%)*
Фибриноген (г/Л)	5	3.0	3.6
Фактор IX (%)	5	124.7	1.9
Протеин S (%)	5	98.5	2.8

ЛИТЕРАТУРА

1. Babson AL and Flanagen ML (1975) Quantitative One Stage Assays for Factors V and X, *AJCP*, **64:** 817-819.
2. Hardisty RM *et al.* (1962) A One Stage Factor VIII Assay and Its Use on Venous and Capillary Plasma. *Thrombosis et Diathesis Haemorrhagica*, **7:**215-229.
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6. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology*, **37:**559-568.
7. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP*, **55:**561-564.
8. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP*, **59:**231-235.

Declaration of Conformity

HL-7-0512DC DOI 2015/08 (5)

In Application of the Council Directive 98/79/EC on the approximation of the laws of the Member States relating to *In Vitro* Diagnostic Medical Devices & CE marking.

Declaration of conformance to applicable sections of Annex I - Essential Requirements and Annex III (EC Declaration of Conformity) imposed by sections 2 to 5. The below listed products are not classified under Annex II Lists A or B. Access to the appropriate technical files will be made available to the appropriate body in the event this is required.

Product Code	**Description**	**GMDN Classification Code**
5556	Clauss Fibrinogen 50	55997

I, the undersigned declare that the devices registered against the above GMDN Classification Code conforms to the said Directives.

Full Name: M.J. Stephenson

Title: Managing Director

Signed:

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Clauss Fibrinogen 50

REF 5556
REF 5556H

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HL-2-1771P 2012/03 (7)

Clauss Fibrinogen 50
Instructions for use

en

INTENDED USE

For the quantitative determination of fibrinogen, based on the Clauss method, in human citrated plasma on Helena Biosciences Europe AC-4, C-1, C-2, C-4 Coagulation Systems.

Clauss Fibrinogen 50 is intended for the quantitative determination of fibrinogen in human plasma. Clauss[1] developed a simple method for the quantitative determination of fibrinogen by measuring the clotting time of dilute plasma after the addition of Thrombin (>30 NIH units/mL). This clot time is proportional to the fibrinogen concentration. Levels of fibrinogen can increase as a result of inflammation, pregnancy or oral contraceptive use[2]. Decreased levels can be found in certain states such as liver disease and DIC. Congenital deficiencies include afibrinogenaemia (no detectable fibrinogen), hypofibrinogenaemia (<1 mg/mL) and dysfibrinogenaemia (abnormal fibrinogen molecule).

WARNINGS AND PRECAUTIONS

The reagents contained in this kit are for *in vitro* diagnostic use only - DO NOT INGEST. Wear gloves when handling all kit components. Refer to the product safety data sheets for risk and safety phrases and disposal information. Plasma products have been screened and found negative (unless otherwise stated on the kit box or vial) for the presence of Hepatitis B Antigen (HbsAg) HIV 1 and 2 antibody and HCV antibody; however they should be handled with the same precautions as a human plasma sample.

COMPOSITION

Component	Content	Description	Preparation
Thrombin: 50 NIH/mL	5 x 4 mL (REF 5556) 5 x 2 mL (REF 5556H)	Contains approximately 200 (REF 5556) / 100 (REF 5556H) units bovine thrombin with stabilisers.	Reconstitute each vial with: 4 mL (REF 5556) 2 mL (REF 5556H) of purified water. Take care when pipetting to avoid contamination. Swirl gently and allow to stand for 15 minutes. Mix well immediatley before use. Do not shake.
Fibrinogen Calibrator	2 x 1 mL (REF 5556) 1 x 1 mL (REF 5556H)	Contains 1 mL of lyophilised normal human plasma assayed for fibrinogen levels.	Reconstitute each vial with exactly 1 mL of purified water. Swirl gently and allow to stand for 10 minutes. Mix gently before use. Do not shake.
Owren's Buffer	2 x 25 mL (REF 5556) 1 x 25 mL (REF 5556H)	Contains 25 mL of buffer which contains barbital and sodium chloride and sodium azide as preservative.	The buffer is ready for use as packaged.

Each kit contains instructions for use.

Each kit contains lot specific reference values insert.

ITEMS REQUIRED BUT NOT PROVIDED

Refer to the Instrument Operator Manual and/or application note for appropriate instructions. The reagents contained in this kit are also available as separate items:

REF 5374	Clauss Fibrinogen (Thrombin only)
REF 5378	Clauss Fibrinogen (Thrombin only)
REF 5379	Fibrinogen Calibrator
REF 5375	Owren's Buffer

STORAGE AND STABILITY

Unopened vials are stable until the given expiry date when stored under conditions indicated on the vial or kit label.

Thrombin: 50 NIH/mL	Once reconstituted, the reagent is stable for 8 hours at +15 – +30°C, 1 week at +2 – +8°C or 1 month at -20°C.
Fibrinogen Calibrator	Once reconstituted, the reagent is stable for 4 hours at +2 – +8°C.
Owren's Buffer	Store at +2 – +8°C once opened.

SAMPLE COLLECTION AND PREPARATION

Plastic or siliconised glass should be used throughout. Blood (9 parts) should be collected into 3.2% or 3.8% sodium citrate anticoagulant (1 part). Separate plasma after centrifugation at 1500 x g for 15 minutes. Plasma should be kept at +2 – +8°C or +18 – +24°C. Testing should be completed within 4 hours of sample collection, or plasma can be stored frozen at -20°C for 2 weeks or -70°C for 6 months. Thaw quickly at +37°C prior to testing. Do not keep at +37°C for more than 5 minutes[3].

PROCEDURE

Refer to the appropriate instrument Operator Manual for detailed instructions or contact Helena Biosciences Europe for instrument specific application guides.

INTERPRETATION OF RESULTS

Expected values for fibrinogen in healthy adults are 150-350 mg/dL (1.5-3.5 g/L)[4,5].

LIMITATIONS

Heparin levels >0.6 units/mL and fibrinolytic degredation products >100 mg/mL may cause falsely low fibrinogen quantitation. If values fall outside the standard curve values for the patient samples, re-assay using an appropriate dilution to bring values into the standard range.

QUALITY CONTROL

Each laboratory should establish a quality control program. Normal and abnormal control plasmas should be tested prior to each batch of patient samples, to ensure satisfactory instrument and operator performance. If controls do not perform as expected, patient results should be considered invalid. Helena Biosciences Europe supply the following controls available for use with this product:

REF 5301	Speciality Assayed Control N
REF 5302	Speciality Assayed Control A
REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA

REFERENCE VALUES

Reference values can vary between laboratories depending on the techniques and systems in use. For this reason each laboratory should establish its own normal range.

PERFORMANCE CHARACTERISTICS

Helena Biosciences Europe or their representatives have determined the following performance characteristics as a guideline. Each laboratory should establish its own performance data. The Clauss Fibrinogen assay is designed to give a linear calibration from 1.5 - 6.5 g/L.

Reproducibility

Intra-assay precision			Inter-assay precision		
Fibrinogen (g/L)	*n*	*CV (%)*	*Fibrinogen (g/L)*	*n*	*CV (%)*
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

REFERENCES

1. Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
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4. Scully RE *et al.* (1980) Normal Reference Laboratory Values, *New England Journal Medcine*, **302**(37):37-48.
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Clauss Fibrinogen 50
Fiche technique

fr

UTILISATION

Sert à la détermination quantitative du fibrinogène, selon la méthode de Clauss, dans le plasma humain citraté avec les analyseurs de coagulation Helena Biosciences Europe AC-4, C-1, C-2, C-4.

Le kit de Fibrinogène Clauss 50 est utilisé pour la détermination quantitative du fibrinogène dans le plasma humain. Clauss[1] a développé une méthode simple de détermination quantitative du fibrinogène en mesurant le temps de coagulation de plasma dilué après l'ajout de Thrombin (>30 unités NIH/mL). Ce temps de coagulation est proportionnel à la concentration en fibrinogène. Le taux de fibrinogène peut augmenter en raison d'une inflammation, d'une grossesse ou de la prise de contraceptifs oraux[2]. Des taux diminués sont trouvés dans certaines pathologies comme une maladie du foie ou une CIVD. L'afibrinogénémie (pas de fibrinogène détectable), l'hypofibrinogénémie (<1 mg/mL) et la dysfibrinogénémie (molécule de fibrinogène anormale) sont des anomalies congénitales.

AVERTISSEMENTS ET PRÉCAUTIONS

Les réactifs du kit sont à usage diagnostic *in vitro* uniquement - NE PAS INGÉRER. Porter des gants pour la manipulation de tous les composants. Se reporter aux fiches de sécurité des composants du kit pour la manipulation et l'élimination. Un dépistage des produits à base de plasma a été réalisé et a donné un résultat négatif (sauf indication contraire sur la boîte du kit ou sur le flacon) pour les antigènes de l'hépatite B (AgHBs), les anticorps anti VIH 1 et 2 et les anticorps anti VHC; il est malgré tout nécessaire de les manipuler avec les mêmes précautions que pour les échantillons de plasma humain.

COMPOSITION

Composant	Contient	Description	Préparation
Thrombin: 50 NIH/mL	5 x 4 mL (REF 5556) 5 x 2 mL (REF 5556H)	Chaque flacon contient environ 200 (REF 5556) / 100 (REF 5556H) unités de Thrombin bovine additionnée de stabilisateurs.	Reconstituer chaque flacon avec: 4 mL (REF 5556) 2 mL (REF 5556H) d'eau distillée. Faire attention lors du pipetage pour éviter toute contamination. Remuer doucement et laisser reposer 15 minutes. Bien mélanger juste avant utilisation. Ne pas agiter.
Fibrinogen Calibrator	2 x 1 mL (REF 5556) 1 x 1 mL (REF 5556H)	Chaque flacon contient 1 mL de plasma humain normal lyophilisé dosé pour les taux de fibrinogène.	Reconstituer chaque flacon avec exactement 1,0 mL d'eau distillée. Remuer doucement et laisser reposer 10 minutes. Mélanger doucement avant utilisation. Ne pas agiter.
Owren's Buffer	2 x 25 mL (REF 5556) 1 x 25 mL (REF 5556H)	Chaque flacon contient 25 mL de tampon contenant du barbital et du chlorure de sodium additionné d'azide de sodium comme conservateur.	Le tampon est prêt à l'emploi.

Chaque kit contient une fiche technique.

Chaque kit contient valeurs de référence spécifiques du lot.

MATÉRIELS NÉCESSAIRES NON FOURNIS

Se référer au manuel d'utilisation de l'instrument et/ou aux notes d'application pour avoir des instructions appropriées. Les réactifs du kit sont aussi disponibles séparément:

REF 5374	Clauss Fibrinogen (Thrombin only)
REF 5378	Clauss Fibrinogen (Thrombin only)
REF 5379	Fibrinogen Calibrator
REF 5375	Owren's Buffer

CONSERVATION ET STABILITÉ

Les flacons non ouverts sont stables jusqu'à la date de péremption indiquée s'ils sont conservés dans les conditions indiquées sur l'étiquette du kit ou du flacon.

Thrombin: 50 NIH/mL	Une fois reconstitué, le réactif est stable 8 heures à température ambiante, 1 semaine entre +2 – +8°C ou 1 mois à -20°C.
Fibrinogen Calibrator	Une fois reconstitué, le réactif est stable 4 heures entre +2 – +8°C.
Owren's Buffer	Conserver entre +2 – +8°C une fois ouvert.

PRÉLÈVEMENTS DES ÉCHANTILLONS

Utiliser tout au long du prélèvement du plastique ou du verre siliconé. Mélanger 9 volumes de sang et 1 volume de citrate de sodium à 3,2% ou 3,8%. Séparer le plasma après centrifugation à 1500 x g pendant 15 minutes. Conserver le plasma entre +2 – +8°C ou +18 – +24°C. L'analyse doit être terminée dans les 4 heures suivant le prélèvement de l'échantillon; sinon, il est possible de congeler le plasma 2 semaines à -20°C ou 6 mois à -70°C. Décongeler rapidement à +37°C avant de réaliser l'analyse. Ne pas laisser à +37°C plus de 5 minutes[3].

PROCÉDURE

Consulter le manuel d'utilisation de l'instrument approprié pour obtenir des instructions détaillées ou contacter Helena Biosciences Europe pour obtenir des notes d'application spécifiques à l'instrument.

INTERPRÉTATION DES RÉSULTATS

Le taux prévu de fibrinogène chez un adulte sain est de 150–350 mg/dL (1,5–3,5 g/L)[4,5].

LIMITES

Des taux d'héparine >0,6 unités/mL et de produits de dégradation fibrinolytique >100 mg/mL peuvent donner une quantification du fibrinogène erronément basse. Si les valeurs de l'échantillon patient se situent hors des valeurs de la courbe d'étalonnage, réaliser à nouveau l'analyse en utilisant la dilution appropriée pour les amener dans la plage de l'étalon.

CONTRÔLE QUALITÉ

Chaque laboratoire doit établir un programme de contrôle qualité. Les plasmas de contrôle, normaux et anormaux, doivent être testés avant chaque lot d'échantillons patients afin de s'assurer que l'instrument et l'opérateur offrent des performances satisfaisantes. Si les contrôles ne donnent pas les résultats prévus, les résultats du patient doivent être considérés comme non valables. Helena Biosciences Europe distribue les contrôles suivants à utiliser avec ce produit:

REF 5301	Speciality Assayed Control N
REF 5302	Speciality Assayed Control A
REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA

VALEURS DE RÉFÉRENCE

Les valeurs de référence peuvent varier d'un laboratoire à l'autre suivant les techniques et les systèmes utilisés. C'est pour cette raison qu'il appartient à chaque laboratoire de déterminer sa propre plage normale.

PERFORMANCES

Helena Biosciences Europe ou ses représentants ont déterminé à titre indicatif les performances suivantes. Chaque laboratoire doit établir ses propres données de performance. Le dosage du fibrinogène est conçu pour donner un étalonnage linéaire sur la plage 1,5 – 6,5 g/L.

Reproductibilité

Précision intra-série			Précision inter-séries		
Fibrinogène (g/L)	*n*	*CV (%)*	*Fibrinogène (g/L)*	*n*	*CV (%)*
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

RÉFÉRENCES

1. Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
2. Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
3. Clinical and Laboratory Standards Institute (2008) Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Haemostasis Assays: Approved Guideline, 5th edn. CLSI: H21-A5
4. Scully RE *et al.* (1980) Normal Reference Laboratory Values, *New England Journal Medcine*, **302**(37):37-48.
5. Okuno T, Selenko V (1972) Plasma fibrinogen determination by automated thrombin time, *American Journal of Medical Technology,* **38**(6):196-201

Clauss Fibrinogen 50
Anleitung

de

ANWENDUNGSBEREICH

Für die quantitative Bestimmung von Fibrinogen nach der Methode nach Clauss im menschlichen Citratplasma auf den Helena Biosciences Europe AC-4, C-1, C-2, C-4 -Gerinnungssystemen.

Das Clauss Fibrinogen 50 dient der quantitativen Bestimmung von Fibrinogen im Humanplasma. Clauss[1] entwickelte zur quantitativen Bestimmung von Fibrinogen eine einfache Methode, bei der die Gerinnungszeit von verdünntem Plasma nach Zugabe von Thrombin gemessen wird (>30 NIH Einheiten/mL). Diese Gerinnungszeit ist der Fibrinogen-Konzentration direkt proportional. Das Fibrinogen kann durch Entzündung, Schwangerschaft oder Einnahme von oralen Verhütungsmitteln erhöht sein[2]. Vermindert wird es durch Lebererkrankung und Verbrauchskoagulopathie. Angeborene Mängelzustände sind insbesondere Afibrinogenämie (kein nachweisbares Fibrinogen), Hypofibrinogenämie (<1 mg/mL) und Dysfibrinogenämie (abnormales Fibrinogenmolekül).

WARNHINWEISE UND VORSICHTSMASSNAHMEN

Die Reagenzien dieses Kits sind nur zur *in vitro* Diagnostik bestimmt - NICHT EINNEHMEN. Beim Umgang mit den Kit-Komponenten ist das Tragen von Handschuhen erforderlich. Siehe die Sicherheitsdatenblätter mit Gefahrenhinweisen und Sicherheitsvorschlägen sowie Informationen zur Entsorgung. Die Plasmaprodukte sind mit negativem Befund auf Hepatitis B Antigen (HBsAg), HIV-1 und HIV-2 Antikörper und HCV-Antikörper getestet worden (wenn nicht auf Kit-Verpackung oder Fläschchen anders bezeichnet). Sie sollten trotzdem mit derselben Vorsicht wie humane Plasmaproben behandelt werden.

INHALT

Komponente	Inhalt	Beschreibung	Vorbereitung
Thrombin: 50 NIH/mL	5 x 4 mL (REF 5556) 5 x 2 mL (REF 5556H)	Jedes Fläschchen enthält ca. 200 (REF 5556) / 100 (REF 5556H) Einheiten Rinder-Thrombin mit Stabilisatoren.	Jedes Fläschchen mit: 4 mL (REF 5556) 2 mL (REF 5556H) destilliertes Wasser. Kontamination beim Pipettieren vermeiden. Leicht schwenken und 15 Minuten stehen lassen. Vor Gebrauch gut mischen. Nicht schütteln.
Fibrinogen Calibrator	2 x 1 mL (REF 5556) 1 x 1 mL (REF 5556H)	Jedes Fläschchen enthält 1 mL lyophilisiertes normales Humanplasma mit bekanntem Fibrinogen-Gehal.	Jedes Fläschchen mit genau 1,0 mL destilliertem Wasser rekonstituieren. Leicht schwenken und 10 minuten stehen lassen. Vor Gebrauch leicht mischen. Nicht schütteln.
Owren's Buffer	2 x 25 mL (REF 5556) 1 x 25 mL (REF 5556H)	Jede Flasche enthält 25 mL Puffer aus Barbital- und Natriumchlorid mit Natriumazid als Konservierungsmittel.	Der Puffer ist gebrauchsfertig verpackt.

Jedes Kit enthält eine Gebrauchsanweisung.

Jedes Kit enthält chargenspezifischen Referenzwerten.

NICHT MITGELIEFERTES, ABER BENÖTIGTES MATERIAL

Zur Bedienung siehe Bedienungsanleitung des Geräts und/oder Anwenderhinweise. Die Reagenzien dieses Kits sind auch einzeln erhältlich:

REF 5374	Clauss Fibrinogen (Thrombin only)
REF 5378	Clauss Fibrinogen (Thrombin only)
REF 5379	Fibrinogen Calibrator
REF 5375	Owren's Buffer

LAGERUNG UND HALTBARKEIT

Ungeöffnete Fläschchen sind unter den auf Verpackung oder Fläschchen angegebenen Lagerbedingungen bis zum aufgedruckten Verfallsdatum stabil.

Thrombin: 50 NIH/mL	Nach Rekonstitution ist das Reagenz 8 Stunden bei Raumtemperatur, 1 Woche bei +2 – +8°C stabil oder 1 monate bei -20°C stabil.
Fibrinogen Calibrator	Rekonstituiert ist das Reagenz bei einer Temperatur von +2 – +8°C für 4 Stunden stabil.
Owren's Buffer	Nach dem Öffnen bei +2 – +8°C lagern.

PROBENENTNAHME UND VORBEREITUNG

Nur Plastik oder Silikonglas verwenden. Blut (9 Teile) sollte in 3,2% oder 3,8% Natriumcitrat als Antikoagulanz (1 Teil) entnommen werden. 15 Minuten bei 1500 g zentrifugieren und Plasma abpipettieren. Plasma bei +2 – +8 °C oder +18 – +24°C lagern. Plasma sollte innerhalb von 4 Stunden verarbeitet oder tief gefroren bei -20°C für 2 Wochen oder -70°C für 6 Monat gelagert werden. Vor dem Testen schnell bei +37°C auftauen. Nicht länger als 5 Minuten bei +37°C belassen[3].

VERFAHREN

Siehe die Bedienungsanleitung des entsprechenden Geräts für genaue Anweisungen oder wenden Sie sich an Helena Biosciences Europe für spezielle anwendungstechnische Hinweise.

AUSWERTUNG DER ERGEBNISSE

Fibrinogen-Normalwerte bei gesunden Erwachsenen sind 150-350 mg/dL (1,5-3,5 g/L)[4,5].

EINSCHRÄNKUNGEN

Heparinwerte >0,6 Einheiten/mL und Fibrinolyse-Abbauprodukte >100 mg/mL können falsch niedrige Fibrinogen-Mengen ergeben. Liegen bei Patientenproben die Werte außerhalb der Standardkurve, die Proben erneut mit verdünntem Plasma testen, um die Werte in den Bereich der Standardkurve zu bringen.

QUALITÄTSKONTROLLE

Jedes Labor muss für eine eigene Qualitätskontrolle sorgen. Vor jeder Testreihe mit Patientenproben müssen normale und pathologische Kontrollplasmen getestet werden, um eine zufrieden stellende Geräteleistung und Bedienung zu gewährleisten. Liegen die Kontrollen außerhalb des Normbereichs, sind die Patientenergebnisse nicht zu verwenden. In Verbindung mit diesem Produkt bietet Helena Biosciences Europe die folgenden Kontrollen an:

REF 5301	Speciality Assayed Control N
REF 5302	Speciality Assayed Control A
REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA

REFERENZWERTE

Referenzwerte können je nach Technik und verwendetem System von Labor zu Labor unterschiedlich sein. Aus diesem Grund sollte jedes Labor seinen eigenen Normalwertbereich erstellen.

LEISTUNGSEIGENSCHAFTEN

Die folgenden Leistungseigenschaften wurden von Helena Biosciences Europe oder in ihrem Auftrag als Richtlinien ermittelt: Jede Labor muss seine eigenen Werte ermitteln.
Der Fibrinogen-Test ist so konzipiert, dass sich eine lineare Kalibration von 1,5 – 6,5 g/L ergibt.

Reproduzierbarkeit

Intra-assay-Präzision			Inter-assay-Präzision		
Fibrinogen (g/L)	*n*	*CV (%)*	*Fibrinogen (g/L)*	*n*	*CV (%)*
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

REFERENZEN

1. Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
2. Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
3. Clinical and Laboratory Standards Institute (2008) Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Haemostasis Assays: Approved Guideline, 5th edn. CLSI: H21-A5
4. Scully RE *et al.* (1980) Normal Reference Laboratory Values, *New England Journal Medcine*, **302**(37):37-48.
5. Okuno T, Selenko V (1972) Plasma fibrinogen determination by automated thrombin time, *American Journal of Medical Technology,* **38**(6):196-201

Clauss Fibrinogen 50
Istruzioni per l'uso

it

USO PREVISTO

Determinazione quantitativa del fibrinogeno secondo il metodo di Clauss presente nel plasma citrato umano su sistemi di coagulazione Helena Biosciences Europe AC-4, C-1, C-2, C-4.

Il kit di Fibrinogeno Clauss 50 è stato formulato per la determinazione quantitativa del fibrinogeno in plasma umano. Clauss[1] ha messo a punto un semplice metodo per la determinazione quantitativa del fibrinogeno misurando il tempo di coagulazione del plasma diluito in seguito all'aggiunta di Thrombin (>30 NIH unità/mL). Questo tempo di coagulazione è proporzionale alla concentrazione di fibrinogeno. I livelli di fibrinogeno possono aumentare in seguito ad infiammazione, gravidanza o impiego di contraccettivi orali[2]. Livelli ridotti di fibrinogeno sono riscontrabili in alcuni stati, come ad esempio le patologie epatiche e la DIC. Tra le carenze congenite rientrano l'afibrinogenemia (assenza di fibrinogeno rilevabile), l'ipofibrinogenemia (<1 mg/mL) e la disfibrinogenemia (molecola di fibrinogeno anomala).

AVVERTENZE E PRECAUZIONI

I reagenti contenuti in questo kit sono destinati esclusivamente alla diagnostica *in vitro* - NON INGERIRE. Indossare guanti protettivi durante l'uso dei componenti del kit. Fare riferimento alle istruzioni del prodotto per avvertenze su rischi e sicurezza ed informazioni sullo smaltimento dei componenti. I prodotti plasmatici sono stati esaminati dando esito negativo (salvo diversamente indicato sulla confezione del kit o sul flacone) relativamente alla presenza dell'antigene dell'epatite B (HbsAg), dell'anticorpo anti-HIV 1 e 2 e dell'anticorpo anti-HCV; questi prodotti devono tuttavia essere manipolati con le stesse misure precauzionali adottate per un campione di plasma umano.

COMPOSIZIONE

Componente	Contiene	Descrizione	Preparazione
Thrombin: 50 NIH/mL	5 x 4 mL (REF 5556) 5 x 2 mL (REF 5556H)	Ogni flacone contiene approssimativamente 200 (REF 5556) / 100 (REF 5556H) unità di Thrombin bovina con stabilizzatori.	Ricostituire ogni flacone con: 4 mL (REF 5556) 2 mL (REF 5556H) di acqua distillate. Durante il pipettaggio, prestare attenzione ad evitare la contaminazione. Agitare delicatamente e lasciare riposare per 15 minuti. Miscelare bene immediatamente prima dell'uso. Non scuotere.
Fibrinogen Calibrator	2 x 1 mL (REF 5556) 1 x 1 mL (REF 5556H)	Ogni flacone contiene 1 mL di plasma umano normale liofilizzato dosato per i livelli di fibrinogeno.	Ricostituire ogni flacone con esattamente 1,0 mL di acqua distillata. Agitare delicatamente e lasciare riposare per 10 minuti. Miscelare delicatamente prima dell'uso. Non scuotere.
Owren's Buffer	2 x 25 mL (REF 5556) 1 x 25 mL (REF 5556H)	Ogni flacone contiene 25 mL di tampone contenente barbital e sodio cloruro con sodio azide come conservante.	Il tampone è pronto all'uso così come viene fornito.

Ogni kit contiene un Istruzioni per l'uso.

Ogni kit contiene un inserto recante i valori di riferimento specifici per il lotto.

MATERIALI NECESSARI, MA NON IN DOTAZIONE

Fare riferimento al manuale utente dello strumento e/o alla nota applicativa per conoscere le istruzioni specifiche. Ireagenti contenuti in questo kit sono disponibili anche come materiale separato:

REF 5374	Clauss Fibrinogen (Thrombin only)
REF 5378	Clauss Fibrinogen (Thrombin only)
REF 5379	Fibrinogen Calibrator
REF 5375	Owren's Buffer

CONSERVAZIONE E STABILITÀ

I flaconi non aperti sono stabili fino alla data di scadenza indicata se conservati nelle condizioni riportate sul flacone o sull'etichetta del kit.

Thrombin: 50 NIH/mL	Dopo la ricostituzione, il reagente è stabile per 8 ore a temperatura ambiente, 1 settimana a $^{+}2$ – $^{+}8$°C o per 1 mesi a -20°C.
Fibrinogen Calibrator	Dopo la ricostituzione, il reagente è stabile per 4 ore a $^{+}2$ – $^{+}8$°C.
Owren's Buffer	Una volta aperto, conservare a $^{+}2$ – $^{+}8$°C.

RACCOLTA DEI CAMPIONI E PREPARAZIONE

Nel corso dell'intera procedura è necessario utilizzare plastica o vetro siliconizzato. Il sangue (9 parti) deve essere raccolto in sodio citrato al 3,2% o al 3,8% come anticoagulante (1 parte). Separare il plasma in seguito a centrifugazione a 1500 x g per 15 minuti. Il plasma deve essere conservato a $^{+}2$ – $^{+}8$°C o $^{+}18$ – $^{+}24$°C. I test devono essere completati entro 4 ore dalla raccolta dei campioni; in alternativa, il plasma può essere conservato congelato a -20°C per 2 settimane o a -70°C per 6 mese. Decongelare rapidamente a $^{+}37$°C prima di eseguire i test. Non conservare a $^{+}37$°C per oltre 5 minuti[3].

PROCEDURA

Fare riferimento al manuale utente dello strumento appropriato per istruzioni dettagliate oppure contattare Helena Biosciences Europe per le note applicative specifiche dello strumento.

INTERPRETAZIONE DEI RISULTATI

Nei soggetti adulti sani i valori previsti per il fibrinogeno sono di 150-350 mg/dL (1,5-3,5 g/L)[4,5].

LIMITAZIONI

I livelli di eparina >0,6 unità/mL e i prodotti fibrinolitici di degradazione >100 mg/mL possono causare una quantificazione del fibrinogeno falsamente bassa. Se i valori fuoriescono dai valori della curva standard per i campioni dei pazienti, ripetere il dosaggio utilizzando una diluizione appropriata per portare i valori all'interno del range standard.

CONTROLLO QUALITÀ

Ogni laboratorio deve definire un programma di controllo qualità. I plasmi di controllo normali e anormali devono essere testati prima di ogni lotto di campioni di pazienti, per garantire un livello prestazionale soddisfacente sia per quanto riguarda lo strumento che per l'operatore. Qualora i controlli non funzionassero come previsto, i risultati relativi ai pazienti dovranno essere considerati non validi. Helena Biosciences Europe mette a disposizione i seguenti controlli utilizzabili con questo prodotto:

REF 5301	Speciality Assayed Control N
REF 5302	Speciality Assayed Control A
REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA

VALORI DI RIFERIMENTO

I valori di riferimento possono variare da un laboratorio all'altro in funzione delle tecniche e dei sistemi in uso. Per tale motivo ciascun laboratorio dovrà elaborare un proprio range normale.

CARATTERISTICHE PRESTAZIONALI

Le caratteristiche prestazionali sotto riportate sono state determinate da Helena Biosciences Europe o dai propri rappresentanti a titolo di linee guida. Ciascun laboratorio dovrà pertanto elaborare i propri dati prestazionali. Il dosaggio del fibrinogeno è stato studiato per fornire calibrazione lineare compresa tra 1,5-6,5 g/L.

Riproducibilità

Precisione intra-dosaggio			Precisione tra i dosaggi		
Fibrinogeno (g/L)	*n*	*CV (%)*	*Fibrinogeno (g/L)*	*n*	*CV (%)*
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

RIFERIMENTI

1. Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
2. Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
3. Clinical and Laboratory Standards Institute (2008) Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Haemostasis Assays: Approved Guideline, 5th edn. CLSI: H21-A5
4. Scully RE *et al.* (1980) Normal Reference Laboratory Values, *New England Journal Medcine*, **302**(37):37-48.
5. Okuno T, Selenko V (1972) Plasma fibrinogen determination by automated thrombin time, *American Journal of Medical Technology,* **38**(6):196-201

Clauss Fibrinogen 50
Instrucciones de uso

es

USO PREVISTO

La determinación cuantitativa de fibrinógeno basada en el método Clauss del plasma humano citrado en sistemas de coagulación Helena Biosciences Europe AC-4, C-1, C-2, C-4.

El Kit de Fibrinógeno de Clauss 50 está previsto para la determinación cuantitativa del fibrinógeno en el plasma humano. Clauss[1] desarrolló un método simple para la determinación cuantitativa de fibrinógeno midiendo el tiempo de coagulación del plasma diluido después de la adición de Thrombin (>30 unidades NIH/mL). Este tiempo de coagulación es proporcional a la concentración de fibrinógeno. Los niveles de fibrinógeno pueden aumentar como consecuencia de inflamación, embarazo o uso de anticonceptivos orales[2]. Pueden encontrarse niveles disminuidos en determinados estados como la hepatopatía y la CID. Entre las deficiencias congénitas están la afibrinogenemia (sin fibrinógeno detectable), la hipofibrinogenemia (<1 mg/mL) y la disfibrinogenemia (molécula de fibrinógeno anormal).

ADVERTENCIAS Y PRECAUCIONES

Los reactivos contenidos en este kit son sólo para uso diagnóstico – NO SE DEBEN INGERIR. Usar guantes para manejar todos los componentes del kit. Consultar la hoja con los datos de seguridad del producto acerca de los riesgos, avisos de seguridad y consejos para su eliminación. Los productos plasmáticos se han sometido a pruebas y han resultado negativos (a menos que se indique otra cosa en la caja del kit o en el vial) para la presencia de antígeno de la hepatitis B (HbsAg), anticuerpos de VIH 1 y 2 y anticuerpo del VHC; sin embargo, deben manipularse con las mismas precauciones que una muestra de plasma humano.

COMPOSICIÓN

Componente	Contiene	Descripción	Preparación
Thrombin: 50 NIH/mL	5 x 4 mL (REF 5556) 5 x 2 mL (REF 5556H)	Cada vial contiene aproximadamente 200 (REF 5556) / 100 (REF 5556H) unidades de trombina bovina con estabilizadores.	Reconstituya cada vial con: 4 mL (REF 5556) 2 mL (REF 5556H) de agua purificada. Tener cuidado al pipetear para evitar la contaminación. Agitar suavemente y permitir que repose durante 15 minutos. Mezclar bien inmediatamente antes de usar. No agitar.
Fibrinogen Calibrator	2 x 1 mL (REF 5556) 1 x 1 mL (REF 5556H)	Cada vial contiene 1,0 mL de plasma humano normal liofilizado estudiado en cuanto a niveles de fibrinógeno.	Reconstituir cada vial con exactamente 1,0 mL de agua destilada. Agitar suavemente y permitir que repose durante 10 minutos. Mezclar suavemente antes de su uso. No agitar.
Owren's Buffer	2 x 25 mL (REF 5556) 1 x 25 mL (REF 5556H)	Cada frasco contiene 25 mL de tampón con barbital y cloruro sódico con azida sódica como conservante.	El tampón viene envasado listo para usar.

Cada kit contiene instrucciones de uso.

Cada kit contiene valores de referencia específicos insertados del lote.

ARTÍCULOS NECESARIOS NO SUMINISTRADOS

Consúltese el Manual del Operador del Instrumento y/o la nota de aplicación para instrucciones adecuadas. Los reactivos contenidos en este kit están también disponibles como artículos separados:

REF 5374	Clauss Fibrinogen (Thrombin only)
REF 5378	Clauss Fibrinogen (Thrombin only)
REF 5379	Fibrinogen Calibrator
REF 5375	Owren's Buffer

ALMACENAJE Y ESTABILIDAD

Los viales no abiertos son estables hasta la fecha de caducidad indicada cuando se conservan en las condiciones indicadas en el vial o en la etiqueta del kit.

Thrombin: 50 NIH/mL	El reactivo reconstituido permanece estable durante 8 horas a temperatura ambiente, 1 semana a $^{+}2$ – $^{+}8$°C o 1 meses a -20°C.
Fibrinogen Calibrator	Una vez reconstituido, el reactivo permanece estable durante 4 horas a $^{+}2$ – $^{+}8$°C.
Owren's Buffer	Conservar a $^{+}2$ – $^{+}8$°C una vez abierto.

RECOGIDA Y PREPARACIÓN DE MUESTRAS

Debe usarse siempre plástico o vidrio siliconizado. Debe recogerse sangre (9 partes) en el anticoagulante citrato sódico al 3,2% o al 3,8% (1 parte). Separar el plasma después de la centrifugación a 1500 x g durante 15 minutos. El plasma debe conservarse a $^{+}2$ – $^{+}8$ºC o $^{+}18$ – $^{+}24$°C. Las pruebas deberían terminarse en 4 horas desde la recogida de las muestras o el plasma puede conservarse congelado a -20°C durante 2 semanas o $^{-}70$°C durante 6 mes. Descongelar rápidamente a $^{+}37$°C antes de realizar la prueba. No conservar a $^{+}37$°C durante más de 5 minutos[3].

PROCEDIMIENTO

Consulte el manual del usuario del instrumento adecuado para instrucciones detalladas o póngase en contacto con Helena Biosciences Europe para notas de aplicación específicas del instrumento.

INTERPRETACIÓN DE RESULTADOS

Los valores esperados para el fibrinógeno en adultos sanos son de 150-350 mg/dL (1,5-3,5 g/L)[4,5].

LIMITACIONES

Los niveles de heparina >0,6 unidades/mL y los productos de degradación fibrinolíticos >100 mg/mL pueden producir una cuantificación falsamente baja del fibrinógeno. Si los valores caen fuera de los valores de la curva estándar para las muestras de pacientes, vuelva a realizar la valoración usando una dilución adecuada para llevar los valores al intervalo estándar.

CONTROL DE CALIDAD

Cada laboratorio debe establecer un programa de control de calidad. Los controles normales y anormales deben estudiarse antes de cada lote de muestras del paciente, para asegurar un funcionamiento adecuado del instrumento y el operador. Si los controles no se realizan como se esperaba, los resultados del paciente deben considerarse inválidos. Helena Biosciences Europe suministra los siguientes controles disponibles para usar con este producto:

REF 5301	Speciality Assay Control N
REF 5302	Speciality Assay Control A
REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA

VALORES DE REFERENCIA

Los valores de referencia pueden variar entre los laboratorios dependiendo de las técnicas y sistemas usados. Por esta razón, cada laboratorio debe establecer su propio intervalo normal.

CARACTERÍSTICAS FUNCIONALES

Helena Biosciences Europeo sus representantes han determinado las siguientes características de rendimiento como directriz. Cada laboratorio debe establecer sus propios datos de rendimiento. La valoración del fibrinógeno está diseñada para dar una calibración lineal de 1,5 a 6,5 g/L.

Reproducibilidad

Precisión intra-ensayo			Precisión inter-ensayo		
Fibrinógeno (g/L)	*n*	*CV (%)*	*Fibrinógeno (g/L)*	*n*	*CV (%)*
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

REFERENCIAS

1. Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
2. Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
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Тест-система "Определение фибриногена методом Клаусса 50"
инструкция

ru

ПРИМЕНЕНИЕ

Тест-система "Определение фибриногена методом Клаусса 50" предназначена для проведения количественного определения фибриногена по Клауссу в плазме крови человека на коагулометрах производства компании Хелена С-1/2/4/АС-4.

Тест-система "Определение фибриногена методом Клаусса 50" предназначена для проведения количественного определения фибриногена по Клауссу в плазме крови человека на коагулометрах. Метод Клаусса[1] – простой метод количественного определения фибриногена, основанный на измерении времени образования сгустка. Метод проводится в разведенной плазме после добавления тромбинового реагента (> 30 МЕ/мл). Время образования сгустка пропорционально концентрации фибриногена. Уровень фибриногена может увеличиваться при воспалении, беременности или при приеме пероральных контрацептивов[2]. Низкие значения могут наблюдаться при заболеваниях печени и ДВС. Изменение содержания фибриногена в плазме помогает диагностике врожденных дефицитных состояний, включая афибриногенемию (полное отсутствие фибриногена), гипофибриногенемию (концентрация фибриногена менее 1 мг/мл) и дисфибриногенемию (структурные нарушения в молекуле фибриногена).

ПРЕДУПРЕЖДЕНИЯ И ПРЕДОСТОРОЖНОСТИ

Реактивы, содержащиеся в наборе, предназначены только для *in-vitro* диагностики. При работе с любым из компонентов набора применяйте соответствующую защитную одежду (одноразовые резиновые или пластиковые перчатки и т.д.). Ознакомьтесь с инструкцией по мерам предосторожности. Тестирование контрольной плазмы (либо реагента) на содержание антигена вируса гепатита В (HBsAg), антител к HIV I и II антител и HCV дало отрицательный результат (за исключением, если последнее не указано на упаковке или флаконе), тем не менее, при работе с ней/ним следует соблюдать такую же осторожность, как и при работе с образцами плазмы крови человека.

СОСТАВ РЕАГЕНТОВ

Компоненты	Состав набора	Описание	Приготовление реагентов
Тромбиновый Реагент: 50 МЕ/мл	5 x 4 мл (Кат. № 5556) 5 x 2 мл (Кат. № 5556H)	содержит 200 единиц (Кат. № 5556) / 100 единиц (Кат. № 5556H) бычьего тромбина со стабилизаторами.	Внести во флакон: 4.0 мл (Кат. № 5556) или 2.0 мл (Кат. № 5556H) дистиллированной (деионизированной воды). Осторожно перемешать и оставить при комнатной температуре в течение 15 минут. Перед использованием еще раз перемешать. Не встряхивать.
Калибратор Фибриногена	2 x 1 мл (Кат. № 5556) 1 x 1 мл (Кат. № 5556H)	Содержит 1.0 мл лиофилизированной нормальной плазмы человека, аттестованной по уровню фибриногена.	Внести во флакон 1.0 мл дистиллированной или деионизированной воды. Осторожно перемешать и оставить при комнатной температуре в течение 10 минут. Перед использованием еще раз перемешать. Не встряхивать.
Буфер Оуренса	2 x 25 мл (Кат. № 5556) 1 x 25 мл (Кат. № 5556H)	Флакон содержит 25.0 мл готового к использованию буфера, содержащего натрия хлорид и натрия азид в качестве стабилизатора	Дополнительные разведения не требуются.

Каждый набор содержит инструкцию по применению.

Паспорт с референсными значениями.

ТРЕБУЕМЫЕ, НО НЕ ПОСТАВЛЯЕМЫЕ МАТЕРИАЛЫ

Адаптации реагентов к различным приборам доступны по запросу у официальных дистрибьюторов и компании Хелена. Реагенты, входящие в набор могут быть заказаны отдельно:

Кат. № 5374	Тест-система "Фибриноген по Клауссу (только тромбиновый реагент)"
Кат. № 5378	Тест-система "Фибриноген по Клауссу (только тромбиновый реагент)"
Кат. № 5379	Калибратор фибриногена
Кат. № 5375	Тестовый реагент "Буфер Оуренса"

ХРАНЕНИЕ И СТАБИЛЬНОСТЬ

Невскрытые флаконы хранятся до истечения срока годности в условиях, указанных на упаковке или этикетке.

Тромбиновый Реагент: 50 МЕ/мл	После растворения, тромбиновый реагент стабилен в течение 7 дней при $^{+}2$ – $^{+}8$°C, 8 часов на борту анализатора при $^{+}15$ – $^{+}30$°C и 1 месяц при -20°C
Калибратор Фибриногена	После растворения, калибратор стабилен в течение 4 часов при $^{+}2$ – $^{+}8$°C
Буфер Оуренса	Вскрытый флакон с буфером следует хранить при $^{+}2$ – $^{+}8$°C

СБОР И ПРИГОТОВЛЕНИЕ ОБРАЗЦОВ

Для работы следует использовать только пластиковые или силиконированные стеклянные пробирки. Кровь забирается в пробирку с цитратным антикоагулянтом (3,2% или 3,8% цитрат натрия) в соотношении 9 + 1. После центрифугирования при 1500 g, в течение 15 минут (использование других параметров должно проверяться лабораторией), полученную плазму необходимо отделить от форменных элементов крови. Плазму следует хранить при температуре $^{+}2$ – $^{+}8$°C или $^{+}18$ – $^{+}24$°C. Тестирование должно быть проведено в течение 4 часов после забора образцов, либо плазму можно однократно заморозить и хранить при температуре -20°C в течение 2 недель или при -70°C в течение 6 месяцев. Перед проведением исследования плазму следует быстро разморозить при $^{+}37$°C. Не держать плазму при $^{+}37$°C более 5 минут[3].

ПРОЦЕДУРА ВЫПОЛНЕНИЯ АНАЛИЗА

Для получения более подробной информации обратитесь к инструкции на автоматический или полуавтоматический коагулометр.

ИНТЕРПРЕТАЦИЯ РЕЗУЛЬТАТОВ

Средний уровень Фибриногена в популяции практически здоровых людей находится между 150-350 мг/дл (1.5-3.5 г/л)[4,5].

ОГРАНИЧЕНИЯ

На низко ложные результаты концентрации фибриногена, полученные на коагулометре, может влиять гепарин в концентрации >0.6 Ед/мл и ПДФ в концентрации >100 мг/мл. Если значения образцов пациентов выпадают за график стандартной кривой, то требуется дальнейшее разведение образца, чтобы значение попадали в линейный диапазон от 1,0 до 6,5 г/л.

КОНТРОЛЬ КАЧЕСТВА

Каждая лаборатория должна установить программу контроля качества. Перед измерением каждой партии образцов пациентов необходимо протестировать нормальную и патологическую плазму, чтобы удостовериться в удовлетворительной работе оборудования и оператора. Если контрольные измерения не совпадают с ожидаемыми значениями, то измеренные данные пациентов следует считать недостоверными. омпания Хелена рекомендует следующие контрольные материалы:

Кат. № 5301	Контроль качества специальные тесты, норма
Кат. № 5302	Контроль качества специальные тесты, патология
Кат. № 5186	Контроль качества, норма
Кат. № 5187	Контроль качества, умеренно выраженная патология
Кат. № 5183	Контроль качества, высокая патология

РЕФЕРЕНСНЫЕ ЗНАЧЕНИЯ

Референсные значения могут варьировать между лабораториями в зависимости от используемых методов и коагулометров. По этой причине каждая лаборатория должна установить свои собственные значения.

АНАЛИТИЧЕСКИЕ ХАРАКТЕРИСТИКИ

Компания Хелена или её дистрибьюторы определили следующие ориентировочные аналитические характеристики. Каждая лаборатория должна определить свои собственные аналитические характеристики. При использовании ручного метода были определены следующие коэффициенты вариации (CV) и линейность в диапазоне от 1,0 до 6,5 г/л (без дополнительных разведений плазмы).

Воспроизводимость

в пределах аналитической серии			между разными аналитическими сериями		
Фибриноген (г/л)	*n*	*CV (%)*	*Фибриноген (г/л)*	*n*	*CV (%)*
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

СПИСОК ЛИТЕРАТУРЫ

1. Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
2. Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
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4. Scully RE *et al.* (1980) Normal Reference Laboratory Values, *New England Journal Medcine*, **302**(37):37-48.
5. Okuno T, Selenko V (1972) Plasma fibrinogen determination by automated thrombin time, *American Journal of Medical Technology,* **38**(6):196-201

Declaration of Conformity

helena
Biosciences Europe

HL-7-0229DC DOI 2015/08 (6)

In Application of the Council Directive 98/79/EC on the approximation of the laws of the Member States relating to *In Vitro* Diagnostic Medical Devices & CE marking.

Declaration of conformance to applicable sections of Annex I - Essential Requirements and Annex III (EC Declaration of Conformity) imposed by sections 2 to 5. The below listed products are not classified under Annex II Lists A or B. Access to the appropriate technical files will be made available to the appropriate body in the event this is required.

Product Code	Description	GMDN Classification Code
5392	Thrombin Time	55987

I, the undersigned declare that the devices registered against the above GMDN Classification Code conforms to the said Directives.

Full Name: M.J. Stephenson Title: Managing Director

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Thrombin Time

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HL-2-0444P 2016/01 (12)

Thrombin Time
Instructions for use

en

INTENDED PURPOSE

The Thrombin Time kit is intended for carrying out clot based haemostasis assays.

The Thrombin Time reagent contains bovine thrombin. The reagent can be used manually or on semi-automated and automated instruments. The test is commonly applied to detect various sources of interference with normal blood coagulation. Prolongation of the thrombin clotting time can be taken as a qualitative indication of abnormal fibrinogen levels (high or low), or the presence of interfering substances such as Fibrin Degradation Products (FDPs) or heparin. Quantitative evaluation of the possible causes of prolonged thrombin clotting time should be performed as follow-up studies, such as aPTT or chromogenic assay for heparin, Clauss fibrinogen, FDP determinations, heparin neutralisation by protamine sulphate or polybrene[1], normal plasma mixing studies[2] or reptilase assay[3] to distinguish between hypofibrinogenaemia and FDP effects.

WARNINGS AND PRECAUTIONS

The reagents contained in this kit are for *in vitro* diagnostic use only – DO NOT INGEST. Wear appropriate personal protective equipment when handling all kit components. Refer to the product safety declaration for the link to appropriate hazard and precautionary statements where applicable. Dispose of components in accordance with local regulations.

COMPOSITION

Composition	Content	Description	Preparation
Thrombin Time	10 x 1 mL (REF 5392H) 10 x 2 mL (REF 5392) 10 x 5 mL (REF 5377)	Each vial contains a lyophilised preparation of bovine thrombin with buffers and stabilisers. The reconstituted reagent contains ≤10 NIH units/mL of thrombin. The reagent should be a white lyophilised plug.	Reconstitute the reagent with the recommended volume of purified water: 1 mL - REF 5392H 2 mL - REF 5392 5 mL - REF 5377 Allow to stand for 5 minutes then mix gently by inversion and transfer to a plastic tube. Reconstituted reagent should be a clear, colourless solution.

Each kit contains Instructions For Use.

ITEMS REQUIRED BUT NOT PROVIDED

Any high quality mechanical, opto-mechanical or photo-optical coagulation instrument capable of performing thrombin clotting time testing may be used.

STORAGE, SHELF-LIFE AND STABILITY

Unopened reagents are stable until the given expiry date when stored under conditions indicated on the vial or kit label.

Thrombin Time	Reconstituted reagent should be stored at $^{+}$2 –$^{+}$8°C and is stable for 14 days or at -20°C for 1 month. Reconstituted reagent can also be stored on-baord a Sysmex CA1500 photo-optical instrument for up to 7 days.

SAMPLE COLLECTION AND PREPARATION

Plastic or siliconised glass should be used throughout. Blood (9 parts) should be collected into 3.2% or 3.8% sodium citrate anticoagulant (1 part). Separate plasma after centrifugation at 1500 x g for 15 minutes. Plasma should be kept at $^{+}$2 –$^{+}$8°C or $^{+}$18 –$^{+}$24°C. Testing should be completed within 4 hours of sample collection, or plasma can be stored frozen at -20°C for 2 weeks or -70°C for 6 months. Thaw quickly at $^{+}$37°C prior to testing. Do not keep at $^{+}$37°C for more than 5 minutes[4].

PROCEDURE

1. Collect and prepare the blood sample according to the directions outlined in "Sample Collection And Preparation".
2. Reconstitute the control plasma according to the package insert provided with each control.
3. Prepare the reagent for use in the procedure according to the reconstitution instructions in the "Composition" section.
4. Perform all tests in duplicate. Calculate the mean clotting time of the duplicate determinations to the nearest 0.1 seconds. Individual values should be within ±5% of the mean value.

Manual Method

1. Pipette 0.2 mL of the patient plasma or control plasma into a reaction tube.
2. Incubate at $^{+}$37°C for 3 minutes.
3. Pipette 0.1 mL of Thrombin Time into the reaction tube containing patient or control plasma whilst simultaneously starting a timer.
4. Record the time taken for clot formation to the nearest 0.1 second.

Automated Method

Refer to the appropriate instrument operator manual for detailed instructions or contact Helena Biosciences Europe for instrument specific application notes.

INTERPRETATION OF RESULTS

The results of the Thrombin Time test should be reported to the nearest 0.1 seconds. The normal range (usually the mean ±2 standard deviations) should be established by each laboratory. Results outside the normal range should be considered abnormal and follow-up testing performed.

LIMITATIONS

Expected values for the Thrombin Time test will vary from one laboratory to another depending on the technique used. The method of clot detection, temperature, pH, collection technique, type of anticoagulant and time and method of sample storage are all very important. Plasma sample collection and storage conditions should be standardised and carefully controlled. Unexpected results should be confirmed by additional testing.
As well as the cause of elongated thrombin times indicated, a report has suggested that many systemic amyloidosis patients with bleeding complications may have a circulating inhibitor which prolongs the Thrombin Time[5]. Also, therapeutic levels of heparin may entirely abolish clotting in the Thrombin Time test, although neutralisation with protamine sulphate or polybrene should correct the Thrombin Time[1].

QUALITY CONTROL

Each laboratory should establish a quality control program. Normal and abnormal control plasmas should be tested prior to each batch of patient samples, to ensure satisfactory instrument and operator performance. If controls do not perform as expected, patient results should be considered invalid.
Helena Biosciences Europe supplies the following controls available for use with this product:

REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA

REFERENCE VALUES

Reference values can vary between laboratories depending on the techniques and systems in use. For this reason each laboratory should establish its own reference ranges.

PERFORMANCE CHARACTERISTICS

The following performance characteristics have been determined by Helena Biosciences Europe or their representatives:

Reproducibility

		Intra-assay precision		Inter-assay precision	
Sample	*n*	*Clot formation (seconds)*	*CV (%)*	*Clot formation (seconds)*	*CV (%)*
Normal	10	12.5	1.43	12.5	1.29

BIBLIOGRAPHY

1. Laposata *et al.*The Clinical Haemostasis Handbook, Yearbook Medical Publishers Inc., p219, 1989
2. Thompson AR and Harker LA. Manual of Haemostasis and Thrombosis. 3rd Ed., F.A. Davis Co., p62, 1983
3. DeMott WR. Laboratory Test Handbook, 2nd Ed., Jacobs D.S. et al Eds., Lexi-Comp Inc., p432-433, 1990.
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Thrombin Time
Fiche technique

fr

UTILISATION

Le kit Thrombin Time est destiné à la réalisation des analyses de l'hémostase basées sur la formation de caillots.

Le réactif Thrombin Time contient de la thrombine bovine. Il est possible d'utiliser le réactif avec une méthode manuelle ou avec des instruments automatisés ou semi-automatisés. Il s'agit d'un test couramment réalisé pour détecter diverses sources d'interférence avec la coagulation sanguine normale. Un allongement du Thrombin Time constitue une indication qualitative de taux de fibrinogène anormaux (élevé ou faible) ou de la présence de substances interférentes comme les produits de dégradation de la fibrine (PDF) ou l'héparine. Il est nécessaire de réaliser une évaluation quantitative des causes potentielles de cet allongement en réalisant d'autres analyses: TCA ou dosage chromogénique pour l'héparine, méthode de Clauss pour le fibrinogène, déterminations des PDF, neutralisation de l'héparine par du sulfate de protamine ou du Polybrene[1], études de mélanges avec du plasma normal[2] ou détermination du temps de reptilase[3] pour différencier une hypofibrinogénémie des effets des PDF.

AVERTISSEMENTS ET PRÉCAUTIONS

Les réactifs du kit sont à usage diagnostique *in vitro* uniquement – NE PAS INGÉRER. Porter un équipement de protection individuelle approprié lors de la manipulation de tous les composants du kit. Consulter la fiche de données de sécurité du produit pour obtenir le lien vers les phrases de risque et les conseils de prudence le cas échéant. Éliminer les composants conformément aux églementations locales.

COMPOSITION

Composant	Contient	Description	Préparation
Thrombin Time	10 x 1 mL (REF 5392H) 10 x 2 mL (REF 5392) 10 x 5 mL (REF 5377)	Chaque flacon contient une préparation lyophilisée de thrombine bovine additionnée de tampons et de stabilisateurs. Le réactif reconstitué contient ≤10 unités NIH/mL de thrombine. Il se présente sous la forme d'un lyophilisat blanc.	Reconstituer le réactif en ajoutant le volume indiqué d'eau distillée: 1 mL - REF 5392H 2 mL - REF 5392 5 mL - REF 5377 Laisser reposer 5 minutes puis mélanger doucement par inversion et transférer dans un tube en plastique. Le réactif reconstitué est une solution transparente et incolore.

Chaque kit contient une fiche technique.

MATÉRIEL NÉCESSAIRE NON FOURNI

Il est possible d'utiliser un instrument de coagulation mécanique opto-mécanique ou photo-optique de haute qualité servant à déterminer le Thrombin Time.

CONSERVATION, DURÉE DE VIE UTILE ET STABILITÉ

Les flacons de réactif non ouverts sont stables jusqu'à la date de péremption indiquée s'ils sont conservés dans les conditions indiquées sur l'étiquette du kit ou du flacon.

Thrombin Time	Une fois reconstitué, le réactif doit être conservé à une température située entre $^{+}$2 –$^{+}$8°C pour rester stable pendant 14 jours, ou à -20°C pour rester stable pendant 1 mois. Le réactif reconstitué peut également être conservé pendant un maximum de 7 jours à bord d'un instrument photo-optique Sysmex CA1500.

PRÉLÈVEMENT ET PRÉPARATION DES ÉCHANTILLONS

Utiliser tout au long du prélèvement du plastique ou du verre siliconé. Mélanger 9 volumes de sang et 1 volume de citrate de sodium à 3,2% ou 3,8%. Séparer le plasma après centrifugation à 1500 x g pendant 15 minutes. Conserver le plasma entre $^{+}$2 –$^{+}$8°C ou $^{+}$18 –$^{+}$24°C. L'analyse doit être terminée dans les 4 heures suivant le prélèvement de l'échantillon; sinon, il est possible de congeler le plasma 2 semaines à -20°C ou 6 mois à -70°C. Décongeler rapidement à $^{+}$37°C avant de réaliser l'analyse. Ne pas laisser à $^{+}$37°C plus de 5 minutes[4].

PROCÉDURE

1. Prélever et préparer l'échantillon de sang conformément aux instructions du paragraphe "Prélèvements des échantillons".
2. Reconstituer le plasma de contrôle en suivant les instructions de la notice fournie avec chaque contrôle.
3. Préparer le réactif à utiliser dans la procédure en suivant les instructions de reconstitution du paragraphe "Composition".
4. Réaliser toutes les analyses en double. Calculer le temps moyen de coagulation des déterminations en arrondissant au dixième de seconde. Les valeurs individuelles doivent se situer dans une plage ±5% de la valeur moyenne.

Méthode Manuelle

1. Pipeter 0,2 mL de plasma patient ou contrôle dans un tube à essai.
2. Incuber 3 minutes à $^{+}$37°C.
3. Pipeter 0,1 mL de réactif Thrombin Time dans le tube à essai contenant le plasma patient ou contrôle et démarrer à ce moment un chronomètre.
4. Relever le temps de formation du caillot en arrondissant au dixième de seconde.

Méthodes Automatisées

Consulter le manuel d'utilisation de l'instrument approprié pour obtenir des instructions détaillées ou contacter Helena Biosciences Europe pour obtenir des notes d'application spécifiques à l'instrument.

INTERPRÉTATION DES RÉSULTATS

Les résultats du Thrombin Time doivent être indiqués en arrondissant au dixième de seconde. La plage normale (en général, écarts-types moyens ± 2) doit être déterminée par chaque laboratoire. Les résultats se situant hors de la plage normale doivent être considérés comme anormaux et il est nécessaire de réaliser des analyses plus approfondies.

LIMITES

Les valeurs prévues du Thrombin Time varient d'un laboratoire à l'autre suivant la technique utilisée. La méthode de détection du caillot, la température, le pH, la technique de prélèvement, le type d'anticoagulant et la durée et le mode de conservation de l'échantillon sont des paramètres très importants. Les conditions de prélèvement et de conservation de l'échantillon de plasma doivent être standardisées et soigneusement contrôlées. Tout résultat hors plage doit être confirmé par un test supplémentaire.
Mis à part les causes de l'allongement du Thrombin Time indiquées, une étude a suggéré que de nombreux patients souffrant d'une amylose systémique avec des complications hémorragiques ont un inhibiteur circulant qui prolonge le Thrombin Time[5]. En outre, un taux thérapeutique d'héparine risque d'annuler complètement la coagulation dans le test de détermination du Thrombin Time, même si une neutralisation avec du sulfate de protamine ou du Polybrene doit corriger le Thrombin Time[1].

CONTRÔLE QUALITÉ

Chaque laboratoire doit établir un programme de contrôle qualité. Les plasmas de contrôle, normaux et anormaux, doivent être testés avant chaque lot d'échantillons patients afin de s'assurer que l'instrument et l'opérateur offrent des performances satisfaisantes. Si les contrôles ne donnent pas les résultats prévus, les résultats du patient doivent être considérés comme non valables.
Helena Biosciences Europe distribue les contrôles suivants à utiliser avec ce produit:

REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA

VALEURS DE RÉFÉRENCE

Les valeurs de référence peuvent varier d'un laboratoire à l'autre suivant les techniques et les systèmes utilisés. C'est pour cette raison qu'il appartient à chaque laboratoire de déterminer ses propres plages de référence.

CARACTÉRISTIQUES DE PERFORMANCES

Helena Biosciences Europe ou ses mandataires ont déterminé les caractéristiques de performance suivantes:

Précision

		Précision intra-série		Précision inter-séries	
Échantillon	*n*	*Formation du caillot (seconde)*	*CV (%)*	*Formation du caillot (seconde)*	*CV (%)*
Normaux	10	12,5	1,43	12,5	1,29

BIBLIOGRAPHIE

1. Laposata *et al.*The Clinical Haemostasis Handbook, Yearbook Medical Publishers Inc., p219, 1989
2. Thompson AR and Harker LA. Manual of Haemostasis and Thrombosis. 3rd Ed., F.A. Davis Co., p62, 1983
3. DeMott WR. Laboratory Test Handbook, 2nd Ed., Jacobs D.S. et al Eds., Lexi-Comp Inc., p432-433, 1990.
4. Clinical and Laboratory Standards Institute (2008) Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Haemostasis Assays: Approved Guideline, 5th edn. CLSI: H21-A5
5. Gastineau DA *et al.* (1991) Inhibitor of the Thrombin Time in Systemic Amyloidosis: A Common Coagulation Abnormality, *Blood,* **77:**2637-40

Thrombin Time
Anleitung

de

VERWENDUNGSZWECK

Das Thrombin Time-Kit ist für koagulometrische Gerinnungstests vorgesehen.

Das Reagenz für die Thrombin Time enthält Rinder-Thrombin. Das Reagenz kann manuell oder in Verbindung mit halbautomatischen oder automatischen Geräten verwendet werden. Der Test wird allgemein zum Nachweis verschiedener Ursachen von Störungen in der normalen Blutgerinnung verwendet. Eine Verlängerung der Thrombin Time kann als qualitativer Hinweis auf abnormale Fibrinogen-Werte (hoch oder niedrig) gelten, oder auf die Anwesenheit gerinnungshemmender Substanzen wie Fibrinogen-Abbauprodukte oder Heparin hindeuten. Quantitative Befundung möglicher Ursachen einer verlängerten Thrombin Time sollte als Verlaufsstudie durchgeführt werden wie z. B. aPTT oder chromogener Heparin-Test, Fibrinogen-Bestimmung (Clauss), Bestimmung der Fibrinogen-Abbauprodukte (FDP), Heparin-Neutralisation mit Protamin-sulfat oder Polybrene[1], Mischtests mit Normalplasma[2] oder Reptilasetest[3], um zwischen Hypofibrinogenämie und FDP-Effekten zu unterscheiden.

WARNHINWEISE UND VORSICHTSMASSNAHMEN

Die in diesem Kit enthaltenen Reagenzien sind ausschließlich für die Verwendung von *in-vitro*-Diagnosen vorgesehen. NICHT VERSCHLUCKEN. Tragen Sie beim Umgang mit sämtlichen Komponenten des Kits geeignete Schutzausrüstung. Beachten Sie gegebenenfalls die Verweise auf entsprechende Gefahren- und Vorbeugeerklärungen in der Produktsicherheitserklärung. Entsorgen Sie die Komponenten gemäß den örtlichen Vorschriften.

ZUSAMMENSETZUNG

Komponent	Inhalt	Beschreibung	Vorbereitung
Thrombin Time	10 x 1 mL (REF 5392H) 10 x 2 mL (REF 5392) 10 x 5 mL (REF 5377)	Jedes Fläschchen enthält eine lyophilisierte Zubereitung von Rinder-Thrombin mit Puffern und Stabilisatoren. Das rekonstituierte Reagenz enthält ≤10 NIH Einheiten/mL Thrombin. Das Reagenz sollte ein weißer lyophilisierter Pfropf sein.	Reagenz mit der empfohlenen Menge destilliertem Wasser rekonstituiert werden: 1 mL - REF 5392H 2 mL - REF 5392 5 mL - REF 5377 5 Minuten stehen lassen, durch Umdrehen leicht mischen und in eine Plastikröhrchen überführen. Rekonstituiertes Reagenz sollte eine klare, farblose Flüssigkeit sein.

Jedes Kit enthält eine Gebrauchsanweisung.

ERFORDERLICHE, ABER NICHT MITGELIEFERTE ARTIKEL

Es kann jedes zur Durchführung der Thrombin Time geeignete, qualitative hochwertige mechanischen, optomechanischen oder lichtoptische Gerät benutzt werden.

LAGERUNG, HALTBARKEIT UND STABILITÄT

Ungeöffnete Reagenzien sind unter den auf Verpackung oder Fläschchen angegebenen Lagerbedingungen bis zum aufgedruckten Verfallsdatum stabil.

Thrombin Time	Rekonstituiertes Reagenz ist bei Lagerung bei $^{+}$2 –$^{+}$8°C 14 Tage, bei -20 °C 1 Monat stabil. Rekonstituiertes Reagenz kann ebenfalls auf dem fotooptischen Gerät Sysmex CA1500 für bis zu 7 Tage aufbewahrt werden.

PROBENENTNAHME UND VORBEREITUNG

Nur Plastik oder Silikonglas verwenden. Blut (9 Teile) sollte in 3,2% oder 3,8% Natriumcitrat als Antikoagulanz (1 Teil) entnommen werden. 15 Minuten bei 1500 g zentrifugieren und Plasma abpipettieren. Plasma bei $^{+}$2 –$^{+}$8°C oder $^{+}$18 –$^{+}$24°C lagern. Plasma sollte innerhalb von 4 Stunden verarbeitet oder tief gefroren bei -20°C für 2 Wochen oder -70°C für 6 Monat gelagert werden. Vor dem Testen schnell bei $^{+}$37°C auftauen. Nicht länger als 5 Minuten bei $^{+}$37°C belassen[4].

VORGEHENSWEISE

1. Blutproben gemäß den Anweisungen in "Probenentnahme und vorbereitung" entnehmen und vorbereiten.
2. Kontrollplasma nach beigefügter Gebrauchsanweisung rekonstituieren.
3. Test-Reagenz entsprechend der Rekonstitutionsanleitung in dem Abschnitt "Inhalt" vorbereiten.
4. Alle Tests im Doppelansatz durchführen. Den Mittelwert der Gerinnungszeit für die Doppelwerte bis auf 0,1 Sekunden berechnen. Die einzelnen Werte sollten sich innerhalb ±5% des Mittelwerts befinden.

Manuelle Methode

1. 0,2 mL Patienten- oder Kontrollplasma in jedes Röhrchen pipettieren.
2. Bei $^{+}$37°C 3 Minuten inkubieren.
3. 0,1 mL Thrombin Time-Reagenz in jedes Röhrchen mit Patienten- oder Kontrollplasma pipettieren und gleichzeitig Stoppuhr starten.
4. Die Zeit bis zur Gerinnselbildung bis auf 0,1 Sekunden genau stoppen.

Automatisierte Methoden

Siehe die Bedienungsanleitung des entsprechenden Geräts für genaue Anweisungen oder wenden Sie sich an Helena Biosciences Europe für spezielle anwendungstechnische Hinweise.

INTERPRETATION DER ERGEBNISSE

Die Ergebnisse der Thrombin Time sollte bis auf 0,1 Sekunden genau angegeben werden. Der Normalbereich (gewöhnlich der Mittelwert von ± 2 Standardabweichungen) sollte von jeden Labor erstellt werden. Ergebnisse außerhalb des Normalbereichs sind als pathologisch zu bewerten, die weitere Tests erforderlich machen.

EINSCHRÄNKUNGEN

Normalwerte für die Thrombin Time variieren je nach angewendeter Technik von Labor zu Labor. Sehr wichtig dafür sind: Methode der Gerinnselerkennung, Temperatur, pH, Entnahmeverfahren, das verwendete Antikoagulanz und Dauer und Art der Probenlagerung. Die Entnahme und Lagerungsbedingungen der Plasmaproben sollten standardisiert sein und sorgfältig überprüft werden. Unerwartete Ergebnisse müssen durch weitere Untersuchungen bestätigt werden.
Wie schon als Grund für eine verlängerte Thrombin Time angedeutet hat ein Bericht darauf hingewiesen, dass viele systemische Amyloidose-Patienten mit Blutungsstörungen einen freien Hemmstoff im Blut besitzen, der die Thrombin Time verlängert[5]. Therapeutische Heparin-Spiegel können dazu führen, dass die Thrombin Time überhaupt nicht zur Gerinnselbildung führt. Neutralisation mit Protamin-sulfat oder Polybrene kann dabei abhelfen[1].

QUALITÄTSKONTROLLE

Jedes Labor muss für eine eigene Qualitätskontrolle sorgen. Vor jeder Testreihe mit Patientenproben müssen normale und pathologische Kontrollplasmen getestet werden, um eine zufrieden stellende Geräteleistung und Bedienung zu gewährleisten. Liegen die Kontrollen außerhalb des Normbereichs, sind die Patientenergebnisse nicht zu verwenden.
In Verbindung mit diesem Produkt bietet Helena Biosciences Europe die folgenden Kontrollen an:

REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA

REFERENZWERTE

Referenzwerte können je nach Technik und verwendetem System von Labor zu Labor unterschiedlich sein. Aus diesem Grund sollte jedes Labor seine eigenen Referenzwertbereiche erstellen.

LEISTUNGSMERKMALE

Die folgenden Leistungseigenschaften wurden von Helena Biosciences Europe oder in ihrem Auftrag:

Präzision

		Intra-assay-Präzision		Inter-assay-Präzision	
Probe	*n*	*Gerinnselbildung (sekunden)*	*CV (%)*	*Gerinnselbildung (sekunden)*	*CV (%)*
Normale	10	12,5	1,43	12,5	1,29

LITERATURVERZEICHNIS

1. Laposata *et al.*The Clinical Haemostasis Handbook, Yearbook Medical Publishers Inc., p219, 1989
2. Thompson AR and Harker LA. Manual of Haemostasis and Thrombosis. 3rd Ed., F.A. Davis Co., p62, 1983
3. DeMott WR. Laboratory Test Handbook, 2nd Ed., Jacobs D.S. et al Eds., Lexi-Comp Inc., p432-433, 1990.
4. Clinical and Laboratory Standards Institute (2008) Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Haemostasis Assays: Approved Guideline, 5th edn. CLSI: H21-A5
5. Gastineau DA *et al.* (1991) Inhibitor of the Thrombin Time in Systemic Amyloidosis: A Common Coagulation Abnormality, *Blood,* **77:**2637-40

Thrombin Time
Istruzioni per l'uso

it

SCOPO PREVISTO

Il kit Thrombin Time è concepito per l'esecuzione di dosaggi di emostasi basati sulla presenza di coaguli.

Il reagente per la determinazione del Thrombin Time contiene trombina bovina. Questo reagente può essere utilizzato manualmente o con strumenti semiautomatici e automatici. Il test viene comunemente impiegato per rilevare varie fonti di interferenza con la normale coagulazione del sangue. Il prolungamento del Thrombin Time può essere considerato come indicazione qualitativa di livelli anormali di fibrinogeno (alti o bassi) oppure della presenza di sostanze interferenti come gli FDP o l'eparina. La valutazione quantitativa delle possibili cause di un Thrombin Time prolungato deve essere eseguita sotto forma di studi di follow-up, come il dosaggio dell'aPTT o il dosaggio cromogenico per l'eparina, il fibrinogeno con metodo Clauss, le determinazioni degli FDP, la neutralizzazione dell'eparina con protamina solfato o polibrene[1], gli studi sulla miscelazione di plasma normale[2] o il dosaggio della reptilasi[3], per distinguere tra l'ipofibrinogenemia e gli effetti degli FDP.

AVVERTENZE E PRECAUZIONI

I reagenti contenuti in questo kit sono destinati esclusivamente alla diagnostica *in vitro* - NON INGERIRE. Indossare un'adeguata attrezzatura protettiva personale durante la manipolazione di tutti i componenti del kit. Per conoscere i relativi simboli precauzionali e di pericolo, laddove pertinente, fare riferimento alla dichiarazione di sicurezza del prodotto. Smaltire i componenti conformemente alle normative locali vigenti.

COMPOSIZIONE

Component	Contiene	Descrizione	Preparazione
Thrombin Time	10 x 1 mL (REF 5392H) 10 x 2 mL (REF 5392) 10 x 5 mL (REF 5377)	Ogni flacone contiene una preparazione liofilizzata di trombina bovina con tamponi e stabilizzatori. Il reagente ricostituito contiene ≤10 NIH unità/mL di trombina. Il reagente deve apparire sotto forma di tappo liofilizzato di colore bianco.	Ricostituire il reagente con il volume raccomandato di acqua distillata: 1 mL - REF 5392H 2 mL - REF 5392 5 mL - REF 5377 Lasciare riposare per 5 minuti, quindi miscelare delicatamente per inversione e trasferire in una provetta in plastica. Il reagente ricostituito deve apparire sotto forma di soluzione incolore trasparente.

Ogni kit contiene un foglio procedurale.

MATERIALI NECESSARI, MA NON IN DOTAZIONE

È possibile utilizzare qualsiasi strumento di coagulazione meccanico, opto-meccanico o foto-ottico di alta qualità in grado di eseguire il test del Thrombin Time.

CONSERVAZIONE, VITA UTILE E STABILITÀ

I reagenti non aperti sono stabili fino alla data di scadenza indicata se conservati nelle condizioni riportate sul flacone o sull'etichetta del kit.

Thrombin Time	Il reagente ricostituito va conservato ad una temperatura di +2 – +8°C e resta stabile per 14 giorni oppure a -20°C per 1 mese. Il reagente ricostituito può essere inoltre conservato all'interno di uno strumento foto-ottico Sysmex CA1500 per max. 7 giorni.

RACCOLTA E PREPARAZIONE DEI CAMPIONI

Nel corso dell'intera procedura è necessario utilizzare plastica o vetro siliconizzato. Il sangue (9 parti) deve essere raccolto in sodio citrato al 3,2% o al 3,8% come anticoagulante (1 parte). Separare il plasma in seguito a centrifugazione a 1500 x g per 15 minuti. Il plasma deve essere conservato a +2 – +8°C o +18 – +24°C. I test devono essere completati entro 4 ore dalla raccolta dei campioni; in alternativa, il plasma può essere conservato congelato a -20°C per 2 settimane o a -70°C per 6 mese. Decongelare rapidamente a +37°C prima di eseguire i test. Non conservare a +37°C per oltre 5 minuti[4].

PROCEDURA

1. Raccogliere e preparare il campione di sangue conformemente alle istruzioni riportate nel paragrafo "Raccolta dei campioni e preparazione".
2. Ricostituire il plasma di controllo seguendo le indicazioni fornite nell'inserto contenuto nella confezione di ciascun controllo.
3. Preparare il reagente da utilizzare nella procedura conformemente alle istruzioni di ricostituzione riportate nel paragrafo "Composizione".
4. Eseguire tutti i test per 2 volte. Calcolare il tempo di coagulazione medio per le ripetizioni dei test con un'approssimazione a 0,1 secondi. I singoli valori devono rientrare in una tolleranza di ±5% rispetto al valore medio.

Metodo Manuale

1. Pipettare 0,2 mL di plasma del paziente o di plasma di controllo in una provetta di reazione.
2. Incubare a +37°C per 3 minuti.
3. Pipettare 0,1 mL di reagente per la determinazione del Thrombin Time nella provetta di reazione contenente il plasma del paziente o il plasma di controllo, azionando contemporaneamente un timer.
4. Registrare il tempo di formazione del coagulo con un'approssimazione a 0,1 secondI.

Metodo Automatico

Fare riferimento al manuale utente dello strumento appropriato per istruzioni dettagliate oppure contattare Helena Biosciences Europe per le note applicative specifiche dello strumento.

INTERPRETAZIONE DEI RISULTATI

I risultati relativi al test del Thrombin Time devono essere indicati con un'approssimazione a 0,1 secondi. Il range normale (solitamente pari alla media ± 2 deviazioni standard) deve essere stabilito da ogni singolo laboratorio. I risultati che fuoriescono dal range normale devono essere considerati come anomali; si raccomanda pertanto di eseguire test di follow-up.

LIMITAZIONI

I valori previsti per il test di determinazione del Thrombin Time possono variare da un laboratorio all'altro in funzione della tecnica utilizzata. Il metodo di rilevamento del coagulo, la temperatura, il pH, la tecnica di raccolta, il tipo di anticoagulante, il tempo e il metodo di conservazione dei campioni sono elementi di estrema importanza. La raccolta dei campioni di plasma e le condizioni di conservazione devono essere standardizzate e controllate con particolare attenzione. I risultati imprevisti devono essere confermati eseguendo ulteriori test.
Oltre alla causa dei tempi di trombina prolungati indicata, secondo un rapporto molti pazienti affetti da amiloidosi sistemica con complicanze emorragiche possono presentare un inibitore circolante, che prolunga il Thrombin Time[5]. Inoltre, i livelli terapeutici di eparina possono eliminare completamente la coagulazione nel test del Thrombin Time, sebbene la neutralizzazione con protamina solfato o polibrene dovrebbe correggere il Thrombin Time[1].

CONTROLLO QUALITÀ

Ogni laboratorio deve definire un programma di controllo qualità. I plasmi di controllo normali e anormali devono essere testati prima di ogni lotto di campioni di pazienti, per garantire un livello prestazionale soddisfacente sia per quanto riguarda lo strumento che per l'operatore. Qualora i controlli non funzionassero come previsto, i risultati relativi ai pazienti dovranno essere considerati non validi.
Helena Biosciences Europe mette a disposizione i seguenti controlli utilizzabili con questo prodotto:

REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA

VALORI DI RIFERIMENTO

Per la sicurezza del paziente, è necessario che il sistema sia monitorato continuamente da un operatore qualificato. Per tale motivo ciascun laboratorio dovrà elaborare i propri range di riferimento.

CARATTERISTICHE PRESTAZIONALI

Le seguenti caratteristiche prestazionali sono state determinate da Helena Biosciences Europe o dai propri rappresentanti:

Precisione

		Precisione intra-dosaggio		Precisione tra i dosaggi	
Campione	*n*	*Formazione del coagulo (secondi)*	*CV (%)*	*Formazione del coagulo (secondi)*	*CV (%)*
Normali	10	12,5	1,43	12,5	1,29

BIBLIOGRAFIA

1. Laposata *et al.*The Clinical Haemostasis Handbook, Yearbook Medical Publishers Inc., p219, 1989
2. Thompson AR and Harker LA. Manual of Haemostasis and Thrombosis. 3rd Ed., F.A. Davis Co., p62, 1983
3. DeMott WR. Laboratory Test Handbook, 2nd Ed., Jacobs D.S. et al Eds., Lexi-Comp Inc., p432-433, 1990.
4. Clinical and Laboratory Standards Institute (2008) Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Haemostasis Assays: Approved Guideline, 5th edn. CLSI: H21-A5
5. Gastineau DA *et al.* (1991) Inhibitor of the Thrombin Time in Systemic Amyloidosis: A Common Coagulation Abnormality, *Blood*, **77:**2637-40

Thrombin Time
Instrucciones de uso

es

USO PREVISTO

El uso previsto del kit Thrombin Time es realizar ensayos de hemostasia basados en la coagulación.

El reactivo de Thrombin Time contiene trombina bovina. El reactivo puede usarse manualmente o en instrumentos semiautomatizados o automatizados. La prueba se aplica con frecuencia para detectar diversas interferencias con la coagulación sanguínea normal. La prolongación del Thrombin Time puede tomarse como una indicación cualitativa de niveles anormales de fibrinógeno (altos o bajos) o la presencia de sustancias que interfieren como los PDF o la heparina. La evaluación cuantitativa de las posibles causas de Thrombin Time prolongado debe realizarse como estudios de seguimiento, como el TTPa o la valoración cromogénica de la heparina, el fibrinógeno de Clauss, las determinaciones de los PDF, la neutralización de la heparina por sulfato de protamina o polibreno[1], los estudios de mezcla de plasma normal[2] o el ensayo de la reptilasa[3] para distinguir entre la hipofibrinogenemia y los efectos de los PDF.

ADVERTENCIAS Y PRECAUCIONES

Los reactivos que contiene este kit son sólo para uso de diagnóstico *in vitro*: NO INGERIR. Lleve el equipo de protección personal adecuado cuando utilice todos los componentes del kit. Consulte la declaración de seguridad del producto para saber más sobre las indicaciones adecuadas de advertencia y riesgo. Desechar los componentes de conformidad con las normativas locales.

COMPOSICIÓN

Component	Contiene	Descripción	Preparación
Thrombin Time	10 x 1 mL (REF 5392H) 10 x 2 mL (REF 5392) 10 x 5 mL (REF 5377)	Cada vial contiene un preparado liofilizado de trombina bovina con tampones y estabilizadores. El reactivo reconstituido contiene ≤10 unidades del NIH/ mL de trombina. El reactivo debe ser un taco liofilizado blanco.	Reconstituya el reactivo con el volumen recomendado de agua destilada: 1 mL - REF 5392H 2 mL - REF 5392 5 mL - REF 5377 Deje que reposen durante 5 minutos y luego, mezcle suavemente mediante inversión y transfiera a un tubo de plástico. El reactivo reconstituido debe ser una solución transparente, incolora.

Cada kit contiene instrucciones de uso.

ARTÍCULOS NECESARIOS NO SUMINISTRADOS

Puede usarse cualquier instrumento de coagulación mecánico opto-mecánico o foto-óptico capaz de realizar pruebas de Thrombin Time.

ALMACENAMIENTO, CADUCIDAD Y ESTABILIDAD

Los reactivos no abiertos son estables hasta la fecha de caducidad indicada cuando se conservan en las condiciones indicadas en el vial o en la etiqueta del kit

Thrombin Time	El reactivo reconstituido debe almacenarse a +2 – +8°C y se mantiene estable durante 14 días o a -20 C durante 1 mes. El reactivo reconstituido también puede almacenarse en un instrumento fotoóptico Sysmex CA1500 durante un máximo de 7 días.

RECOGIDA Y PREPARACIÓN DE LAS MUESTRAS

Debe usarse siempre plástico o vidrio siliconizado. Debe recogerse sangre (9 partes) en el anticoagulante citrato sódico al 3,2% o al 3,8% (1 parte). Separar el plasma después de la centrifugación a 1500 x g durante 15 minutos. El plasma debe conservarse a +2 – +8°C o +18 – +24°C. Las pruebas deberían terminarse en 4 horas desde la recogida de las muestras o el plasma puede conservarse congelado a -20°C durante 2 semanas o -70°C durante 6 mes. Descongelar rápidamente a +37°C antes de realizar la prueba. No conservar a +37°C durante más de 5 minutos[4].

PROCEDIMIENTO

1. Recoja y prepare la muestra de sangre de acuerdo con las instrucciones esbozadas en "Recogida y preparación de muestras".
2. Reconstituya el plasma control de acuerdo con el prospecto incluido con cada control.
3. Prepare el reactivo para su uso en el procedimiento de acuerdo con las instrucciones de reconstitución en la sección "Composición".
4. Realice todas las pruebas por duplicado. Calcule el tiempo de coagulación medio de las determinaciones duplicadas hasta una exactitud de 0,1 segundos. Los valores individuales deben estar dentro de ±5% del valor medio.

Método Manual

1. Pipetee 0,2 mL del plasma del paciente o el plasma control en un tubo de reacción.
2. Incube a +37°C durante 3 minutos.
3. Pipetee 0,1 mL de reactivo de Thrombin Time en el tubo de reacción que contiene plasma del paciente o control mientras se pone en marcha simultáneamente un temporizador.
4. Registre el tiempo hasta la formación del coágulo procurando afinar en la décima de segundo más próxima.

Método Automatizado

Consulte el manual del usuario del instrumento adecuado para instrucciones detalladas o póngase en contacto con Helena Biosciences Europe para notas de aplicación específicas del instrumento.

INTERPRETACIÓN DE LOS RESULTADOS

Los resultados de la prueba de Thrombin Time deben comunicarse en los 0,1 segundos más próximos. Cada laboratorio debe establecer el intervalo normal (habitualmente, la media ±2 desviaciones estándar). Los resultados fuera del intervalo normal deben considerarse anormales y deben realizarse pruebas de seguimiento.

LIMITACIONES

Los valores esperados para la prueba del Thrombin Time variarán de un laboratorio a otro dependiendo de la técnica usada. El método de detección de los coágulos, la temperatura, el pH, la técnica de recogida, el tipo de anticoagulante y el tiempo y el método de almacenamiento de la muestra son todos muy importantes. Las condiciones de recogida y conservación de las muestras de plasma deben estandarizarse y controlarse cuidadosamente. Los resultados inesperados deben confirmarse mediante pruebas adicionales.
Además de la causa de alargamiento de los Tiempos de Coagulación de la trombina indicada, un informe ha sugerido que muchos pacientes con amiloidosis sistémica con complicaciones de sangrado pueden tener un inhibidor circulante que prolonga el Thrombin Time[5]. Además, los niveles terapéuticos de hepatina pueden abolir por completo la coagulación en la prueba del Thrombin Time, aunque la neutralización con sulfato de protamina o polibreno debe corregir el Thrombin Time[1].

CONTROL DE CALIDAD

Cada laboratorio debe establecer un programa de control de calidad. Los controles normales y anormales deben estudiarse antes de cada lote de muestras del paciente, para asegurar un funcionamiento adecuado del instrumento y el operador. Si los controles no se realizan como se esperaba, los resultados del paciente deben considerarse inválidos.
Helena Biosciences Europe suministra los siguientes controles disponibles para usar con este producto:

REF 5186	Routine Control N
REF 5187	Routine Control A
REF 5183	Routine Control SA

VALORES DE REFERENCIA

Los valores de referencia pueden variar entre los laboratorios dependiendo de las técnicas y sistemas usados. Por esta razón, cada laboratorio debe establecer sus propios intervalos de referencia.

CARACTERÍSTICAS FUNCIONALES

Las siguientes características de rendimiento han sido determinadas por Helena Biosciences Europe o sus representantes:

Precisión

		Precisión intra-ensayo		Precisión inter-ensayo	
Muestra	*n*	*Formación del coágulo (segundo)*	*CV (%)*	*Formación del coágulo (segundo)*	*CV (%)*
Normales	10	12,5	1,43	12,5	1,29

BIBLIOGRAFÍA

1. Laposata *et al.*The Clinical Haemostasis Handbook, Yearbook Medical Publishers Inc., p219, 1989
2. Thompson AR and Harker LA. Manual of Haemostasis and Thrombosis. 3rd Ed., F.A. Davis Co., p62, 1983
3. DeMott WR. Laboratory Test Handbook, 2nd Ed., Jacobs D.S. et al Eds., Lexi-Comp Inc., p432-433, 1990.
4. Clinical and Laboratory Standards Institute (2008) Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Haemostasis Assays: Approved Guideline, 5th edn. CLSI: H21-A5
5. Gastineau DA *et al.* (1991) Inhibitor of the Thrombin Time in Systemic Amyloidosis: A Common Coagulation Abnormality, *Blood*, **77:**2637-40

Тест-система "Тромбиновое время"
инструкция

ru

НАЗНАЧЕНИЕ

Комплект «Тромбиновое время» предназначен для выполнения анализов гемостаза на основе кровяного сгустка.

Тест-система «Тромбиновое время» содержит бычий тромбин. Реагент может использоваться в ручном режиме исследования, в полуавтоматическом и автоматическом приборе. Тест-система обычно применяется для определения различных источников влияния на нормальную свертываемость крови. Увеличение времени свертывания тромбина может считаться качественным показателем атипичных уровней фибриногена (высокого или низкого) или наличия интерферирующих веществ, таких как продукты распада фибрина или гепарин. Количественная оценка возможных случаев увеличенного времени свертывания тромбина должна быть выполнена в качестве последующих исследований, таких как определение АЧТВ или хромогенное исследование на гепарин, определение фибриногена по Клауссу, определение продуктов распада фибрина, нейтрализация гепарина сульфатом протамина или полибреном[1], исследования на смешивание нормальной плазмы[2] или рептилазное исследование[3] для установления различия между гипофибриногенемией и действием продуктов распада фибрина.

ПРЕДУПРЕЖДЕНИЯ И МЕРЫ ПРЕДОСТОРОЖНОСТИ

Содержащиеся в данном наборе реагенты предназначены только для *in vitro* диагностики– НЕ ПРИНИМАТЬ ВНУТРЬ! При работе со всеми компонентами набора использовать соответствующие средства индивидуальной защиты. В случае необходимости см. свидетельство о безопасности изделия для ознакомления с соответствующими описаниями опасного воздействия и сведениями о мерах предосторожности. Удаление компонентов в отходы производите в соответствии с местными правилами.

СОСТАВ

Состав	Содержимое набора	Описание	Приготовление
Тест-система «Тромбиновое время»	10 х 1 мл (Кат. № 5392H) 10 х 2 мл (Кат. № 5392) 10 х 5 мл (Кат. № 5377)	Каждый флакон содержит лиофилизированный препарат из бычьего тромбина с буферами и стабилизаторами. Восстановленный реагент содержит ≤10 NIH ЕД/мл тромбина. Реагентом должна быть лиофилизированная тромбоцитная пробка.	Восстановите реагент с рекомендуемым объемом очищенной воды: 1 мл для - кат № 5392H 2 мл для - кат. № 5392 5 мл для - кат. № 5377 Дайте постоять 5 минут, затем осторожно перемешайте путем переворачивания и поместите в пластиковую пробирку. Восстановленный реагент должен представлять собой чистый бесцветный раствор.

В каждом наборе имеется инструкция по применению.

НЕОБХОДИМЫЕ КОМПОНЕНТЫ, НЕ ВКЛЮЧЕННЫЕ В КОМПЛЕКТ ПОСТАВКИ

Может использоваться любой высококачественный механическое, оптико-механического или фотооптический прибор, который может проверять время свертывания тромбина.

ХРАНЕНИЕ, СРОК ГОДНОСТИ И УСТОЙЧИВОСТЬ

Невскрытые флаконы остаются стабильными до истечения срока годности при хранении в условиях, указанных на флаконе или этикетке набора.

Тест-система «Тромбиновое время»	Помещенный на хранение восстановленный реагент сохраняет стабильность в течение 14 дней при температуре от +2 – +8°C и в течение 1 месяца при -20°C. Срок хранения реагента в фотооптическом приборе Sysmex CA1500 не должен превышать 7 дней.

ОТБОР И ПОДГОТОВКА ОБРАЗЦОВ

Для работы следует использовать только пластиковые или силиконизированные стеклянные пробирки. Кровь (9 частей) забирается в пробирку с антикоагулянтом цитрата натрия 3,2% или 3,8% (1 часть). Отделите плазму после центрифугирования при 1500 g в течение 15 минут. Плазму следует хранить при температуре +2 – +8°C или +18 – +24°C. Исследование должно быть завершено в течение 4 часов после забора образцов, либо плазму можно заморозить при -20°C и хранить 2 недели, а при замораживании при -70°C она может храниться в течение 6 месяцев. Размораживайте быстро при +37°C перед проведением исследования. Не держите более 5 минут при температуре +37°C[4].

ПРОЦЕДУРА

1. Проведите забор и подготовку пробы крови в соответствии с указаниями документа ЗАБОР И ПОДГОТОВКА ОБРАЗЦОВ.
2. Восстановите контрольную плазму в соответствии с приложенным листком-вкладышем.
3. Подготовьте реагент к использованию в порядке, указанном в инструкции по восстановлению в разделе СОСТАВ.
4. Проведите все исследования дважды. Рассчитайте среднее время свертывания каждого из двух дублирующих исследований образца до ближайших 0.1 секунд. Индивидуальные показатели должны быть в колебаться пределах ±5% от среднего значения.

Ручной Метод

1. С помощью пипетки поместите 0,2 мл плазмы пациента или контрольной плазмы в реакционную пробирку.
2. Инкубируйте 3 минуты при температуре +37°C.
3. С помощью пипетки поместите 0,1 мл тест-системы «Тромбиновое время» в реакционную пробирку, содержащую плазму пациента или контрольную плазму, и одновременно включите таймер.
4. Зафиксируйте время, потребовавшееся на формирование тромбов до ближайшей 0,1 секунды.

Автоматизированный Метод

Обратитесь к соответствующей инструкции по эксплуатации прибора за подробной информацией или обратитесь в компанию "Хелена Байосайенсес Европ" за получением справочной информации применительно к конкретному прибору.

ИНТЕРПРЕТАЦИЯ РЕЗУЛЬТАТОВ

Результаты определения тромбинового времени должны указываться до ближайшей 0,1 секунды. Нормальный диапазон (обычно средний ±2 стандартные отклонения) должен устанавливаться для каждой лаборатории. Результаты, выходящие за значения нормального диапазона должны считаться атипичными и должно проводиться последующее исследование.

ОГРАНИЧЕНИЯ

Ожидаемые результаты исследования на тромбиновое время будут различными в разных лабораториях в зависимости от используемого метода. Метод клоттингового определения, температура, pH, техника забора, тип антикоагулянта, время и способ хранения образца очень важны. Забор образца плазмы и условия хранения должны быть стандартизованы и тщательно контролироваться. Непредвиденные результаты должны быть подтверждены дополнительными тестами.
Также как и для указанного случая увеличенного тромбинового времени, в отчете указывается, что многие пациенты с системным амилоидозом, осложненным кровотечениями, могут иметь циркулирующий ингибитор, который увеличивает тромбиновое время[5]. Также терапевтические дозы гепарина могут полностью прекратить свертывание в тесте на тромбиновое время, хотя нейтрализация сульфатом протамина или полибреном должна скорректировать тромбиновое время[1].

КОНТРОЛЬ КАЧЕСТВА

Каждая лаборатория должна создать программу контроля качества. Нормальная контрольная плазма и контрольная плазма с отклонениями должны тестироваться перед каждой партией образцов плазмы пациентов для обеспечения правильной работы прибора и лаборанта. Если контрольные образцы не дают ожидаемых результатов, результаты анализа образцов пациентов считаются недействительными.
Компания "Хелена Байосайенсес Европ" предоставляет следующие контрольные образцы для использования с данным продуктом:

Кат. № 5186	Контроль качества, норма
Кат. № 5187	Контроль качества, умеренно выраженная патология
Кат. № 5183	Контроль качества, высокая патология

НОРМАЛЬНЫЕ ПОКАЗАТЕЛИ

Контрольные значения могут быть различными в разных лабораториях, в зависимости от используемых методов и систем. В связи с этим каждая лаборатория должна установить собственные показатели контрольных диапазонов.

ЭКСПЛУАТАЦИОННЫЕ ХАРАКТЕРИСТИКИ

Следующие рабочие характеристики были определены компанией "Хелена Байосайенсес Европ" или ее представителями:

Изучение повторяемости

		Внутрианалитическая сходимость		Внутрианалитическая сходимость	
Образец	*Число образцов*	*Время свертывания (секунды)*	*CV (%)*	*Время свертывания (секунды)*	*CV (%)*
нормальным	10	12,5	1,43	12,5	1,29

ЛИТЕРАТУРА

1. Laposata *et al.*The Clinical Haemostasis Handbook, Yearbook Medical Publishers Inc., p219, 1989
2. Thompson AR and Harker LA. Manual of Haemostasis and Thrombosis. 3rd Ed., F.A. Davis Co., p62, 1983
3. DeMott WR. Laboratory Test Handbook, 2nd Ed., Jacobs D.S. et al Eds., Lexi-Comp Inc., p432-433, 1990.
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5. Gastineau DA *et al.* (1991) Inhibitor of the Thrombin Time in Systemic Amyloidosis: A Common Coagulation Abnormality, *Blood*, **77:**2637-40

Declaration of Conformity

HL-7-0137DC DOI 2015/07 (7)

In Application of the Council Directive 98/79/EC on the approximation of the laws of the Member States relating to *In Vitro* Diagnostic Medical Devices & CE marking.

Declaration of conformance to applicable sections of Annex I - Essential Requirements and Annex III (EC Declaration of Conformity) imposed by sections 2 to 5. The below listed products are not classified under Annex II Lists A or B. Access to the appropriate technical files will be made available to the appropriate body in the event this is required.

Product Code	**Description**	**GMDN Classification Code**
5186	Routine Control N	30590

I, the undersigned declare that the devices registered against the above GMDN Classification Code conforms to the said Directives.

Full Name: M.J. Stephenson Title: Managing Director

Signed: Date: 28 Jul 2015

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Declaration of Conformity

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HL-7-0138DC DOI 2015/07 (7)

In Application of the Council Directive 98/79/EC on the approximation of the laws of the Member States relating to *In Vitro* Diagnostic Medical Devices & CE marking.

Declaration of conformance to applicable sections of Annex I - Essential Requirements and Annex III (EC Declaration of Conformity) imposed by sections 2 to 5. The below listed products are not classified under Annex II Lists A or B. Access to the appropriate technical files will be made available to the appropriate body in the event this is required.

Product Code	**Description**	**GMDN Classification Code**
5187	Routine Control A	30590

I, the undersigned declare that the devices registered against the above GMDN Classification Code conforms to the said Directives.

Full Name: M.J. Stephenson

Title: Managing Director

Signed: Michael Stephenson

Date: 28 Jul 2015

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Declaration of Conformity

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HL-7-0135DC DOI 2015/07 (7)

In Application of the Council Directive 98/79/EC on the approximation of the laws of the Member States relating to *In Vitro* Diagnostic Medical Devices & CE marking.

Declaration of conformance to applicable sections of Annex I - Essential Requirements and Annex III (EC Declaration of Conformity) imposed by sections 2 to 5. The below listed products are not classified under Annex II Lists A or B. Access to the appropriate technical files will be made available to the appropriate body in the event this is required.

Product Code	**Description**	**GMDN Classification Code**
5183	Routine Control SA	30590

I, the undersigned declare that the devices registered against the above GMDN Classification Code conforms to the said Directives.

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Coagulation Control Plasmas

REF 5186 Routine Control N
REF 5187 Routine Control A
REF 5183 Routine Control SA
REF 5482 Routine Coagulation Control Set

IVD

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HL-2-0482P 2016/01 (16)

Coagulation Control Plasmas
Instructions for use

en

INTENDED PURPOSE

The Coagulation Control Plasmas kit is intended for use as a quality control material.

Routine Control N, Routine Control A and Routine Control SA are for use as normal, moderately prolonged and markedly prolonged controls for PT and aPTT assays. They are also assayed for Fibrinogen, TCT and ATIII, and are prepared from normal human plasma.

WARNINGS AND PRECAUTIONS

The reagents contained in this kit are for *in vitro* diagnostic use only – DO NOT INGEST. Wear appropriate personal protective equipment when handling all kit components. Refer to the product safety declaration for the link to appropriate hazard and precautionary statements where applicable. Dispose of components in accordance with local regulations.

Blood products have been screened and found negative (unless otherwise stated on the kit box or vial) for the presence of:
Hepatitis B Antigen (HbsAg)
HIV 1 antibody HIV 2 antibody
HCV antibody
However they should be handled with the same precautions as a human patient sample.

COMPOSITION

REF	Component	Content	Description
5186	Routine Control - N	10 x 1 mL	Prepared from pooled normal plasma.
5187	Routine Control - A	10 x 1 mL	Prepared from adsorbed human plasma.
5183	Routine Control - SA	10 x 1 mL	Prepared from adsorbed human plasma.
5482	Routine Coagulation Control Set:		
	Routine Control - N	4 x 1 mL	
	Routine Control - A	3 x 1 mL	
	Routine Control - SA	3 x 1 mL	

Each kit contains instructions for use.
Each kit contains lot specific reference values insert.

Each vial contains 1 mL of buffered, lyophilised human plasma.
Preparation: Reconstitute each vial of the appropriate control with 1 mL of distilled or deionised water. Swirl gently. Allow to stand for 10 minutes for complete dissolution and mix well before use.

ITEMS REQUIRED BUT NOT PROVIDED

Coagulation Control Plasmas may be used when performing tests on any mechanical or photo-optical coagulation instrument in conjunction with all suitable, commercial reagents.

STORAGE, SHELF-LIFE AND STABILITY

Unopened vials are stable until the given expiry date when stored under conditions indicated on the vial or kit label. The reconstituted controls are stable for 8 hours when kept at +2 – +8°C or 4 weeks at -20°C when flash frozen. Keep covered.

SAMPLE COLLECTION AND PREPARATION

Not applicable.

PROCEDURE

Each control should be treated in the same manner as the unknown specimen in accordance with the instructions outlined in each particular test protocol.

INTERPRETATION OF RESULTS

Routine Control N should give values within the laboratory normal range for PT, aPTT and fibrinogen assays. Routine Control A and Routine Control SA have been standardised to give prolonged and markedly prolonged PT and aPTT times respectively. Lot and instrument specific expected values are provided with each pack of controls.

LIMITATIONS

The results obtained with Coagulation Control Plasmas depend on several factors strongly associated with instrumentation, types of reagents, deficient substrates and laboratory to laboratory variations[1,2,3]. Each laboratory should establish an expected range for the particular instrument-reagent system.

QUALITY CONTROL

Each laboratory should establish a quality control program. Normal and abnormal control plasmas should be tested prior to each batch of patient samples, to ensure satisfactory instrument and operator performance. If controls do not perform as expected, patient results should be considered invalid.

REFERENCE VALUES

Reference values can vary between laboratories depending on the techniques and systems in use. For this reason each laboratory should establish its own reference ranges.

PERFORMANCE CHARACTERISTICS

The following performance characteristics have been determined by Helena Biosciences Europe or their representatives using an opto-mechanical coagulation instrument. Each laboratory should establish its own performance data.

Reproducibility

		Intra-assay precision	
Sample	*n*	*aPTT CV (%)*	*PT CV (%)*
Routine Control N	5	2.83	1.01
Routine Control A	5	2.76	1.71
Routine Control SA	5	1.72	1.03

BIBLIOGRAPHY

1. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology*, **37:**559-568.
2. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP*, **55:**561-564.
3. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP*, **59:**231-235.

Plasmas de contrôle de coagulation
Fiche technique

fr

UTILISATION

Le kit Coagulation Control Plasmas est destiné à être utilisé comme produit de contrôle qualité.

Les contrôles Routine Control N, Routine Control A et Routine Control SA servent de témoins normal, modérément prolongé et nettement prolongé dans les déterminations du TP et du TCA. Le fibrinogène, la TCT et l'ATIII ont été dosés et ils sont préparés à partir de plasma humain normal.

AVERTISSEMENTS ET PRÉCAUTIONS

Les réactifs du kit sont à usage diagnostique *in vitro* uniquement – NE PAS INGÉRER. Porter un équipement de protection individuelle approprié lors de la manipulation de tous les composants du kit. Consulter la fiche de données de sécurité du produit pour obtenir le lien vers les phrases de risque et les conseils de prudence le cas échéant. Éliminer les composants conformément aux églementations locales.

Un dépistage des produits sanguins a été réalisé et a donné un résultat négatif (sauf indication contraire sur la boîte du kit ou sur le flacon) quant à la présence de :
Antigène de l'hépatite B (AgHBs)
Anticorps anti-VIH 1
Anticorps anti-VIH 2
Anticorps anti-VHC
Cependant, ils doivent être manipulés avec les mêmes précautions que celles prises pour les échantillons patients humains.

COMPOSITION

REF	Composant	Contient	Description
5186	Routine Control - N	10 x 1 mL	Préparé à partir d'un pool de plasma normal.
5187	Routine Control - A	10 x 1 mL	Préparés à partir de plasma humain adsorbé.
5183	Routine Control - SA	10 x 1 mL	Préparés à partir de plasma humain adsorbé.
5482	Routine Coagulation Control Set:		
	Routine Control - N	4 x 1 mL	
	Routine Control - A	3 x 1 mL	
	Routine Control - SA	3 x 1 mL	

Chaque kit contient une fiche technique.
Chaque kit contient valeurs de référence spécifiques du lot.

Chaque flacon contient 1 mL de plasma humain tamponné lyophilisé.
Préparation: Reconstituer chaque flacon du contrôle approprié avec 1 mL d'eau distillée ou désionisée. Agiter doucement. Attendre 10 minutes jusqu'à dissolution totale et bien mélanger avant d'utiliser.

MATÉRIEL NÉCESSAIRE NON FOURNI

Le Coagulation Control Plasmas peut être utilisé dans les analyses réalisées sur des instruments de coagulation mécanique ou photo-optique avec les réactifs appropriés vendus dans le commerce.

CONSERVATION, DURÉE DE VIE UTILE ET STABILITÉ

Les flacons non ouverts sont stables jusqu'à la date de péremption indiquée s'ils sont conservés dans les conditions indiquées sur l'étiquette du kit ou du flacon. Une fois reconstitués, les contrôles sont stables 8 heures entre +2 – +8°C ou 4 semaines à -20 °C en cas de congélation instantanée. Couvrir le produit.

PRÉLÈVEMENT ET PRÉPARATION DES ÉCHANTILLONS

Non applicable.

PROCÉDURE

Chaque contrôle doit être traité de la même manière que l'échantillon à analyser en observant les instructions de chaque protocole spécifique.

INTERPRÉTATION DES RÉSULTATS

Le Routine Control N doit donner des valeurs se situant dans la plage normale du laboratoire pour le TP, le TCA et le fibrinogène. Le Routine Control A et le Routine Control SA ont été standardisés pour donner des temps TP et TCA prolongés et très prolongés respectivement. Les valeurs prévues spécifiques du lot et de l'instrument sont fournies avec chaque kit de contrôles.

LIMITES

Les résultats obtenus avec le Coagulation Control Plasmas dépendent de plusieurs facteurs fortement corrélés avec l'instrument, les types de réactifs, les substrats carencés et les variations inter-laboratoires[1,2,3]. Le laboratoire doit déterminer une plage prévue pour chaque système instrument-réactif.

CONTRÔLE QUALITÉ

Chaque laboratoire doit établir un programme de contrôle qualité. Les plasmas de contrôle, normaux et anormaux, doivent être testés avant chaque lot d'échantillons patients afin de s'assurer que l'instrument et l'opérateur offrent des performances satisfaisantes. Si les contrôles ne donnent pas les résultats prévus, les résultats du patient doivent être considérés comme non valables.

VALEURS DE RÉFÉRENCE

Les valeurs de référence peuvent varier d'un laboratoire à l'autre suivant les techniques et les systèmes utilisés. C'est pour cette raison qu'il appartient à chaque laboratoire de déterminer ses propres plages de référence.

CARACTÉRISTIQUES DE PERFORMANCES

Helena Biosciences Europe ou ses mandataires ont déterminé les caractéristiques de performance suivantes en utilisant un instrument de coagulation opto-mécanique. Chaque laboratoire doit établir ses propres données de performance.

Reproductibilité

		Précision intra-série	
Échantillon	*n*	*TCA CV (%)*	*TP CV (%)*
Routine Control N	5	2.83	1.01
Routine Control A	5	2.76	1.71
Routine Control SA	5	1.72	1.03

BIBLIOGRAPHIE

1. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology*, **37:**559-568.
2. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP*, **55:**561-564.
3. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP*, **59:**231-235.

Kontrollplasma für die Gerinnung
Anleitung

de

VERWENDUNGSZWECK

Das Coagulation Control Plasmas-Kit ist für die Qualitätskontrolle vorgesehen.

Routine Control N, Routine Control A und Routine Control SA sind als normale, mäßig verzögerte und stark verzögerte Kontrollen für PT und aPTT Tests geeignet. Sie sind auch auf Fibrinogen, TZ und AT-III getestet und werden aus normalem Humanplasma hergestellt.

WARNHINWEISE UND VORSICHTSMASSNAHMEN

Die in diesem Kit enthaltenen Reagenzien sind ausschließlich für die Verwendung von *in-vitro*-Diagnosen vorgesehen. NICHT VERSCHLUCKEN. Tragen Sie beim Umgang mit sämtlichen Komponenten des Kits geeignete Schutzausrüstung. Beachten Sie gegebenenfalls die Verweise auf entsprechende Gefahren- und Vorbeugeerklärungen in der Produktsicherheitserklärung. Entsorgen Sie die Komponenten gemäß den örtlichen Vorschriften.

Die Blutprodukte wurden untersucht und sind für folgende Gene ohne Befund (soweit nicht anderweitig auf der Verpackung oder den Ampullen angegeben):
Hepatitis-B-Antikörper (HbsAg)
HIV-Antikörper 1
HIV-Antikörper 2
HCV-Antikörper
Sie sind jedoch mit den gleichen Vorkehrungen zu behandeln wie Proben von menschlichen Patienten.

ZUSAMMENSETZUNG

REF	Komponente	Inhalt	Beschreibung
5186	Routine Control - N	10 x 1 mL	Aus gepooltem Humanplasma hergestellt.
5187	Routine Control - A	10 x 1 mL	Adsorbiertem Humanplasma hergestellt.
5183	Routine Control - SA	10 x 1 mL	Adsorbiertem Humanplasma hergestellt.
5482	Routine Coagulation Control Set:		
	Routine Control - N	4 x 1 mL	
	Routine Control - A	3 x 1 mL	
	Routine Control - SA	3 x 1 mL	

Jedes Kit enthält eine Gebrauchsanweisung.
Jedes Kit enthält chargenspezifischen Referenzwerten.

Jedes Fläschchen enthält 1 mL gepuffertes, lyophilisiertes Humanplasma.
Vorbereitung: Jedes Fläschchen Kontrollplasma mit 1 mL destilliertem oder entionisiertem Wasser rekonstituieren. Leicht schwenken. Zum vollständigen Auflösen 10 Minuten stehen lassen und vor Gebrauch gut mischen.

ERFORDERLICHE, ABER NICHT MITGELIEFERTE ARTIKEL

Coagulation Control Plasmas kann in Verbindung mit allen entsprechenden kommerziellen Reagenzien bei der Durchführung von Tests an mechanischen oder lichtoptischen Koagulometern verwendet werden.

LAGERUNG, HALTBARKEIT UND STABILITÄT

Ungeöffnete Fläschchen sind unter den auf Verpackung oder Fläschchen angegebenen Lagerbedingungen bis zum aufgedruckten Verfallsdatum stabil. Rekonstituierte Kontrollen sind bei +2 – +8°C 4 Wochen stabil bzw. 4 Wochen bei -20 °C, wenn schockgefroren. Verschlossen aufbewahren.

PROBENENTNAHME UND VORBEREITUNG

Entfällt.

VORGEHENSWEISE

Jede Kontrolle sollte gemäß den Anleitungen der einzelnen Testprotokolle wie unbekannte Probe behandelt werden.

INTERPRETATION DER ERGEBNISSE

Routine Control N sollte für PT, aPTT und Fibrinogen Tests Werte im Normalbereich ergeben. Routine Control A und Routine Control SA wurden standardisiert, um verlängerte bzw. stark verlängerte PT und aPTT Zeiten zu ergeben. Chargen und Geräte spezifische Normalwerte sind in jeder Packung mit Kontrollen enthalten.

EINSCHRÄNKUNGEN

Die mit Coagulation Control Plasmas erzielten Resultate hängen von mehreren Faktoren ab, die stark mit dem Gerät, den verwendeten Reagenzien, mangelnden Substraten und Unterschieden zwischen den Labors in Verbindung stehen[1,2,3]. Jedes Labor sollte daher für jedes Geräte-Reagenzien-System einen eigenen Normalwertebereich erstellen.

QUALITÄTSKONTROLLE

Jedes Labor muss für eine eigene Qualitätskontrolle sorgen. Normale und pathologische Kontrollplasmen müssen vor jeder Testreihe mit Patientenproben getestet werden, um eine zufrieden stellende Gerätleistung und Bedienung zu gewährleisten. Liegen die Kontrollen außerhalb des Normbereichs, sind die Patientenergebnisse nicht zu verwenden.

REFERENZWERTE

Referenzwerte können je nach Technik und verwendetem System von Labor zu Labor unterschiedlich sein. Aus diesem Grund sollte jedes Labor seine eigenen Referenzwertbereiche erstellen.

LEISTUNGSMERKMALE

Die folgenden Leistungseigenschaften wurden von Helena Biosciences Europe oder in ihrem Auftrag mit einem optomechanischen Gerinnungsgerät ermittelt. Jede Labor muss seine eigenen Werte ermitteln.

Reproduzierbarkeit

		Intra-assay-Präzision	
Probe	*n*	*aPTT CV (%)*	*PT CV (%)*
Routine Control N	5	2.83	1.01
Routine Control A	5	2.76	1.71
Routine Control SA	5	1.72	1.03

LITERATURVERZEICHNIS

1. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology,* **37:**559-568.
2. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP,* **55:**561-564.
3. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP,* **59:**231-235.

Plasmi di controllo della coagulazione
Istruzioni per l'uso

it

SCOPO PREVISTO

Il kit Coagulation Control Plasmas è concepito per l'uso come materiale di controllo qualità.

Routine Control N, Routine Control A e Routine Control SA sono destinati ad essere utilizzati come controlli normali, moderatamente prolungati e marcatamente prolungati per i dosaggi di PT e aPTT. Essi vengono dosati anche per fibrinogeno, TCT e ATIII e sono preparati con plasma umano normale.

AVVERTENZE E PRECAUZIONI

I reagenti contenuti in questo kit sono destinati esclusivamente alla diagnostica *in vitro* - NON INGERIRE. Indossare un'adeguata attrezzatura protettiva personale durante la manipolazione di tutti i componenti del kit. Per conoscere i relativi simboli precauzionali e di pericolo, laddove pertinente, fare riferimento alla dichiarazione di sicurezza del prodotto. Smaltire i componenti conformemente alle normative locali vigenti.

I prodotti ematici sono stati sottoposti a screening e trovati negativi (salvo diversa indicazione sulla confezione del kit o sulla fiala) per la presenza di:
Antigene dell'epatite B (HbsAg)
Anticorpo HIV 1
Anticorpo HIV 2
Anticorpo HCV
Questi prodotti devono tuttavia essere manipolati con le stesse misure precauzionali adottate per un campione paziente umano.

COMPOSIZIONE

REF	Componente	Contiene	Descrizione
5186	Routine Control - N	10 x 1 mL	Preparato con un pool di plasma normale.
5187	Routine Control - A	10 x 1 mL	Preparati con plasma umano adsorbito.
5183	Routine Control - SA	10 x 1 mL	Preparati con plasma umano adsorbito.
5482	Routine Coagulation Control Set:		
	Routine Control - N	4 x 1 mL	
	Routine Control - A	3 x 1 mL	
	Routine Control - SA	3 x 1 mL	

Ogni kit contiene un Istruzioni per l'uso.

Ogni kit contiene un inserto recante i valori di riferimento specifici per il lotto.

Ogni flacone contiene 1 mL di plasma umano tamponato liofilizzato.

Preparazione: Ricostituire ogni flacone di controllo appropriato con 1 mL di acqua distillata o deionizzata. Agitare delicatamente. Attendere 10 minuti per consentire al prodotto di sciogliersi completamente e miscelare bene prima dell'uso.

MATERIALI NECESSARI, MA NON IN DOTAZIONE

Il Coagulation Control Plasmas può essere utilizzato durante l'esecuzione di test su qualsiasi strumento di coagulazione meccanico o foto-ottico in combinazione con tutti i reagenti idonei disponibili in commercio.

CONSERVAZIONE, VITA UTILE E STABILITÀ

Ogni riferimento a nomi e dati utilizzati negli esempi è casuale, se non specificato diversamente. I controlli ricostituiti sono stabili per 8 ore se conservati a $^{+}2$ —$^{+}8$°C oppure 4 settimane a -20ºC se congelato molto velocemente. Mantenere i prodotti coperti.

RACCOLTA E PREPARAZIONE DEI CAMPIONI

Non applicabile.

PROCEDURA

Ogni controllo deve essere trattato seguendo la stessa procedura adottata per il campione non noto, conformemente alle istruzioni riportate in ciascun protocollo di test specifico.

INTERPRETAZIONE DEI RISULTATI

Routine Control N deve fornire valori compresi nel range normale di laboratorio per i dosaggi di PT, aPTT e fibrinogeno. Routine Control A e Routine Control SA sono stati standardizzati per fornire, rispettivamente, tempi di PT e aPTT prolungati e marcatamente prolungati. I valori previsti specifici per il lotto e lo strumento vengono forniti con ciascuna confezione di controlli.

LIMITAZIONI

I risultati ottenuti con il Coagulation Control Plasmas dipendono da innumerevoli fattori, strettamente legati alla strumentazione, ai tipi di reagenti, a substrati carenti e alle variazioni dovute ai singoli laboratori[1,2,3]. Ogni laboratorio dovrà definire un range di previsione per il sistema strumento-reagente specificamente utilizzato.

CONTROLLO QUALITÀ

Ogni laboratorio deve definire un programma di controllo qualità. I plasmi di controllo normali e anormali devono essere testati prima di ogni lotto di campioni di pazienti, per garantire un livello prestazionale soddisfacente sia per quanto riguarda lo strumento che per l'operatore. Qualora i controlli non funzionassero come previsto, i risultati relativi ai pazienti dovranno essere considerati non validi.

VALORI DI RIFERIMENTO

Per la sicurezza del paziente, è necessario che il sistema sia monitorato continuamente da un operatore qualificato. Per tale motivo ciascun laboratorio dovrà elaborare i propri range di riferimento.

CARATTERISTICHE PRESTAZIONALI

Le seguenti caratteristiche prestazionali sono state determinate da Helena Biosciences Europe o dai propri rappresentanti con l'utilizzo di uno strumento di coagulazione opto-meccanico. Ciascun laboratorio dovrà pertanto elaborare i propri dati prestazionali.

Riproducibilità

		Precisione intra-dosaggio	
Campione	*n*	*aPTT CV (%)*	*PT CV (%)*
Routine Control N	5	2.83	1.01
Routine Control A	5	2.76	1.71
Routine Control SA	5	1.72	1.03

BIBLIOGRAFIA

1. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology,* **37:**559-568.
2. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP,* **55:**561-564.
3. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP,* **59:**231-235.

Plasmas de control de la coagulación
Instrucciones de uso

es

USO PREVISTO

El uso previsto del kit Coagulation Control Plasmas es como material de control de calidad.

Routine Control N, Routine Control A y Routine Control SA se usan como controles normal, moderadamente prolongado y notablemente prolongado para las valoraciones de TP y TTPa. También se valoran para fibrinógeno, TCT y ATIII y se elaboran a partir de plasma humano normal.

ADVERTENCIAS Y PRECAUCIONES

Los reactivos que contiene este kit son sólo para uso de diagnóstico *in vitro*: NO INGERIR. Lleve el equipo de protección personal adecuado cuando utilice todos los componentes del kit. Consulte la declaración de seguridad del producto para saber más sobre las indicaciones adecuadas de advertencia y riesgo. Desechar los componentes de conformidad con las normativas locales.

La sangre se ha sometido a pruebas que han resultado negativas (a menos que se indique lo contrario en la caja del kit o en el vial) de la presencia de:
Antígeno de la hepatitis B (HbsAg)
Anticuerpos del VIH 1
Anticuerpos del VIH 2
Anticuerpos del VHC
Sin embargo, deben manipularse con las mismas precauciones que una muestra de un paciente.

COMPOSICIÓN

REF	Componente	Contiene	Descripción
5186	Routine Control - N	10 x 1 mL	Elabora a partir de plasma normal de reserva.
5187	Routine Control - A	10 x 1 mL	Elaboran a partir de plasma humano adsorbido.
5183	Routine Control - SA	10 x 1 mL	Elaboran a partir de plasma humano adsorbido.
5482	Routine Coagulation Control Set:		
	Routine Control - N	4 x 1 mL	
	Routine Control - A	3 x 1 mL	
	Routine Control - SA	3 x 1 mL	

Cada kit contiene instrucciones de uso.

Cada kit contiene valores de referencia específicos insertados del lote.

Cada vial contiene 1 mL de plasma humano tamponado, liofilizado.

Preparación: Reconstituya cada vial del control adecuado con 1 mL de agua destilada o desionizada. Agite suavemente. Deje que repose durante 10 minutos para que la disolución sea completa y mezcle bien antes de su uso.

ARTÍCULOS NECESARIOS NO SUMINISTRADOS

El Coagulation Control Plasmas puede usarse cuando se realizan pruebas con cualquier instrumento de coagulación mecánica o foto-óptica junto con todos los reactivos adecuados, comerciales.

ALMACENAMIENTO, CADUCIDAD Y ESTABILIDAD

Los viales no abiertos son estables hasta la fecha de caducidad indicada cuando se conservan en las condiciones indicadas en el vial o en la etiqueta del kit. Los controles reconstituidos son estables durante 8 horas cuando se conservan a $^{+}2$ —$^{+}8$°C o durante 4 semanas a -20ºC cuando se conserva con congelación instantánea. Manténgase cubierto.

RECOGIDA Y PREPARACIÓN DE LAS MUESTRAS

No aplicable.

PROCEDIMIENTO

Cada control debe tratarse de la misma forma que la muestra desconocida, de acuerdo con las instrucciones indicadas en cada protocolo de prueba concreto.

INTERPRETACIÓN DE LOS RESULTADOS

Routine Control N debe dar valores dentro del intervalo normal de laboratorio para TP, TTPa y valoraciones de fibrinógeno. El Routine Control A y el Routine Control SA han sido estandarizados para dar tiempos de TP y TTPa prolongados y notablemente prolongados, respectivamente. Se aportan los valores esperados específicos de lote y de instrumento con cada paquete de controles.

LIMITACIONES

Los resultados obtenidos con Coagulation Control Plasmas dependen de varios factores fuertemente asociados a la instrumentación, los tipos de reactivos, sustratos deficientes y variaciones entre laboratorios[1,2,3]. Cada laboratorio debe establecer un intervalo esperado para el sistema instrumento-reactivo concreto.

CONTROL DE CALIDAD

Cada laboratorio debe establecer un programa de control de calidad. Los plasmas de control normales y anormales deben estudiarse antes de cada lote de muestras del paciente, para asegurar un funcionamiento adecuado del instrumento y el operador. Si los controles no se realizan como se esperaba, los resultados del paciente deben considerarse inválidos.

VALORES DE REFERENCIA

Los valores de referencia pueden variar entre los laboratorios dependiendo de las técnicas y sistemas usados. Por esta razón, cada laboratorio debe establecer sus propios intervalos de referencia.

CARACTERÍSTICAS FUNCIONALES

Las siguientes características de rendimiento han sido determinadas por Helena Biosciences Europe o sus representantes usando un instrumento de coagulación opto-mecánico. Cada laboratorio debe establecer sus propios datos de rendimiento.

Riproducibilità

		Precisión intra-ensayo	
Muestra	*n*	*TTPa CV (%)*	*TP CV (%)*
Routine Control N	5	2.83	1.01
Routine Control A	5	2.76	1.71
Routine Control SA	5	1.72	1.03

BIBLIOGRAFÍA

1. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology,* **37:**559-568.
2. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP,* **55:**561-564.
3. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP,* **59:**231-235.

КОНТРОЛЬНЫЕ ПЛАЗМЫ
инструкция

ru

НАЗНАЧЕНИЕ

Комплект Coagulation Control Plasmas предназначен для использования в качестве материала для контроля качества.

Контрольные плазмы: «Контроль качества, норма», «Контроль качества, высокая патология», «Контроль качества, умеренно выраженная патология» – контроли качества с нормальным, умеренно увеличенным и значительно увеличенным активированным парциальным тромбопластиновым временем (АПТВ/АЧТВ) и протромбиновым временем (ПВ). Их также можно использовать для определения количества фибриногена, тромбинового времени (ТВ) и антитромбина III (AT-III). Контроли приготовлены из человеческой плазмы практически здоровых людей.

ПРЕДУПРЕЖДЕНИЯ И МЕРЫ ПРЕДОСТОРОЖНОСТИ

Содержащиеся в данном наборе реагенты предназначены только для *in vitro* диагностики– НЕ ПРИНИМАТЬ ВНУТРЬ! При работе со всеми компонентами набора использовать соответствующие средства индивидуальной защиты. В случае необходимости см. свидетельство о безопасности изделия для ознакомления с соответствующими описаниями опасного воздействия и сведениями о мерах предосторожности. Удаление компонентов в отходы производите в соответствии с местными правилами.

Препараты крови были подвергнуты скринингу и показали отрицательный результат (если на коробке, в которую упакован комплект или на пробирке не указано иное) на:
Антиген к гепатиту В (HbsAg)
Антитела к ВИЧ 1
Антитела к ВИЧ 2
Антитела к вирусу гепатита С (HCV)
Тем не менее с ними следует обращаться, соблюдая те же меры предосторожности, что и при обращении с образцом, полученным от человека.

СОСТАВ

Кат. №	Компоненты	Состав набора	Описание
5186	Контроль качества, норма	10 x 1 мл	приготовлен из пула нормальной плазмы.
5187	Контроль качества, умеренно выраженная патология	10 x 1 мл	приготовлен из адсорбированной плазмы.
5183	Контроль качества, высокая патология	10 x 1 мл	приготовлен из адсорбированной плазмы.
5482	Контроль коагуляции, уровень П1:		
	Контроль качества, норма	4 x 1 мл	
	Контроль качества, умеренно выраженная патология	3 x 1 мл	
	Контроль качества, высокая патология	3 x 1 мл	

Каждый набор содержит инструкцию по применению.

Паспорт с референсными значениями (допустимых/контрольных пределов).

Каждый флакон содержит 1.0 мл лиофилизированной плазмы человека.

Подготовка: Разведите соответствующую контрольную плазму добавлением во флакон 1.0 мл дистиллированной или деионизированной воды. Осторожно перемешайте и оставьте при комнатной температуре в течение 10 минут. Перед использованием флакон с разведенной плазмой переворачивайте (без встряхивания).

НЕОБХОДИМЫЕ КОМПОНЕНТЫ, НЕ ВКЛЮЧЕННЫЕ В КОМПЛЕКТ ПОСТАВКИ

Контрольные плазмы могут быть использованы с анализаторами, имеющими различный метод детекции (механический, оптический и т.д.) в сочетании с реагентами различных производителей.

ХРАНЕНИЕ, СРОК ГОДНОСТИ И УСТОЙЧИВОСТЬ

Невскрытые флаконы с лиофилизированной плазмой хранятся до истечения срока годности в условиях, указанных на этикетке. Разведенная контрольная плазма в закрытом флаконе может храниться при $^{+}2$ —$^{+}8$°C или 4 недель при -20°C в случае мгновенной заморозки. в течение 8 часов.

ОТБОР И ПОДГОТОВКА ОБРАЗЦОВ

Не относится.

ПРОЦЕДУРА

Каждый образец контрольной плазмы должен анализироваться так же, как образец плазмы больного, в соответствии с инструкциями к используемому реагенту и прибору.

ИНТЕРПРЕТАЦИЯ РЕЗУЛЬТАТОВ

«Контроль качества, норма», должен показывать значения в пределах нормального диапазона используемого в лаборатории для ПВ, АПТВ и определения концентрации фибриногена. «Контроль качества, умеренно выраженная патология» и «Контроль качества, высокая патология», были стандартизированы, таким образом, чтобы показывать соответственно умеренно или выраженное увеличение АПТВ и ПВ. Номер партии и допустимые/контрольные пределы для различных коагулометров поставляются с каждым набором контролей.

ОГРАНИЧЕНИЯ

Референсные значения могут варьировать между лабораториями в зависимости от используемых реагентов, методов, коагулометров и других факторов[1,2,3]. По этой причине каждая лаборатория должна установить свои собственные нормативные параметры метода.

КОНТРОЛЬ КАЧЕСТВА

Каждая лаборатория должна установить программу контроля качества. Перед измерением каждой партии образцов пациентов необходимо протестировать нормальную и патологическую плазму, чтобы удостовериться в удовлетворительной работе оборудования и оператора. Если контрольные измерения не совпадают с ожидаемыми значениями, то измеренные данные пациентов следует считать недостоверными.

НОРМАЛЬНЫЕ ПОКАЗАТЕЛИ

Референсные значения могут варьировать между лабораториями в зависимости от используемых методов и коагулометров. По этой причине каждая лаборатория должна установить свои собственные значения.

ЭКСПЛУАТАЦИОННЫЕ ХАРАКТЕРИСТИКИ

Компания Хелена или её дистрибьюторы определили следующие ориентировочные аналитические характеристики. Каждая лаборатория должна определить свои собственные аналитические характеристики.
При использовании оптико-механического коагулометра и реагентов Хелена были определены следующие коэффициенты вариации (CV):

Воспроизводимость

		в пределах аналитической серии	
Контрольная плазма	*Кол-во образцов*	*CV (%) АПТВ*	CV (%) ПВ
Контроль качества, норма	5	2.83	1.01
Контроль качества, умеренно выраженная патология	5	2.76	1.71
Контроль качества, высокая патология	5	1.72	1.03

ЛИТЕРАТУРА

1. Kirkwood TBL *et al.* (1977) Identification of Sources of Variation in Factor VIII Assay, *British Journal of Haematology,* **37:**559-568.
2. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, *AJCP,* **55:**561-564.
3. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, *AJCP,* **59:**231-235.

helena
Biosciences Europe

16/02/2021

LETTER OF DISTRIBUTION

To Whom It May Concern,

This letter is to serve notice that GBG-MLD SRL Global Biomarketing Group, located at str. Tighina, 65, of. 607 MD2001 Chisinau, Municipiul Chisinau, Moldova is authorized to distribute the Helena Biosciences Europe Haemostasis and Electrophoresis range of products in the whole Republic of Moldova territory. As such, GBG-MLD SRL Global Biomarketing Group is responsible for promotion, support, installation, and after-sales service for Helena Biosciences Europe products.

GBG-MLD SRL Global Biomarketing Group will maintain appropriate, up-to-date and accurate records to enable the immediate recall of any Products or batches of Products. These records shall include records of deliveries to customers (including batch numbers, expiry dates, delivery date, name and address of customer, telephone number, fax number and e-mail address). These records should be kept for a minimum of one year past the expiry of the product that has been delivered.

This agreement is effective for a period of 3 years from the date of this letter, unless terminated by either party by giving 90 days notice, and can be extended through the mutual agreement of both parties based on sales performance.

Sincerely

Dmitri Alexandrov

Helena Biosciences Europe (UK) Helena Biosciences helena Biosciences Europe

International Business Manager

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Helena Laboratories (UK) Ltd trading as Helena Biosciences Europe. Registered in England: 1796207. ISO 13485

Avantor Performance Materials Poland Spółka Akcyjna
Sowińskiego 11
44-101 Gliwice
Tel. 48 32 2392 000

Declaration of conformity

Avantor Performance Materials Poland S.A. who is an established manufacturer of reagents and products for diagnostic in vitro located at:

Sowińskiego 11 Street
44-101, Gliwice
Poland

Herewith declares the following:
Reagents mentioned in attached list are labeled with J.T.Baker label, comply with the In Vitro Diagnostic Medical Devices Directive 98/79/EC and the requirements of ISO 13485 Standard.
This declaration is the basic for CE marking of the In Vitro Diagnostic Medical Devices.
The products are not part of List A and List B of Annex II of the IVD Directive 98/79/EC but are subject to self registration.
This declaration is valid for all the IVD medical devices described above and which are placed on the market by ourselves on or after the date hereof and which bear the CE marking

Gliwice, Poland

January 25, 2019

Anna Szuba

Anna Szuba
Quality Director

NIP 631-010-13-07
Numer w KRS: 0000010108
Sąd rejestrowy: Sąd Rejonowy w Gliwicach
X Wydział Gospodarczy KRS
Kapitał zakładowy 2 360 793,00 zł
Regon: 271563380

J.T.Baker product list for CE marked products

Product	Product number	Pack size
Diluents		
Diluid™ 100 Plus	3961	20 L
Diluid™ 22	2990.9010PC	10 L
Diluid™ 610	3969	20 L
	3969-00	20 L
Diluid™ Abacus	3430,9020	20 L
	3430,9010	10 L
	3430-00	20 L
Diluid™ AC 900	3996	20 L
Diluid™ APR	3476.9020PC	20 L
Diluid™ Azide free	3957	20 L
Diluid™ III Diff	3963	20 L
	3963.9010	10 L
	3963-00	20 L
Diluid™ Erma	3459,9020	20 L
	3459-00	20 L
Diluid™ Mindray	3439.9020PC	20 L
	3439-00	20 L
Diluid™ NR	3483.9020PC	20 L
	3483-00	20 L
Diluid™ Ruby	2987.9020PC	20 L
Diluid™/Sheath 3200-4000	3832,9020	20 L
Diluid™ ST1600/2000	3976	20 L
Sheath D	3495.9010PC	10 L
Sheath Fluid 3000/3500	3471.9020PC	20 L
Lyses		
CN-free Lyse Diff AC 900	3998	5 L
CyMet™ 22 CN Free	2986.0500PE	500 ml
CyMet™ 3000	3469.9010PC	10 L
CyMet™ 3200 CN free	3823,1000	1 L
CyMet™ 3500	3839.5000PC	5 L
CyMet™ 3500 CN free	3825	5 L
CyMet™ 610 CN free	3970	10 L
	3970-00	10 L
	3977	5 L
CyMet™ Abacus CN free	3431,1000	1 L
	3431-00	1 L
CyMet™ APR Baso II	3479.1000PE	1 L
CyMet™ APR CN free	3417.0500PE	500 ml
CyMet™ APR EO	3478.1000PE	1 L
CyMet™ ASA	2950.2500PE	2.5 L
CyMet™ ASB	2951.0500PE	500 ml
CyMet™ AS CN free	2952.9010PC	10 L
CyMet™ BS3 CN free	2982.0500PE	500 ml
CyMet™ III Diff	3968	1 L
	3968-00	500 ml
CyMet™ III Diff CN free	3511,1000	1 L
	3511-00	5 L
CyMet™ Erma	3416-00	500 ml
	3416,0500	500 ml
CyMet™ H20	3853,1000	1 L
CyMet™ KX CN Free	3425-00	500 ml
	3425,0500	500 ml
CyMet™ Micro	3852,1000	1 L
CyMet™ Micro CN free	3863,1000	1 L micros
	3863-00	1 L micros
CyMet™ Mindray	3441-00	500 ml
CyMet™ Mindray CN Free	3440.0500PE	500 ml

J.T.Baker product list for CE marked products

Product	Product number	Pack size
CyMet™ NR III	3484.1000PE	1 L
CyMet™ NR III CN Free	3486-00	1 L
	3486.1000PE	1 L
CyMet™ NR V	3485.1000PE	1 L
CyMet™ Ruby CN Free	2988.5000PC	5 L
CyMet™ ST 1600/2000 CN free	3759.5000	5 L
LeucoLyse	3475.5000PC	5 L
LeucoLyse Ruby	2989.5000PC	5 L
Cleaners		
Blanking Solution 1600/2000	3947	20 L
DetectoTerge™	3763	5 L
	3766	1 L
DetectoTerge™ BS	2970.0900PE	900 ml
ProClean™	3900	5 L
	3900-00	5 L
	3768,1000	1 L micros
ProClean™ Abacus	3432,5000	5 L
	3432.1000PE	1 L
ProClean™ CD	3902.0100PE	100 ml
ProClean™ Extra	3862,5000	5 L
	3862.9020PC	20 L
	3862-00	5 L
	3867-00	1 L micros
	3867.1000PE	1 L micros
ProClean™ Plus	3901	100 ml
Rinse Mindray	3442.5000PE	5 L
Hematology Controls		
8-Parameter Control L/N/H	3427/3428/3429	2.5 ml
	3463/3464/3465	2.5 ml
8-Parameter Control 4xN	3747	4 x 2.5 ml
8-Parameter Control 1xL+4xN+1xH	3751	6 x 2.5 ml
8-Parameter Control extended L/N/H	3633/3634/3635	2.5 ml
3-Diff Control L/N/H	3433/3434/3435	2.5 ml
	3502/3503/3504	4.5 ml
3-Diff Control extented L/N/H	3421/3422/3423	2.5 ml
CD-Diff Control L/N/H	3452/3453/3454	3.0 ml
CD-Diff Control 2xL+2xN+2xH	3838	6 x 3.0 ml
K-Diff Control L/N/H	3455/3456/3457	2.5 ml
Platelet Control- Extended value	3424	5 x 3.0 ml
WBC Reduced RBC L/H	3698/3699	3.0 ml
XE-Diff Control L/N/H	3731/3732/3733	4.5 ml
Fixatives		
Cervix Spray Fixative	3869,1200	12 x 125 ml
10% v/v Buffered Formaldehyde (4% w/v)	3933,1000	1 L
	3933.5000PC	5 L
	3933,9010	10 L
	3933,9020	20 L
	3933.1000MB	1000 L
	3933.9020PE	20 L
	3933.9010JL	10 L
	3933.9020JL	20 L
Clearing agents		
UltraClear™	3905.2500PE	2.5 L
	3905.5000PE	5 L
	3905.9010PE	10 L

J.T.Baker product list for CE marked products

Product	Product number	Pack size
Stains and Dyes		
Eosin-Y Alcoholic	3800.1000PE	1 L
	3800.2500PE	2.5 L
Giemsa	3856,1000	1 L
	3856,2500	2.5 L
	3856.9180ST	180 L
Hematoxylin er (Mayer)	3870,1000	1 L
	3870,2500	2.5 L
Hematoxylin Modified (Harris, Gill II)	3873,1000	1 L
	3873,2500	2.5 L
May-Grünwald	3855,1000	1 L
	3855,2500	2.5 L
Papanicolaou 2A	3554.1000PE	1 L
	3554.2500PE	2.5 L
Papanicolaou 2B	3555.1000PE	1 L
	3555,2500PE	2,5 L
Papanicolaou 3B	3556,1000PE	1 L
	3556.2500PE	2.5 L
Mounting media		
UltraKitt™	3921,0500	500 ml
	3921,0600	6 x 100 ml
	3921,9025ST	25 L
Mounting medium High	3882,0500	500 ml
Mounting medium Low	3883,0500	500 ml
PBS		
PBS	3059	20 L
	3059.9010PC	10 L

Declaration of CE conformity

Avantor Performance Materials B.V. reg. No. 38013066 who is an established manufacturer of Hematology- Reagents, Stains, Controls and Calibrators and products for Histopathology located at:

Teugseweg 20
7418 AM Deventer
the Netherlands

herewith declares the following:

The reagents (see attached list) are labeled with the J.T. Baker label and have the CE mark on the label where applicable. The devices comply with the In Vitro Diagnostic Medical Devices Directive 98/79/EC and the conformity assessment procedure according to Annex III.
The products are not part of List A and List B of Annex II of the IVD Directive 98/79/EC but are subject to self registration.
This declaration is valid for all the IVD medical devices described above and which are placed on the market by ourselves on or after the date hereof and which bear the CE marking.

Deventer, the Netherlands.
22 November 2011

Dr. J. Mittendorf
QA & RA Manager

J.T.Baker product list for CE marked products

Prod.no.	Product	Pack size
Reagents for diluting and lysing		
3961	Diluid™ 100 Plus	20 liter
3954	Diluid 590	20 liter
3969	Diluid 610	20 liter
3430.9010	Diluid Abacus	10 liter
3430.9020	Diluid Abacus	20 liter
3996	Diluid AC 900	20 liter
3996.9010PC	Diluid AC 900	10 liter
3476.9020PC	Diluid APR	20 liter
3957	Diluid Azide free	20 liter
3958	Diluid Azide free	10 liter
3963.9010	Diluid III Diff	10 liter
3963	Diluid III Diff	20 liter
3974	Diluid III Diff Seaccontainer	20 liter
3459.9020	Diluid Erma	20 liter
3483.9020PC	Diluid NR	20 liter
3439.9020PC	Diluid Mindray	20 liter
3832.9020	Diluid Sheath 3200-4000	20 liter
3976	Diluid ST 1600/2000	20 liter
3496.9020PC	Diluid M5	20 liter
3495.9010PC	Sheath D	10 liter
3826	Sheath Fluid 3000/3500	20 liter
3826.5000	Sheath Fluid 3000/3500	5 liter
3827.5000PC	LeucoLyse	5 liter
3998	CN-free Lyse Diff AC 900	5 liter
3744	CyMet™ 1000 CN free	5 liter
3773.5000PC	CyMet 4500 CN free	5 liter
3824	CyMet 3000	10 liter
3823.1000	CyMet 3200 CN free	1 liter
3825	CyMet 3500 CN free	5 liter
3839.5000PC	CyMet 3500	5 liter
3975	CyMet 530+ CN free	10 liter
3971	CyMet 590 CN free	5 liter
3970	CyMet 610 CN free	10 liter
3977	CyMet 610 CN free	5 liter
3918.5000	CyMet 9000 CN free	5 liter
3431.1000	CyMet Abacus CN free	1 liter
3444.1000PE	CyMet Abacus EO	1 liter
3445.1000PE	CyMet Abacus Baso	1 liter
3477.0500PE	CyMet APR CN free	500 ml
3478.1000PE	CyMet APR EO	1 liter
3479.1000PE	CyMet APR Baso II	1 liter
3755	CyMet Automated	5 liter
3757	CyMet Automated	500 ml
3780	CyMet Automated CN Free	1 liter
3460.0500	CyMet Erma	500 ml
3841.1000PE	CyMet H12 CN Free	1 liter
3842.1000	EO Reagent Autocounter	1 liter
3853.1000	CyMet H20	1 liter
3968	CyMet III Diff	1 liter
3964	CyMet III Diff	5 liter
3972.1000	CyMet III Diff CN free	1 liter
3972.5000	CyMet III Diff CN free	5 liter
3740.0500	CyMet KX CN Free	500 ml
3852.1000	CyMet Micro	1 liter
3852.0500	CyMet Micro	500 ml
3857.1000	CyMet Micro CN free	1 liter
3857.0500	CyMet Micro CN free	500 ml
3863.1000	CyMet Micro CN free	1L micros
3440.0500PE	CyMet Mindray CN Free	500 ml
3441.0500PE	CyMet Mindray	500 ml
3480.5000PC	CyMet SF Baso	5L
3481.5000PC	CyMet SF Diff 1	5L
3482.0500PE	CyMet SF Diff 2	500 ml
3775.1000	CyMet ST 1600/2000	1 liter
3759.1000	CyMet ST 1600/2000 CN free	1 liter
3759.5000	CyMet ST 1600/2000 CN free	5 liter
3788	CyMet STX/STL	1 liter
3919	CyMet STX/STL	5 liter
3484.1000PE	CyMet NR III	1 liter
3486.1000PE	CyMet NR III, CN Free	1 liter
3485.1000PE	CyMet NR V	1 liter
3497.0500PE	CyMet MH CN Free	500 ml
3489.1000PE	CyMet MBA	1 liter
3487.1000PE	CyMet MD(I)	1 liter
3488.0500PE	CyMet MD(II)	500 ml
3077	LyzerGlobin™	500 ml
3769	LyzerGlobin	6 x 15 ml
3771	LyzerGlobin PCE	6 x 15 ml
3770	LyzerGlobin II	10 x 10 ml
3850	LyzerGlobin CN free	6 x 15 ml
Cleaners		
3766.0500	DetectoTerge	500 ml
3763	DetectoTerge	5 liter
3766	DetectoTerge	1 liter
3900	ProClean™	5 liter
3768.1000	ProClean	1L micros
3867.1000PE	ProClean Extra	1L micros
3862.1000	ProClean Extra	1 liter
3862.5000	ProClean Extra	5 liter
3901	ProClean Plus	100 ml
3902.0100PE	ProClean CD	100 ml
3432.5000	ProClean Abacus	5 liter
3946	Blanking Solution Hgb	20 liter
3947	Blanking Solution 1600/2000	20 liter
3917	Hypochlorite 0.5%	1liter
3917.5000	Hypochlorite 0.5%	5 liter
3936.1000	Hypochlorite 5%	1liter
3442.5000PE	Rinse Mindray	5 liter
3915	Rinsing Solution Serono 9000	20 liter
3941.1000PE	HypoChlorite NR	1 liter
3941.5000PC	HypoChlorite NR	5 liter
3498.1000PE	ProClean MX5	1 liter
Reagents for 5-part WBC diff. on STKS and MaxM.		
3938	RBCLyse™	1 liter
3938G.1000PE	RBCLyse G	1 liter
3939	WBCStabilise™	500 ml
3492.0090	RetiCount MH	6 x 15 ml
3493.0500PE	RetiClear MHG	500 ml
3493.1000PE	RetiClear MHG	1 liter
3494.0200PE	RetiCount G	200 ml
3774	Reticount™	30 ml
3777	Reticount CD	15 x 3.5 ml

Hematology Controls		
3721/3722/3723	8 PMC Low/Normal/High	8 ml
3724/3725/3726	8 PMC Low/Normal/High	2.5 ml
3633/3634/3635	8 PMC Low/Normal/High ext	2.5 ml
3701/3702/3703	8 PMC Low/Normal/High	4.5 ml
3922/3923/3924	8 PMC L/N/H Swelab	4.5 ml
3746	8 PMC 1 x L,1 x N,1 x H	3 x 2.5 ml
3747	8 PMC 4 x Normal	4 x 2.5 ml
3748	8 PMC 4 x Normal	4 x 8 ml
3749	8 PMC 4 x Low	4 x 2.5 ml
3751	8 PMC 1x L, 4 x N, 1x H	6 x 2.5 ml
3734/3735/3736	3-Diff Control L/N/H	2.5 ml
3630/3631/3632	3-Diff Control L/N/H ext	2.5 ml
3820/3821/3822	3-Diff Control L/N/H	4.5 ml
3752	3-Diff Control 4 x Low	4 x 2.5 ml
3753	3-Diff Control 4 x Norm	4 x 2.5 ml
3754	3-Diff Control 4 x High	4 x 2.5 ml
3782/3783/3784	CA-Diff Control L/N/H	4.5 ml
3607/3608/3609	CA-Diff Control L/N/H	2.5 ml
3610/3611/3612	DIA Diff 5 Control L/N/H	4.5 ml
3731/3732/3733	XE-Diff Control L/N/H	4.5 ml
3693/3694/3695	SF-Diff Control L/N/H	4.5 ml
3613/3614/3615	BC Diff 5 Control L/N/H	4.5 ml

3684/3685/3686	ADV-Diff Control L/N/H	3.5 ml
3690/3691/3692	ADV Retic 1/2/3	4.0 ml
3828/3829/3830	CD-Diff Control	3.0 ml
3838	CD-Diff Control 2x L,N,H	6 x 3.0 ml
3687/3688	CD 4K Retic 1/2	3.0 ml
3892/3893/3894	AC-Diff Control	2.5 ml
3896/3897/3898	K-Diff Control	2.5 ml
3696/3697	WBC reduced Plt Control L/H	3.0 ml
3698/3699	WBC reduced RBC Control L/H	3.0 ml
Laser controls for Coulter MaxM, GenS and STKS		
3681/3682/3683	5D Control Low /N /H	5.0 ml
Calibration Set for Cell Analysers.		
3940	Cal Set 1	2 x 2.5 ml
3720	Platelet Control Ext. value	5 x 3 ml
Phosphate Buffered Saline.		
3059	PBS, diluting fluid for bloodgrouping	20 liter
3059.9010PC	PBS, diluting fluid for bloodgrouping	10 liter

Number	Product	Content
	Stains and Dyes	
3554.1000PE	Papanicolaou Solution 2A	1 liter
3554.2500PE	Papanicolaou Solution 2A	2.5 liter
3554.9200PE	Papanicolaou Solution 2A	200 liter
3555.1000PE	Papanicolaou Solution 2B	1 liter
3555.2500PE	Papanicolaou Solution 2B	2.5 liter
3556.1000PE	Papanicolaou Solution 3B	1 liter
3556.2500PE	Papanicolaou Solution 3B	2.5 liter
3556.9200PE	Papanicolaou Solution 3B	200 liter
3800.1000PE	Eosine-Y Alcoholic	1 liter
3800.2500PE	Eosine-Y Alcoholic	2.5liter
3801.1000PE	Eosin Y 0.5% Aqueous	1 liter
3801.2500PE	Eosin Y 0.5% Aqueous	2.5liter
3871.1000	Eosine Solution 0.2% ready to use	1 liter
3871.2500	Eosine Solution 0.2% ready to use	2.5 liter
3856.0100	Giemsa	0.1 liter
3856.0500	Giemsa	0.5 liter
3856.1000	Giemsa	1 liter
3856.2500	Giemsa	2.5 liter
3870.1000	Hematoxyline er (Mayer)	1 liter
3870.2500	Hematoxyline er (Mayer)	2.5 liter
3873.1000	Hematoxyline (Harris, Gill II)	1 liter
3873.2500	Hematoxyline (Harris, Gill II)	2.5 liter
3879.1000	Leishman	1 liter
3855.0500	May Grünwald	0.5 liter
3855.1000	May Grünwald	1 liter
3855.2500	May Grünwald	2.5 liter

3864.1000	Papanicolaou 2A OG6	1 liter
3864.2500	Papanicolaou 2A OG6	2.5 liter
3865.1000	Papanicolaou 2B Orange II	1 liter
3865.2500	Papanicolaou 2B Orange II	2,5 liter
3866.1000	Papanicolaou 3B EA 50	1 liter
3866.2500	Papanicolaou 3B EA 50	2,5 liter
3876.1000	Shorr	1 liter
3878.1000	Wright	1 liter
	Clearing agent	
3905.2500PE	UltraClear	2.5 liter
3905.5000PE	UltraClear	5 liter
3905.9010PE	UltraClear	10 liter
3905.9200	UltraClear	200 liter
	Mounting media	
3921.0500	UltraKitt	500 ml
3921.0600	UltraKitt	6 x 100 ml
	Fixatives	
3933.1000	10% v/v Buffered Formaldehyde	1 liter
3933.5000PC	10% v/v Buffered Formaldehyde	5 liter
3933.9010 (PE)	10% v/v Buffered Formaldehyde	10 liter (PE)
3933.9020 (PE)	10% v/v Buffered Formaldehyde	20 liter (PE)
3869.1200	Cervix Fixative	12 x 125 ml
3880.1000	Bouin's Fixative	1 liter
3058.9010	Immuno PBS 20x concentrated	10 liter

22 November 2011

avantor™

<u>To whom this may concern</u>

Date: March 01, 2021 Letter of Authorization

Avantor Performance Materials Poland S.A., reg. No. 0000010108 who is an established manufacturer of Hematology- Reagents, Stains, Controls and Calibrators and products for Histology located at:

Sowińskiego 11
44-101 Gliwice
Poland

herewith confirms that:

I.M Global Biomarketing Group Moldova S.R.L
Republic of Moldova
MD-2001, Chisinau
Tighina str. 65, 607 office
Tel (373 22) 549 120, 549 121
Fax (373 22) 547 373

is authorized to act as our distributor for our hematology/histology reagents and controls (Products) in Moldova
.
We declare that we will supply the Products for the needs of tenders.
We declare that we will supply the Products for tenders with warranty as per the Avantor General Conditions of Sale.

Furthermore I.M Global Biomarketing Group is duly entitled to:

- Register, promote, offer, negotiate prices and sell our Products in Moldova;
- carry out the required product training of the medical and technical personnel who will use these products.

The product specialists of I.M Global Biomarketing Group have been duly trained and are qualified for providing all services in regards to consulting, sales, maintenance and training.

In all the above activities I.M Global Biomarketing Group is acting in its own name and on its own account.
This authorization letter is valid until about 1 year after date.

Avantor Performance Materials S.A.
Poland

HvdBerg

H van den Berg,
Marketing Product Manager Diagnostics

Certificate of Completion

This is to certify

Mr. Alexei Legun

Has successfully completed

The technical maintenance training course

On

Fully Automatic Blood Cell Counter

PCE-210

Particle(Blood Cell)Counter

PCE-170/PCE-170N

Hemoglobin meter

Hb-20N

March 24, 2005

H. Shimosaka

Hiroshi Shimosaka
President
ERMA INC.

BeneSphera™

3 PART DIFFERENTIAL

Hematology Analyzer

BeneSphera™ TRAINING

Mr / ~~Ms~~ Sergiu Sorocovici

Global Biomarketing Group

str. Tighina 65, of. 607

2001 Chisinau, Moldau

has attended a 2-days training on goods manufactured or distributed by us.

April 12th – April 13th, 2012

H. J. Maas

P.O. Box 1 - 0570-687500 AVANTOR PERFORMANCE MATERIALS B.V. 7400 AA DEVENTER - Holland

Deventer, The Netherlands

Place, Date 13.04.2012

BeneSphera™ | AVANTOR™ PERFORMANCE MATERIALS

Certificate of Registration

nqa global assurance

This is to certify that the Quality Management System of:

Avantor Fluid Handling B.V.

Maidstone 50
5026 SK Tilburg
The Netherlands

applicable to:

The design, engineering, manufacturing and distribution of Single Use Systems and supporting hardware, including installation-, service- and maintenance activities for the pharmaceutical and biotech industry.

has been assessed and approved by
National Quality Assurance, U.S.A., against the provisions of:

ISO 9001:2015

Certificate Number:	16880
EAC Code:	34
Certified Since:	March 22, 2012
Valid Until:	March 19, 2024
Reissued:	March 20, 2021
Cycle Issued:	March 20, 2021

For and on behalf of NQA, USA

ANAB ACCREDITED ISO/IEC 17021 MANAGEMENT SYSTEMS CERTIFICATION BODY

This approval is subject to the company maintaining its system to the required standard, which will be monitored by NQA, USA, 289 Great Road, Suite 105, Acton, MA 01720, an accredited organization under the ANSI National Accreditation Board.

CERTIFICADO CE DE SISTEMA DE GARANTÍA DE CALIDAD TOTAL
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Certificado nº/*Certificate no*	Fecha de validez/*Date of validity*	ON nº/*NB no*
2003 12 0388 CT	**Desde/*From* 27/11/2018 Hasta/*To* 18/11/2023**	**0318**

A favor de /*In favour of:*

Fabricante/*Manufacturer*:
Nombre/*Name:* DIA. Pro Diagnostic Bioprobes S.r.l.
Dirección/*Address:* Via G. Carducci, 27 -20099- Sesto San Giovanni – Milano (Italy).
Representante autorizado ante la UE/*Authorized EU representative*:
Nombre/*Name:* Idem Dirección/*Address:* Idem

Para los productos/*For the products:*

Categoría/*Category:* Productos Sanitarios para Diagnóstico "In Vitro" / *In Vitro Diagnostic Medical Devices*
Grupo genérico/*Generic group*: Diagnóstico de enfermedades infecciosas / *Diagnostic of infectious diseases*
Tipo/*Type*: Especificados en Anexos de este Certificado/*Specified in Annexes to this Certificate.*

Elaborado en/*In the facilities:*

Dia. Pro Diagnostic Bioprobes S.r.l.
Via G. Carducci, 27 -20099- Sesto San Giovanni – Milano (Italy).

Este certificado debe ir acompañado por certificado de examen de diseño: SI
This certificate must be accompanied by design examination certificate: YES

Este certificado es consecuencia de la auditoria del Sistema Completo de Garantía de Calidad y del examen de la documentación técnica contenida en el expediente nº 2003 05 0240, y garantiza que los productos descritos cumplen los requisitos de la Directiva. / *This certificate is issued on the full quality assurance system audit, and the examination of the technical documentation contained in dossier nº 2003 05 02405, and guarantees that the described products fulfil the requirements of the Directive.*

Madrid, 26 de noviembre de 2018
DIRECTORA DE LA AGENCIA ESPAÑOLA DE MEDICAMENTOS Y PRODUCTOS SANITARIOS

agencia española de medicamentos y productos sanitarios

Fdo. Mª Jesús Lamas Díaz

CORREO ELECTRÓNICO
on0318@aemps.es
C/ CAMPEZO, 1 - EDIFICIO 8
28022 MADRID
Tel.: (+34) 902.101.322 /(+34) 91.822.59.97
Fax: (+34) 91.822.52.89

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Representante autorizado ante la UE/*Authorized EU representative:*
Nombre/*Name:* Idem Dirección/*Address:* Idem

Tipo de producto / *Device type*: Reactivos y productos reactivos, calibradores y materiales de control para el diagnóstico de enfermedades infecciosas / *Reagents, and reagent products, calibrators and control materials for diagnostic of human infectious diseases.*

Clasificación/*Classification:* Lista A, anexo II / *List A, Annex II*

1. **Reactivos y productos reactivos para la determinación, confirmación y cuantificación de marcadores de infección en muestras humanas mediante técnicas de Inmunoabsorción enzimática (ELISA)/** *Reagents and reactive products for the determination, confirmation and quantification of infection markers in human samples by Enzyme-linked immunosorbent assay (ELISA)* **[NANDO: IVD 0201; IVD 0202; IVD 0203]**

1.1. HBs Ag one

- SAG1.CE (192 tests) - SAG1.CE.96 (96 tests) - SAG1.CE.480 (480 tests) - SAG1.CE.960 (960 tests)	Descrito en el certificado / *Described in the certificate* 2003 12 0389 ED

1.2. HBs Ab

- SAB.CE (96 tests)	Descrito en el certificado / *Described in the certifícate* 2003 12 0390 ED

1.3. HBc Ab

- BCAB.CE (96 tests)	Descrito en el certificado / *Described in the certifícate* 2003 12 0391 ED

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1.4. HBc IgM

- BCM.CE (96 tests)

Descrito en el certificado / *Described in the certificate* 2004 03 0424 ED

1.5. HBe Ag & Ab

- HBE.CE (96 tests)

Descrito en el certificado / *Described in the certificate* 2004 03 0425 ED

1.6. HBs Ag Confirmation

- SCONF.CE (20 tests)
- SCONF.CE.40 (40 tests)

Descrito en el certificado / *Described in the certificate* 2006 11 0511 ED

1.7. HBs Ag one Version ULTRA

- SAG1ULTRA.CE (192 tests)
- SAG1ULTRA.CE.96 (96 tests)
- SAG1ULTRA.CE.480 (480 tests)
- SAG1ULTRA.CE.960 (960 tests)
- SAG1ULTRA.CE.DB (192 tests)

Descrito en el certificado / *Described in the certificate* 2008 12 0588 ED

1.8. HCV Ab

- CVAB.CE (192 tests)
- CVAB.CE.96 (96 tests)
- CVAB.CE.480 (480 tests)
- CVAB.CE.960 (960 tests)
- CVAB.CE.DB (192 tests)

Descrito en el certificado / *Described in the certificate* 2003 12 0392 ED

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1.9. HCV Ab Confirmation

- CCONF.CE (12 tests) — Descrito en el certificado / *Described in the certifícate* 2005 09 0485 ED

1.10. HCV IgM

- CVM.CE (96 tests) — Descrito en el certificado / *Described in the certifícate* 2007 09 0532 ED

1.11. HCV Ab (Format 20)

- CVAB.CE.EG (192 tests)
- CVAB.CE.EG.96 (96 tests)
- CVAB.CE.EG.480 (480 tests)
- CVAB.CE.EG.960 (960 tests)

Descrito en el certificado / *Described in the certifícate* 2015 10 0842 ED

1.12. HDV Ab

- DAB.CE (96 tests) — Descrito en el certificado / *Described in the certificate* 2003 12 0393 ED

1.13. HDV Ag

- DAG.CE (96 tests) — Descrito en el certificado / *Described in the certifícate* 2003 12 0394 ED

1.14. HDV IgM

- DIM.CE (96 tests) — Descrito en el certificado / *Described in the certifícate* 2003 12 0395 ED

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1.15. HTLV I & II Ab

- HTLVAB.CE (192 tests)
- HTLVAB.CE.96 (96 tests)
- HTLVAB.CE.480 (480 tests)
- HTLVAB.CE.960 (960 tests)

Descrito en el certificado/ *Described in the certifícate* 2005 12 0493 ED

1.16. HTLV I & II Ab Version ULTRA

- HTLVABULTRA.CE (192 tests)
- HTLVABULTRA.CE.96 (96 tests)
- HTLVABULTRA.CE.480 (480 tests)
- HTLVABULTRA.CE.960 (960 tests)
- HTLVABULTRA.CE.DB (192 tests)

Descrito en el certificado/ *Described in the certifícate* 2011 11 0775 ED

1.17. HIV Ab & Ag

- IVCOMB.CE (192 tests)
- IVCOMB.CE.96 (96 tests)
- IVCOMB.CE.480 (480 tests)
- IVCOMB.CE.960 (960 tests)
- IVCOMB.CE.DB (192 tests)

Descrito en el certificado/ *Described in the certifícate* 2008 02 0539 ED

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2. **Reactivos y productos reactivos para la determinación, confirmación y cuantificación de marcadores de infección en muestras humanas mediante técnicas de PCR en tiempo real/** *Reagents and reactive products for the determination, confirmation and quantification of infection markers in human samples by Real-Time PCR* **[NANDO: IVD 0203]**

2.1. HBV DNA Quantitation (QT)

- HBVDNAQT.CE (50 tests)
- HBVDNAQT.CE.25 (25 tests)
- HBVDNAQT.CE.100 (100 tests)
- HBVDNAQT.CE.150 (150 tests)

Descrito en el certificado / *Described in the certifícate* 2012 09 0790 ED

2.2. HDV RNA Quantitation (QT)

- DRNA.CE (50 tests)
- DRNA.CE.25 (25 tests)
- DRNA.CE.100 (100 tests)
- DRNA.CE.150 (150 tests)

Descrito en el certificado / *Described in the certifícate* 2009 11 0660 ED

3. **Reactivos y productos reactivos para la determinación, confirmación y cuantificación de marcadores de infección en muestras humanas mediante ensayos de quimioluminiscencia (CLIA)/** *Reagents and reactive products for the determination, confirmation and quantification of infection markers in human samples by Chemiluminescence Immunoassay (CLIA)* **[NANDO: IVD 0201; IVD 0202; IVD 0203]**

3.1. DIA.CHEMILUX HCV Ab

- RACVAB.CE (100 tests)

Descrito en el certificado / *Described in the certifícate* 2015 01 0834 ED

3.2. DIA.CHEMILUX HBs Ag

- RASAG.CE (100 tests)

Descrito en el certificado / *Described in the certifícate* 2015 10 0841 ED

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3.3. DIA.CHEMILUX HIV Ab & Ag

- RAIVCOMB.CE (100 tests) — Descrito en el certificado / *Described in the certifícate* 2016 02 0844 ED

3.4. DIA.CHEMILUX HBc Ab

- RABCAB.CE (100 tests) — Descrito en el certificado / *Described in the certifícate* 2017 07 0863 ED

3.5. DIA.CHEMILUX HTLV I & II Ab

- RAHTLVAB.CE (100 tests) — Descrito en el certificado / *Described in the certifícate* 2018 11 0878 ED

Este certificado ampara todas las marcas de estos productos incluidas por el fabricante en su declaración de conformidad. / *This certificate covers all trademarks of these products included by the manufacturer in his declaration of conformity*.

Madrid, 26 de noviembre de 2018

DIRECTORA DE LA AGENCIA ESPAÑOLA DE MEDICAMENTOS Y PRODUCTOS SANITARIOS

agencia española de medicamentos y productos sanitarios

Fdo. Mª Jesús Lamas Díaz

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HBsAg one

Version ULTRA

Fourth generation Enzyme Immunoassay (ELISA) for the determination of Hepatitis B surface Antigen or HBsAg in human serum and plasma

- for "in vitro" diagnostic use only -

DIA.PRO
Diagnostic Bioprobes Srl
Via G. Carducci n° 27
20099 Sesto San Giovanni (Milano) - Italy
Phone +39 02 27007161
Fax +39 02 26007726
e-mail: info@diapro.it

REF SAG1ULTRA.CE
96/192/480/960 Tests

HBsAg One version ULTRA

A. INTENDED USE
Fourth generation Enzyme Immunoassay (ELISA) for the one-step determination of Hepatitis B surface Antigen or HBsAg in human plasma and sera.
The kit is intended for the screening of blood units, is able to detect HBsAg mutants and finds application in the follow-up of HBV-infected patients.
For "in vitro" diagnostic use only.

B. INTRODUCTION

The World Health Organization (WHO) defines Hepatitis B Virus infection as follows:

"Hepatitis B is one of the major diseases of mankind and is a serious global public health problem. Hepatitis means inflammation of the liver, and the most common cause is infection with one of 5 viruses, called hepatitis A,B,C,D, and E. All of these viruses can cause an acute disease with symptoms lasting several weeks including yellowing of the skin and eyes (jaundice); dark urine; extreme fatigue; nausea; vomiting and abdominal pain. It can take several months to a year to feel fit again. Hepatitis B virus can cause chronic infection in which the patient never gets rid of the virus and many years later develops cirrhosis of the liver or liver cancer.

HBV is the most serious type of viral hepatitis and the only type causing chronic hepatitis for which a vaccine is available. Hepatitis B virus is transmitted by contact with blood or body fluids of an infected person in the same way as human immunodeficiency virus (HIV), the virus that causes AIDS. However, HBV is 50 to 100 times more infectious than HIV. The main ways of getting infected with HBV are: (a) perinatal (from mother to baby at the birth); (b) child- to-child transmission; (c) unsafe injections and transfusions; (d) sexual contact.

Worldwide, most infections occur from infected mother to child, from child to child contact in household settings, and from reuse of un-sterilized needles and syringes. In many developing countries, almost all children become infected with the virus. In many industrialized countries (e.g. Western Europe and North America), the pattern of transmission is different. In these countries, mother-to-infant and child-to-child transmission accounted for up to one third of chronic infections before childhood hepatitis B vaccination programmes were implemented. However, the majority of infections in these countries are acquired during young adulthood by sexual activity, and injecting drug use. In addition, hepatitis B virus is the major infectious occupational hazard of health workers, and most health care workers have received hepatitis B vaccine.

Hepatitis B virus is not spread by contaminated food or water, and cannot be spread casually in the workplace. High rates of chronic HBV infection are also found in the southern parts of Eastern and Central Europe. In the Middle East and Indian sub-continent, about 5% are chronically infected. Infection is less common in Western Europe and North America, where less than 1% are chronically infected.

Young children who become infected with HBV are the most likely to develop chronic infection. About 90% of infants infected during the first year of life and 30% to 50% of children infected between 1 to 4 years of age develop chronic infection. The risk of death from HBV-related liver cancer or cirrhosis is approximately 25% for persons who become chronically infected during childhood. Chronic hepatitis B in some patients is treated with drugs called *interferon or lamivudine*, which can help some patients. Patients with cirrhosis are sometimes given liver transplants, with varying success. It is preferable to prevent this disease with vaccine than to try and cure it.

Hepatitis B vaccine has an outstanding record of safety and effectiveness. Since 1982, over one billion doses of hepatitis B vaccine have been used worldwide. The vaccine is given as a series of three intramuscular doses. Studies have shown that the vaccine is 95% effective in preventing children and adults from developing chronic infection if they have not yet been infected. In many countries where 8% to 15% of children used to become chronically infected with HBV, the rate of chronic infection has been reduced to less than 1% in immunized groups of children. Since 1991, WHO has called for all countries to add hepatitis B vaccine into their national immunization programs."

Hepatitis B surface Antigen or HBsAg is the most important protein of the envelope of Hepatitis B Virus, responsible for acute and chronic viral hepatitis.
The surface antigen contains the determinant "a", common to all the known viral subtypes, immunologically distinguished by two distinct subgroups (ay and ad).
The ability to detect HBsAg with high sensitive immunoassays in the last years has led to an understanding of its distribution and epidemiology worldwide and to radically decrease the risk of infection in transfusion.

C. PRINCIPLE OF THE TEST
A mix of mouse monoclonal antibodies specific to the determinants "a", "d" and "y" of HBsAg is fixed to the surface of microwells. Patient's serum/plasma is added to the microwell together with a second mix of mouse monoclonal antibodies, conjugated with Horseradish Peroxidase (HRP) and directed against a different epitope of the determinant "a" and against "preS".
The specific immunocomplex, formed in the presence of HBsAg in the sample, is captured by the solid phase.
At the end of the one-step incubation, microwells are washed to remove unbound serum proteins and HRP conjugate.
The chromogen/substrate is then added and, in the presence of captured HBsAg immunocomplex, the colorless substrate is hydrolyzed by the bound HRP conjugate to a colored end-product. After blocking the enzymatic reaction, its optical density is measured by an ELISA reader.
The color intensity is proportional to the amount of HBsAg present in the sample.
The version ULTRA is particularly suitable for automated screenings and is able to detect "s" mutants.

D. COMPONENTS
The standard configuration contains reagents to perform 192 tests and is made of the following components:

1. Microplate MICROPLATE
n° 2. 12 strips of 8 breakable wells coated with anti HBsAg, affinity purified mouse monoclonal antibodies, specific to "a", "y" and "d" determinants, and sealed into a bag with desiccant.

2. Negative Control CONTROL -
1x4.0ml/vial. Ready to use control. It contains goat serum, 10 mM phosphate buffer pH 7.4+/-0.1, 0.09% Na-azide and 0.1% Kathon GC as preservatives. The negative control is pale yellow color coded.

3. Positive Control CONTROL +
1x4.0ml/vial. Ready to use control. It contains goat serum, non infectious recombinant HBsAg, 10 mM phosphate buffer pH 7.4+/-0.1, 0.02% gentamicine sulphate and 0.1% Kathon GC as preservatives. The positive control is color coded green.

4. Calibrator CAL ….
n° 2 vials. Lyophilized calibrator. To be dissolved with EIA grade water as reported in the label. Contains fetal bovine serum, non infectious recombinant HBsAg at 0.5 IU/ml (2nd WHO international standard for HBsAg, NIBSC code 00/588), 10 mM phosphate buffer pH 7.4+/-0.1, 0.02% gentamicine sulphate and 0.1% Kathon GC as preservatives.
Note: The volume necessary to dissolve the content of the vial may vary from lot to lot. Please use the right volume reported on the label .

5. Wash buffer concentrate WASHBUF 20X
2x60ml/bottle. 20X concentrated solution. Once diluted, the wash solution contains 10 mM phosphate buffer pH 7.0+/-0.2, 0.05% Tween 20 and 0.1% Kathon GC.

6. Enzyme Conjugate Diluent CONJ DIL
2x16ml/vial. Ready to use and pink/red color coded regent. It contains 10 mM Tris buffer pH 6.8+/-0.1, 1% normal mouse serum, 5% BSA, 0.1% Kathon GC and 0.02% gentamicine sulphate as preservatives. The solution is normally opalescent.

7. Enzyme Conjugate CONJ 20X
2x1ml/vial. 20X concentrated reagent. It contains Horseradish Peroxidase (HRP) labeled mouse monoclonal antibodies to HBsAg, determinant "a" and "preS", 10 mM Tris buffer pH 6.8+/-0.1, 5% BSA, 0.1% Kathon GC and 0.02% gentamicine sulphate as preservatives.

8. Chromogen/Substrate SUBS TMB
2x25ml/bottle. It contains a 50 mM citrate-phosphate buffered solution at pH 3.5-3.8, 4% dimethylsulphoxide, 0.03% tetra-methyl-benzidine (TMB) and 0.02% hydrogen peroxide (H2O2).
Note: To be stored protected from light as sensitive to strong illumination.

9. Sulphuric Acid H_2SO_4 O.3 M
1x25ml/bottle. It contains 0.3 M H2SO4 solution.
Note: Attention: Irritant (H315; H319; P280; P302+P352; P332+P313; P305+P351+P338; P337+P313; P362+P363)

10. Plate sealing foils n° 4

11. Package insert

Important note:
Only upon specific request , Dia.Pro can supply reagents for 96, 480, 960 tests , as reported below**:**

Microplates	N°1	N°5	N°10
Negative Control	1x2ml/vial	1x10ml/vial	1x20ml/vial
Positive Control	1x2ml/vial	1x10ml/vial	1x20ml/vial
Calibrator	N° 1 vial	N° 5 vials	N° 10 vials
Wash buffer concentrate	1x60ml/vial	5x60ml/vial	4x150ml/vial
Enzyme conjugate	1x0.8ml/vial	1x4ml/vial	2x4ml/vial
Conjugate Diluent	1x16ml/vial	2x40ml/vial	2x80ml/vial
Chromogen/Substrate	1x25ml/vial	3x42ml/vial	2x125ml/vial
Sulphuric Acid	1x15ml/vial	2x40ml/vial	2x80ml/vial
Plate sealing foils	N° 2	N° 10	N° 20
Package insert	N° 1	N° 1	N° 1
Number of tests	96	480	960
Code SAG1ULTRA.CE	96	480	960

E. MATERIALS REQUIRED BUT NOT PROVIDED
1. Calibrated Micropipettes (150ul, 100ul and 50ul) and disposable plastic tips.
2. EIA grade water (double distilled or deionised, charcoal treated to remove oxidizing chemicals used as disinfectants).
3. Timer with 60 minute range or higher.
4. Absorbent paper tissues.
5. Calibrated ELISA microplate thermostatic incubator (dry or wet), capable to provide shaking at 1300 rpm+/-150, set at +37°C.
6. Calibrated ELISA microwell reader with 450nm (reading) and with 620-630nm (blanking) filters.
7. Calibrated ELISA microplate washer.
8. Vortex or similar mixing tools.

F. WARNINGS AND PRECAUTIONS
1. The kit has to be used by skilled and properly trained technical personnel only, under the supervision of a medical doctor responsible of the laboratory.
2. When the kit is used for the screening of blood units and blood components, it has to be used in a laboratory certified and qualified by the national authority in that field (Ministry of Health or similar entity) to carry out this type of analysis.
3. All the personnel involved in performing the assay have to wear protective laboratory clothes, talc-free gloves and glasses. The use of any sharp (needles) or cutting (blades) devices should be avoided. All the personnel involved should be trained in biosafety procedures, as recommended by the Center for Disease Control, Atlanta, U.S. and reported in the National Institute of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
4. All the personnel involved in sample handling should be vaccinated for HBV and HAV, for which vaccines are available, safe and effective.
5. The laboratory environment should be controlled so as to avoid contaminants such as dust or air-born microbial agents, when opening kit vials and microplates and when performing the test. Protect the Chromogen (TMB) from strong light and avoid vibration of the bench surface where the test is undertaken.
6. Upon receipt, store the kit at 2..8°C into a temperature controlled refrigerator or cold room.
7. Do not interchange components between different lots of the kits. It is recommended that components between two kits of the same lot should not be interchanged.
8. Check that the reagents are clear and do not contain visible heavy particles or aggregates. If not, advise the laboratory supervisor to initiate the necessary procedures for kit replacement.
9. Avoid cross-contamination between serum/plasma samples by using disposable tips and changing them after each sample.
10. Avoid cross-contamination between kit reagents by using disposable tips and changing them between the use of each one.
11. Do not use the kit after the expiration date stated on the external container and internal (vials) labels. A study conducted on an opened kit has not pointed out any relevant loss of activity up to 6 re-use of the device and up to 6 months.
12. Treat all specimens as potentially infective. All human serum specimens should be handled at Biosafety Level 2, as recommended by the Center for Disease Control, Atlanta, U.S. in compliance with what reported in the Institutes of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
13. The use of disposable plastic-ware is recommended in the preparation of the liquid components or in transferring components into automated workstations, in order to avoid cross contamination.
14. Waste produced during the use of the kit has to be discarded in compliance with national directives and laws concerning laboratory waste of chemical and biological substances. In particular, liquid waste generated from the washing procedure, from residuals of controls and from samples has to be treated as potentially infective material and inactivated before waste. Suggested procedures of inactivation are treatment with a 10% final concentration of household bleach for 16-18 hrs or heat inactivation by autoclave at 121°C for 20 min..
15. Accidental spills from samples and operations have to be adsorbed with paper tissues soaked with household bleach and then with water. Tissues should then be discarded in proper containers designated for laboratory/hospital waste.
16. The Stop Solution is an irritant. In case of spills, wash the surface with plenty of water
17. Other waste materials generated from the use of the kit (example: tips used for samples and controls, used microplates) should be handled as potentially infective and disposed according to national directives and laws concerning laboratory wastes.

G. SPECIMEN: PREPARATION AND WARNINGS

1. Blood is drawn aseptically by venepuncture and plasma or serum is prepared using standard techniques of preparation of samples for clinical laboratory analysis. No influence has been observed in the preparation of the sample with citrate, EDTA and heparin.
2. Avoid any addition of preservatives to samples; especially sodium azide as this chemical would affect the enzymatic activity of the conjugate, generating false negative results.
3. Samples have to be clearly identified with codes or names in order to avoid misinterpretation of results. When the kit is used for the screening of blood units, bar code labeling and electronic reading is strongly recommended.
4. Haemolysed (red) and lipemic ("milky") samples have to be discarded as they could generate false results. Samples containing residues of fibrin or heavy particles or microbial filaments and bodies should be discarded as well as they could give rise to false positive results. Specimens with an altered pathway of coagulation, presenting particles after blood collection and preparation of serum/plasma as those coming from hemodialized patients, could give origin to false positive results.
5. Sera and plasma can be stored at +2°..8°C for up to seven days after collection. For longer storage periods, samples can be stored frozen at –20°C for several months. Any frozen sample should not be frozen/thawed more than once as this may generate particles that could affect the test result. If some turbidity is present or presence of microparticles is suspected after thawing, filter the sample on a disposable 0.2-0.8u filter to clean it up for testing or use the two-steps alternative method.

H. PREPARATION OF COMPONENTS AND WARNINGS

A study conducted on an opened kit has not pointed out any relevant loss of activity up to 6 re-uses of the device and up to 6 months.

1. Microplates:
Allow the microplate to reach room temperature (about 1 hr) before opening the container. Check that the desiccant has not turned green, indicating a defect in conservation.
In this case, call Dia.Pro's customer service.
Unused strips have to be placed back inside the aluminum pouch, with the desiccant supplied, firmly zipped and stored at +2°..8°C. After first opening, remaining strips are stable until the humidity indicator inside the desiccant bag turns from yellow to green.

2. Negative Control:
Ready to use. Mix well on vortex before use.

3. Positive Control:
Ready to use. Mix well on vortex before use. The positive control does not contain any infective HBV as it is composed of recombinant synthetic HBsAg.

4. Calibrator:
Add the volume of ELISA grade water, reported on the label, to the lyophilized powder; let fully dissolve and then gently mix on vortex. The solution is not stable. Store the Calibrator frozen in aliquots at –20°C.

5. Wash buffer concentrate:
The 20x concentrated solution has to be diluted with EIA grade water up to 1200 ml and mixed gently end-over-end before use. As some salt crystals may be present into the vial, take care to dissolve all the content when preparing the solution.
In the preparation avoid foaming as the presence of bubbles could give origin to a bad washing efficiency.
Note: *Once diluted, the wash solution is stable for 1 week at +2..8° C.*

6. Enzyme conjugate:
The working solution is prepared by diluting the 20X concentrated reagent into the Conjugate
Mix well on vortex before use.
Avoid any contamination of the liquid with oxidizing chemicals, dust or microbes. If this component has to be transferred, use only plastic sterile disposable containers.
Important note*: The working solution is not stable. Prepare only the volume necessary for the work of the day. As an example when the kit is used in combination with other instruments or manually, dilute 0.1 ml 20X Conjugate with 1.9 ml Conjugate Diluent into a disposable plastic vial and mix carefully before use.*

7. Chromogen/Substrate:
Ready to use. Mix well by end-over-end mixing.
Avoid contamination of the liquid with oxidizing chemicals, air-driven dust or microbes. Do not expose to strong light, oxidizing agents and metallic surfaces.
If this component has to be transferred use only plastic, and if possible, sterile disposable container.

8. Sulphuric Acid:
Ready to use. Mix well by end-over-end mixing.
Attention*: Irritant* (H315; H319; P280; P302+P352; P332+P313; P305+P351+P338; P337+P313; P362+P363).

Legenda:

Warning ***H statements:***
H315 *– Causes skin irritation.*
H319 *– Causes serious eye irritation.*

Precautionary ***P statements:***
P280 *– Wear protective gloves/protective clothing/eye protection/face protection.*
P302 + P352 *– IF ON SKIN: Wash with plenty of soap and water.*
P332 + P313 *– If skin irritation occurs: Get medical advice/attention.*
P305 + P351 + P338 *– IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.*
P337 + P313 *– If eye irritation persists: Get medical advice/attention.*
P362 + P363 *- Take off contaminated clothing and wash it before reuse.*

I. INSTRUMENTS AND TOOLS USED IN COMBINATION WITH THE KIT

1. **Micropipettes** have to be calibrated to deliver the correct volume required by the assay and must be submitted to regular decontamination (70% ethanol, 10% solution of bleach, hospital grade disinfectants) of those parts that could accidentally come in contact with the sample or the components of the kit. They should also be regularly maintained in order to show a precision of 1% and a trueness of ±2%.
2. The **ELISA incubator** has to be set at +37°C (tolerance of ±1°C) and regularly checked to ensure the correct temperature is maintained. Both dry incubators and water baths are suitable for the incubations, provided that the instrument is validated for the incubation of ELISA tests.
3. In case of **shaking** during incubations, the instrument has to ensure 350 rpm ±150. Amplitude of shaking is very important as a wrong one could give origin to splashes and therefore to some false positive result.
4. The **ELISA washer** is extremely important to the overall performances of the assay. The washer must be carefully validated and correctly optimized using the kit controls/calibrator and reference panels, before using the kit for routine laboratory tests. Usually 4-5 washing cycles (aspiration + dispensation of 350ul/well of washing solution = 1 cycle) are sufficient to ensure that the assay performs as expected. A soaking time of 20-30 seconds between cycles is suggested. In order to set correctly their number, it

is recommended to run an assay with the kit controls/calibrator and well-characterized negative and positive reference samples, and check to match the values reported below in the section "Internal Quality Control". Regular calibration of the volumes delivered and maintenance (decontamination and cleaning of needles) of the washer has to be carried out according to the instructions of the manufacturer.

5. **Incubation times** have a tolerance of $\pm$5%.
6. The **microplate reader** has to be equipped with a reading filter of 450nm and with a second filter (620-630nm, strongly recommended) for blanking purposes. Its standard performances should be (a) bandwidth $\leq$ 10 nm; (b) absorbance range from 0 to $\geq$ 2.0; (c) linearity to $\geq$ 2.0; (d) repeatability $\geq$ 1%. Blanking is carried out on the well identified in the section "Assay Procedure". The optical system of the reader has to be calibrated regularly to ensure that the correct optical density is measured. It should be regularly maintained according to the manufacturer 's instructions.
7. When using **ELISA automated workstations**, all critical steps (dispensation, incubation, washing, reading, shaking, data handling, etc.) have to be carefully set, calibrated, controlled and regularly serviced in order to match the values reported in the sections "Internal Quality Control". The assay protocol has to be installed in the operating system of the unit and validated by checking full matching the declared performances of the kit. In addition, the liquid handling part of the station (dispensation and washing) has to be validated and correctly set paying particular attention to avoid carry over by the needles used for dispensing samples and for washing. The carry over effect must be studied and controlled to minimize the possibility of contamination of adjacent wells due to strongly reactive samples, leading to false positive results. The use of ELISA automated work stations is recommended for blood screening and when the number of samples to be tested exceed 20-30 units per run.
8. When using automatic devices, in case the vial holder of the instrument does not fit with the vials supplied in the kit, transfer the solution into appropriate containers and label them with the same label peeled out from the original vial. This operation is important in order to avoid mismatching contents of vials, when transferring them. When the test is over, return the secondary labeled containers to 2..8°C, firmly capped.
9. **Dia.Pro's customer service** offers support to the user in the setting and checking of instruments used in combination with the kit, in order to assure full compliance with the essential requirements of the assay. Support is also provided for the installation of new instruments to be used in combination with the kit.

L. PRE ASSAY CONTROLS AND OPERATIONS

1. Check the expiration date of the kit printed on the external label of the kit box. Do not use if expired.
2. Check that the liquid components are not contaminated by naked-eye visible particles or aggregates. Check that the Chromogen/Substrate is colorless or pale blue. Check that no breakage occurred in transportation and no spillage of liquid is present inside the box. Check that the aluminum pouch, containing the microplate, is not punctured or damaged.
3. Dilute all the content of the 20x concentrated Wash Solution as described above.
4. Dilute the 20X concentrated Enzyme Conjugate with its Diluent as reported.
5. Dissolve the Calibrator as described above.
6. Allow all the other components to reach room temperature (about 1 hr) and then mix as described.
7. Set the ELISA incubator at +37°C and prepare the ELISA washer by priming with the diluted washing solution, according to the manufacturers instructions. Set the right number of washing cycles as found in the validation of the instrument for its use with the kit.
8. Check that the ELISA reader has been turned on at least 20 minutes before reading.
9. If using an automated workstation, turn it on, check settings and be sure to use the right assay protocol.
10. Check that the micropipettes are set to the required volume.
11. Check that all the other equipment is available and ready to use.
12. In case of problems, do not proceed further with the test and advise the supervisor.

M. ASSAY PROCEDURE

The assay has to be carried out according to what reported below, taking care to maintain the same incubation time for all the samples in testing.

Automated assay:

In case the test is carried out automatically with an ELISA system, we suggest to make the instrument dispense first 150 ul controls & calibrator, then all the samples and finally 100 ul diluted Enzyme Conjugate.

For the pre-washing step (point 1 of the assay procedure) and all the next operations follow the operative instructions reported below for the Manual Assay.

It is strongly recommended to check that the time lap between the dispensation of the first and the last sample will be calculated by the instrument and taken into consideration by delaying the first washing operation accordingly.

Manual Assay:

1. Place the required number of strips in the plastic holder and wash them once to hydrate wells. Carefully identify the wells for controls, calibrator and samples.

Important note: *Pre washing (1 cycle: dispensation of 350ul/well of washing solution+ aspiration) is fundamental to obtain reliable and specific results both in the manual and in the automatic procedures. Do not omit it !*

2. Leave the A1 well empty for blanking purposes.
3. Pipette 150µl of the Negative Control in triplicate, 150ul of the Calibrator in duplicate and then 150ul of the Positive Control in single followed by 150ul of each of the samples.
4. Check for the presence of samples in wells by naked eye (there is a marked color difference between empty and full wells) or by reading at 450/620nm. (samples show OD values higher than 0.100).
5. Dispense 100ul diluted Enzymatic Conjugate in all wells, except for A1, used for blanking operations.

Important note: *Be careful not to touch the inner surface of the well with the pipette tip when the conjugate is dispensed. Contamination might occur.*

6. Following addition of the conjugate, check that the color of the samples have changed from yellowish to pink/red and then incubate the microplate for **120 min at +37°C**.

Important notes:

a. *Strips have to be sealed with the adhesive sealing foil, only when the test is performed manually. Do not cover strips when using ELISA automatic instruments.*
b. *If the procedure is carried out on shaking, be sure to deliver the rpm reported for in Section I.3 as otherwise intra-well contamination could occur.*

7. When the first incubation is over, wash the microwells as previously described (section I.4)

8. Pipette 200 µl Chromogen/Substrate into all the wells, A1 included.

Important note: *Do not expose to strong direct light as a high background might be generated.*

9. Incubate the microplate protected from light at **18-24°C for 30 min.** Wells dispensed with the positive control, the calibrator and positive samples will turn from clear to blue.
10. Pipette 100 µl Sulphuric Acid into all the wells to stop the enzymatic reaction, using the same pipetting sequence as in step 8. Addition of the acid solution will turn the positive control, the calibrator and positive samples from blue to yellow/brown.
11. Measure the color intensity of the solution in each well, as described in section I.6 using a 450nm filter (reading) and a 620-630nm filter (background subtraction, strongly recommended), blanking the instrument on A1.

Important general notes:

1. *If the second filter is not available, ensure that no fingerprints or dust are present on the external bottom of the microwell before reading at 450nm. They could generate false positive results on reading.*
2. *Reading should ideally be performed immediately after the addition of the acid solution but definitely no longer than 20 minutes afterwards. Some self-oxidation of the chromogen can occur leading to a higher background.*
3. *When samples to be tested are not surely clean or have been stored frozen, the assay procedure reported below is recommended as long as it is far less sensitive to interferences due to hemolysis, hyperlipaemia, bacterial contamination and fibrin microparticles. The assay is carried out in two-steps at +37°C on shaking at* 350 rpm <u>+</u>150 *as follows:*
   - *dispense 100 ul of controls, calibrator and samples*
   - *incubate 60 min at +37°C on shaking*
   - *wash according to instructions (section I.4)*
   - *dispense 100 ul diluted enzyme tracer*
   - *incubate 30 min at +37°C on shaking*
   - *wash*
   - *dispense 100 ul TMB&H2O2 mix*
   - *incubate 30 min at r.t. on shaking*
   - *stop and read*

   In this procedure the pre-wash can be omitted.
   This method shows performances similar to the standard one and therefore can be used in alternative.
4. *The Calibrator (CAL) does not affect the cut-off calculation and therefore the test results calculation. The Calibrator may be used only when a laboratory internal quality control is required by the management.*

N. ASSAY SCHEME

Operations	Procedure
Pre-Washing step	n° 1 cycle
Controls&Calibrator&samples Diluted Enzyme Conjugate	150 ul 100 ul
1st incubation	**120 min**
Temperature	+37°C
Washing steps	n° 4-5
Chromogen/Substrate	200ul
2nd incubation	**30 min**
Temperature	room
Sulphuric Acid	100 ul
Reading OD	450nm

An example of dispensation scheme is reported in the following section:

Microplate

	1	2	3	4	5	6	7	8	9	10	11	12
A	BLK	S2										
B	NC	S3										
C	NC	S4										
D	NC	S5										
E	CAL	S6										
F	CAL	S7										
G	PC	S8										
H	S1	S9										

Legenda: BLK = Blank NC = Negative Control
CAL = Calibrator PC = Positive Control S = Sample

O. INTERNAL QUALITY CONTROL

A check is performed on the controls/calibrator any time the kit is used in order to verify whether the expected OD450nm or S/Co values have been matched in the analysis.

Ensure that the following results are met:

Parameter	Requirements
Blank well	< 0.100 OD450nm value
Negative Control (NC)	< 0.050 mean OD450nm value after blanking
Calibrator 0.5 IU/ml	S/Co <u>></u> 2
Positive Control	> 1.000 OD450nm value

If the results of the test match the requirements stated above, proceed to the next section.
If they do not, do not proceed any further and perform the following checks:

Problem	Check
Blank well > 0.100 OD450nm	1. that the Chromogen/Substrate solution has not become contaminated during the assay
Negative Control (NC) > 0.050 OD450nm after blanking	1. that the washing procedure and the washer settings are as validated in the pre qualification study; 2. that the proper washing solution has been used and the washer has been primed with it before use; 3. that no mistake has been done in the assay procedure (dispensation of positive control instead of the negative one); 4. that no contamination of the negative control or of the wells where the control was dispensed has occurred due to spills of positive samples or of the enzyme conjugate; 5. that micropipettes have not become contaminated with positive samples or with the enzyme conjugate 6. that the washer needles are not blocked or partially obstructed.

Calibrator S/Co < 2	1. that the procedure has been correctly performed; 2. that no mistake has occurred during its distribution (ex.: dispensation of negative control instead of calibrator) 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the calibrator has occurred.
Positive Control < 1.000 OD450nm	1. that the procedure has been correctly performed; 2. that no mistake has occurred during the distribution of the control (dispensation of negative control instead of positive control. In this case, the negative control will have an OD450nm value > 0.050). 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the positive control has occurred.

If any of the above problems have occurred, report the problem to the supervisor for further actions.

P. CALCULATION OF THE CUT-OFF

The test results are calculated by means of a cut-off value determined on the mean OD450nm value of the negative control (NC) with the following formula:

NC + 0.050 = Cut-Off (Co)

The value found for the test is used for the interpretation of results as described in the next paragraph.

Important note*: When the calculation of results is performed by the operating system of an ELISA automated work station, ensure that the proper formulation is used to calculate the cut-off value and generate the correct interpretation of results.*

Q. INTERPRETATION OF RESULTS

Test results are interpreted as a ratio of the sample OD450nm (S) and the Cut-Off value (Co), mathematically S/Co, according to the following table:

S/Co	Interpretation
< 0.9	Negative
0.9 – 1.1	Equivocal
> 1.1	Positive

A negative result indicates that the patient is not infected by HBV and that the blood unit may be transfused.
Any patient showing an equivocal result should be retested on a second sample taken 1-2 weeks after the initial sample; the blood unit should not be transfused.
A positive result is indicative of HBV infection and therefore the patient should be treated accordingly or the blood unit should be discarded.

Important notes:

1. *Interpretation of results should be done under the supervision of the laboratory supervisor to reduce the risk of judgment errors and misinterpretations.*
2. *Any positive result must be confirmed first by repeating the test on the sample, after having filtered it on 0.2-0.8 u filter to remove any microparticles interference. Then, if still positive, the sample has to be submitted to a confirmation test before a diagnosis of viral hepatitis is released.*
3. *When test results are transmitted from the laboratory to another department, attention must be paid to avoid erroneous data transfer.*
4. *Diagnosis of viral hepatitis infection has to be taken and released to the patient by a suitably qualified medical doctor.*

An example of calculation is reported below.

The following data must not be used instead or real figures obtained by the user.

Negative Control: 0.012 – 0.008 – 0.010 OD450nm
Mean Value: 0.010 OD450nm
Lower than 0.050 – Accepted
Positive Control: 2.489 OD450nm
Higher than 1.000 – Accepted
Cut-Off = 0.010+0.050 = 0.060
Calibrator: 0.350 - 0.370 OD450nm
Mean value: 0.360 OD450nm S/Co = 6.0
S/Co higher than 2.0 – Accepted
Sample 1: 0.028 OD450nm
Sample 2: 1.690 OD450nm
Sample 1 S/Co < 0.9 = negative
Sample 2 S/Co > 1.1 = positive

R. PERFORMANCE CHARACTERISTICS

Evaluation of Performances has been conducted in accordance to what reported in the Common Technical Specifications or CTS (art. 5, Chapter 3 of IVD Directive 98/79/EC). Version ULTRA proved to be at least equivalent to the original design in a study conducted for the validation of the new version.

1. Analytical Sensitivity

The limit of detection of the assay has been calculated on the 2nd WHO international standard, NIBSC code 00/588.
In the following table, results are given for three lots (P1, P2 and P3) of the version ULTRA in comparison with the reference device (Ref.):

WHO IU/ml	Lot # P1 S/Co	Lot # P2 S/Co	Lot # P3 S/Co	Ref. S/Co
0.4	**4.6**	**4.8**	**4.6**	**4.6**
0.2	**2.3**	**2.4**	**2.4**	**2.4**
0.1	**1.4**	**1.4**	**1.5**	**1.2**
0.05	0.8	0.8	***1.0***	0.7
0.025	0.6	0.6	0.6	0.4
FCS (NC)	0.3	0.2	0.3	0.1

The assay shows an Analytical Sensitivity better than 0.1 WHO IU/ml of HBsAg.

In addition two panels of sensitivity supplied by EFS, France, and by SFTS, France, were tested and gave in the best conditions the following results:

Panel EFS Ag HBs HB1-HB6 lot n° 04

Sample ID	Characteristics	ng/ml	S/Co
HB1	diluent	/	0,2
HB2	adw2+ayw3	0.05	0,6
HB3	adw2+ayw3	0.1	**1,0**
HB4	adw2+ayw3	0.2	**1,8**
HB5	adw2+ayw3	0.3	**2,4**
HB6	adw2+ayw3	0.5	**4,2**

Sensitivity panel SFTS, France, Ag HBs 2005

Sample ID	Characteristics	ng/ml	S/Co
171	Adw2 + ayw3	2.21 ± 0.15	**15,4**
172	Adw2 + ayw3	1.18 ± 0.10	**8,7**
173	Adw2 + ayw3	1.02 ± 0.05	**6,1**
174	Adw2 + ayw3	0.64 ± 0.04	**4,0**
175	Adw2 + ayw3	0.49 ± 0.03	**3,4**
176	Adw2 + ayw3	0.39 ± 0.02	**2,6**
177	Adw2 + ayw3	0.25 ± 0.02	**2,0**
178	Adw2 + ayw3	0.11 ± 0.02	**1,3**
179	Adw2 + ayw3	0.06 ± 0.01	***0,9***
180	Adw2 + ayw3	0.03 ± 0.01	0,8
181	Adw2	0.5 – 1.0	**4,7**
182	Adw4	0.5 – 1.0	**3,6**
183	Adr	0.5 – 1.0	**4,5**
184	Ayw1	0.5 – 1.0	**5,1**
185	Ayw2	0.5 – 1.0	**6,4**
186	Ayw3	0.5 – 1.0	**7,3**
187	Ayw3	0.5 – 1.0	**5,8**
188	Ayw4	0.5 – 1.0	**6,9**
189	Ayr	0.5 – 1.0	**6,1**
190	diluent	/	0,6

The panel # 808, supplied by Boston Biomedical Inc., USA, was also tested to define the limit of sensitivity.
Results in the best conditions are as follows :

BBI panel PHA 808

Sample ID	Characteristics	ng/ml	S/Co
01	ad	2,49	**10,2**
02	ad	1,17	**4,8**
03	ad	1,02	**4,3**
04	ad	0,96	**3,8**
05	ad	0,69	**2,9**
06	ad	0,50	**2,2**
07	ad	0,41	**1,5**
08	ad	0,37	**1,3**
09	ad	0,30	**1,2**
10	ad	0,23	***1,0***
11	ay	2,51	**11,2**
12	ay	1,26	**5,9**
13	ay	0,97	**4,1**
14	ay	0,77	**3,7**
15	ay	0,63	**2,0**
16	ay	0,48	**2,4**
17	ay	0,42	**2,0**
18	ay	0,33	**1,8**
19	ay	0,23	**1,6**
20	ay	0,13	**1,1**
21	negative	/	0,6

2. Diagnostic Sensitivity:
The diagnostic sensitivity was tested according to what required by Common Technical Specifications (CTS) of the directive 98/79/EC on IVD for HBsAg testing.
Positive samples, including HBsAg subtypes and a panel of “s” mutants from most frequent mutations, were collected from different HBV pathologies (acute, a-symptomatic and chronic hepatitis B) or produced synthetically, and were detected positive in the assay.
All the HBsAg known subtypes, “ay” and “ad”, and isoforms “w” and “r”, supplied by CNTS, France, were tested in the assay and determined positive by the kit as expected.
An overall value of 100% has been found in a study conducted on a total number of more than 400 samples positive with the original reference IVD code SAG1.CE, CE marked.
A total of 30 sero-conversions were studied, most of them produced by Boston Biomedica Inc., USA.

Results obtained by examining eight panels supplied by Boston Biomedica Inc., USA, are reported below for the version ULTRA in comparison with the reference device code SAG1.CE.

Panel ID	1st sample positive	HBsAg subtype	HBsAg ng/ml	Version ULTRA S/Co	Ref. device S/Co
PHM 906	02	ad	0.5	**3.7**	**1.4**
PHM 907 (M)	06	ay	1.0	**4.4**	**2.9**
PHM 909	04	ad	0.3	**1.2**	0.8
PHM 914	04	ad	0.5	**1.1**	**1.1**
PHM 918	02	ad	0.1	**1.8**	0.5
PHM 923	03	ay	< 0.2	**2.2**	**1.2**
PHM 925	03	Ind.	n.d.	**1.4**	*0.9*
PHM 934	01	ad	n.d.	**1.0**	0.8

3. Diagnostic Specificity:
It is defined as the probability of the assay of scoring negative in the absence of specific analyte. In addition to the first study, where more than 5000 negative samples from blood donors (two blood centers), classified negative with a CE marked device in use at the laboratory of collection were examined, the diagnostic specificity was recently assessed by testing a total of 2288 negative blood donors on seven different lots. A value of specificity of 100% was found.
Both plasma, derived with different standard techniques of preparation (citrate, EDTA and heparin), and sera have been used to determine the specificity.
No false reactivity due to the method of specimen preparation has been observed.
Frozen specimens have also been tested to check whether samples freezing interferes with the performance of the test. No interference was observed on clean and particle free samples.
Samples derived from patients with different viral (HCV, HAV) and non viral pathologies of the liver that may interfere with the test were examined. No cross reaction were observed.

4. Precision:
It has been calculated for the version ULTRA on two samples examined in 16 replicates in 3 different runs for three lots.
Results are reported in the following tables:

Average values Total n = 144	Negative Sample	Calibrator 0.5 IU/ml
OD450nm	0.026	0.332
Std.Deviation	0.004	0.027
CV %	16%	8%

The variability shown in the tables did not result in sample misclassification.

S. LIMITATIONS
Repeatable false positive results were assessed on freshly collected specimens in less than 0.1% of the normal population, mostly due to high titers Heterophilic Anti Mouse Antibodies (HAMA).
Interferences in fresh samples were also observed when they were not particles-free or were badly collected (see chapter G).
Old or frozen samples, presenting fibrin clots, crioglobulins, lipid-containing micelles or microparticles after storage or thawing, can generate false positive results.

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All the IVD Products manufactured by the company are under the control of a certified Quality Management System approved by an EC Notified Body. Each lot is submitted to a quality control and released into the market only if conforming with the EC technical specifications and acceptance criteria.

Manufacturer:
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CE
0318

HBsAb

Enzyme Immunoassay for qualitative/quantitative determination of antibodies to Hepatitis B surface Antigen in human serum and plasma

- for "in vitro" diagnostic use only -

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REF SAB.CE
96 Tests

HBs Ab

A. INTENDED USE

Enzyme ImmunoAssay (ELISA) for both the quantitative and qualitative determination of antibodies to the Surface Antigen of Hepatitis B Virus in human plasma and sera.
For "in vitro" diagnostic use only.

B. INTRODUCTION

The World Health Organization (WHO) defines Hepatitis B Virus infection as follows:

"Hepatitis B is one of the major diseases of mankind and is a serious global public health problem. Hepatitis means inflammation of the liver, and the most common cause is infection with one of 5 viruses, called hepatitis A,B,C,D, and E. All of these viruses can cause an acute disease with symptoms lasting several weeks including yellowing of the skin and eyes (jaundice); dark urine; extreme fatigue; nausea; vomiting and abdominal pain. It can take several months to a year to feel fit again. Hepatitis B virus can cause chronic infection in which the patient never gets rid of the virus and many years later develops cirrhosis of the liver or liver cancer.

HBV is the most serious type of viral hepatitis and the only type causing chronic hepatitis for which a vaccine is available. Hepatitis B virus is transmitted by contact with blood or body fluids of an infected person in the same way as human immunodeficiency virus (HIV), the virus that causes AIDS. However, HBV is 50 to 100 times more infectious than HIV. The main ways of getting infected with HBV are: (a) perinatal (from mother to baby at the birth); (b) child- to-child transmission; (c) unsafe injections and transfusions; (d) sexual contact.

Worldwide, most infections occur from infected mother to child, from child to child contact in household settings, and from reuse of un-sterilized needles and syringes. In many developing countries, almost all children become infected with the virus. In many industrialized countries (e.g. Western Europe and North America), the pattern of transmission is different. In these countries, mother-to-infant and child-to-child transmission accounted for up to one third of chronic infections before childhood hepatitis B vaccination programmes were implemented. However, the majority of infections in these countries are acquired during young adulthood by sexual activity, and injecting drug use. In addition, hepatitis B virus is the major infectious occupational hazard of health workers, and most health care workers have received hepatitis B vaccine.

Hepatitis B virus is not spread by contaminated food or water, and cannot be spread casually in the workplace. High rates of chronic HBV infection are also found in the southern parts of Eastern and Central Europe. In the Middle East and Indian sub-continent, about 5% are chronically infected. Infection is less common in Western Europe and North America, where less than 1% are chronically infected.

Young children who become infected with HBV are the most likely to develop chronic infection. About 90% of infants infected during the first year of life and 30% to 50% of children infected between 1 to 4 years of age develop chronic infection. The risk of death from HBV-related liver cancer or cirrhosis is approximately 25% for persons who become chronically infected during childhood.

Chronic hepatitis B in some patients is treated with drugs called *interferon or lamivudine*, which can help some patients. Patients with cirrhosis are sometimes given liver transplants, with varying success. It is preferable to prevent this disease with vaccine than to try and cure it.

Hepatitis B vaccine has an outstanding record of safety and effectiveness. Since 1982, over one billion doses of hepatitis B vaccine have been used worldwide. The vaccine is given as a series of three intramuscular doses. Studies have shown that the vaccine is 95% effective in preventing children and adults from developing chronic infection if they have not yet been infected. In many countries where 8% to 15% of children used to become chronically infected with HBV, the rate of chronic infection has been reduced to less than 1% in immunized groups of children. Since 1991, WHO has called for all countries to add hepatitis B vaccine into their national immunization programmes."

Hepatitis B surface Antigen (HBsAg) is the major structural polypeptide of the envelope of the Hepatitis B Virus (HBV).
This antigen is composed mainly of the type common determinant "a" and the type specific determinants "d" and "y", present only on the specific serotypes.
Upon infection, a strong immunological response develops firstly against the type specific determinants and in a second time against the "a" determinant.
Anti "a" antibodies are however recognised to be most effective in the neutralisation of the virus, protecting the patient from other infections and leading it to convalescence.
The detection of HBsAb has become important for the follow up of patients infected by HBV and the monitoring of recipients upon vaccination with synthetic and natural HBsAg.

C. PRINCIPLE OF THE TEST

Microplates are coated with a preparation of highly purified HBsAg that in the first incubation with sample specifically captures anti HBsAg antibodies to the solid phase.
After washing, captured antibodies are detected by an HBsAg, labelled with peroxidase (HRP), that specifically binds the second available binding site of these antibodies.
The enzyme specifically bound to wells, by acting on the substrate/chromogen mixture, generates an optical signal that is proportional to the amount of HBsAb in the sample and can be detected by an ELISA reader.
The amount of antibodies may be quantitated by means of a standard curve calibrated against the W.H.O reference preparation.
Samples are pre treated in the well with an specimen diluent able to block interference present in vaccinated individuals.

D. COMPONENTS

Each kit contains sufficient reagents to perform 96 tests.

1. Microplate: $\boxed{\text{MICROPLATE}}$

8x12 microwell strips coated with purified heat-inactivated HBsAg of both subtypes (ad and ay) from human origin and sealed into a bag with desiccant.
Allow the microplate to reach room temperature before opening; reseal unused strips in the bag with desiccant and store at 4°C.

2. Calibration Curve: CAL N° …
5x2.0 ml/vial. Ready to use and colour coded standard curve, derived from HBsAb positive plasma titrated on WHO standard for anti HBsAg (1st reference preparation 1977, lot 17-2-77), ranging: CAL1 = 0 mIU/ml // CAL2 = 10 mIU/ml // CAL3 = 50 mIU/ml // CAL4 = 100 mIU/ml // CAL 5 = 250 mIU/ml.
Contains human serum proteins, 5% BSA, 10 mM phosphate buffer pH 7.4+/-0.1, 0.09% sodium azide and 0.1% Kathon GC as preservatives. Standards are blue coloured.

3. Wash buffer concentrate: WASHBUF 20X
1x60ml/bottle. 20x concentrated solution.
Once diluted, the wash solution contains 10 mM phosphate buffer pH 7.0+/-0.2, 0.05% Tween 20 and 0.1% Kathon GC.

4. Enzyme conjugate : CONJ
1x16.0 ml/vial. Ready-to-use solution and red color coded.
It contains inactivated purified HBsAg of both subtypes ad and ay, labelled with HRP, 5% BSA, 10 mM Tris buffer pH 6.8+/-0.1, 0.3 mg/ml gentamicine sulphate and 0.1% Kathon GC as preservatives.

5. Chromogen/Substrate: SUBS TMB
1x16ml/vial. Contains a 50 mM citrate-phosphate buffered solution at pH 3.5-3.8, 4% dimethylsulphoxide, 0.03% tetra-methyl-benzidine (TMB) and 0.02% hydrogen peroxide (H2O2).
Note: To be stored protected from light as sensitive to strong illumination.

6. Sulphuric Acid: H2SO4 0.3 M
1x15ml/vial. Contains 0.3 M H_2SO_4 solution.
Attention: Irritant (H315, H319; P280, P302+P352, P332+P313, P305+P351+P338, P337+P313, P362+P363).

7. Specimen Diluent: DILSPE
1x8ml. 10 mM Tris Buffered solution ph 7.4 +/-0.1,suggested to be used in the follow up of vaccination. It contains 0.09% sodium azide as preservatives.

8. Control Serum: CONTROL …ml
1 vial. Lyophilized.
Contains fetal bovine serum proteins, human anti HBsAg antibodies calibrated at 50 ± 10% WHO mIU/ml. 0.3 mg/ml gentamicine sulphate and 0.1% Kathon GC as preservatives.

9. Plate sealing foil n° 2

10. Package insert n° 1

E. MATERIALS REQUIRED BUT NOT PROVIDED

1. Calibrated Micropipettes (100ul and 50ul) and disposable plastic tips.
2. EIA grade water (double distilled or deionised, charcoal treated to remove oxidizing chemicals used as disinfectants).
3. Timer with 60 minute range or higher.
4. Absorbent paper tissues.
5. Calibrated ELISA microplate thermostatic incubator (dry or wet), set at +37°C (+/-1°C tolerance)..
6. Calibrated ELISA microwell reader with 450nm (reading) and with 620-630nm (blanking, strongly recommended) filters.
7. Calibrated ELISA microplate washer.
8. Vortex or similar mixing tools.

F. WARNINGS AND PRECAUTIONS

1. The kit has to be used by skilled and properly trained technical personnel only, under the supervision of a medical doctor responsible of the laboratory.
2. All the personnel involved in performing the assay have to wear protective laboratory clothes, talc-free gloves and glasses. The use of any sharp (needles) or cutting (blades) devices should be avoided. All the personnel involved should be trained in biosafety procedures, as recommended by the Center for Disease Control, Atlanta, U.S. and reported in the National Institute of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
3. All the personnel involved in sample handling should be vaccinated for HBV and HAV, for which vaccines are available, safe and effective.
4. The laboratory environment should be controlled so as to avoid contaminants such as dust or air-born microbial agents, when opening kit vials and microplates and when performing the test. Protect the Chromogen (TMB) from strong light and avoid vibration of the bench surface where the test is undertaken.
5. Upon receipt, store the kit at 2..8°C into a temperature controlled refrigerator or cold room.
6. Do not interchange components between different lots of the kits. It is recommended that components between two kits of the same lot should not be interchanged.
7. Check that the reagents are clear and do not contain visible heavy particles or aggregates. If not, advise the laboratory supervisor to initiate the necessary procedures for kit replacement.
8. Avoid cross-contamination between serum/plasma samples by using disposable tips and changing them after each sample.
9. Avoid cross-contamination between kit reagents by using disposable tips and changing them between the use of each one.
10. Do not use the kit after the expiration date stated on the external container and internal (vials) labels. A study conducted on an opened kit did not pointed out any relevant loss of activity up to six 6 uses of the device and up to 6 months.
11. Treat all specimens as potentially infective. All human serum specimens should be handled at Biosafety Level 2, as recommended by the Center for Disease Control, Atlanta, U.S. in compliance with what reported in the Institutes of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
12. The use of disposable plastic-ware is recommended in the preparation of the liquid components or in transferring components into automated workstations, in order to avoid cross contamination.
13. Waste produced during the use of the kit has to be discarded in compliance with national directives and laws concerning laboratory waste of chemical and biological substances. In particular, liquid waste generated from the washing procedure, from residuals of controls and from samples has to be treated as potentially infective material and inactivated before waste. Suggested procedures of inactivation are treatment with a 10% final concentration of household bleach for 16-18 hrs or heat inactivation by autoclave at 121°C for 20 min..
14. Accidental spills from samples and operations have to be adsorbed with paper tissues soaked with household bleach and then with water. Tissues should then be discarded in proper containers designated for laboratory/hospital waste.
15. The Sulphuric Acid is an irritant. In case of spills, wash the surface with plenty of water
16. Other waste materials generated from the use of the kit (example: tips used for samples and controls, used microplates) should be handled as potentially infective and disposed according to national directives and laws concerning laboratory wastes.

G. SPECIMEN: PREPARATION AND WARNINGS

1. Blood is drawn aseptically by venipuncture and plasma or serum is prepared using standard techniques of preparation of samples for clinical laboratory analysis. No influence has been observed in the preparation of the sample with citrate, EDTA and heparin.

2. Samples have to be clearly identified with codes or names in order to avoid misinterpretation of results. Bar code labeling and electronic reading is strongly recommended.
3. Haemolysed ("red") and visibly hyperlipemic ("milky") samples have to be discarded as they could generate false results. Samples containing residues of fibrin or heavy particles or microbial filaments and bodies should be discarded as they could give rise to false results.
4. Sera and plasma can be stored at +2°..8°C for up to five days after collection. For longer storage periods, samples can be stored frozen at –20°C for several months. Any frozen samples should not be freezed/thawed more than once as this may generate particles that could affect the test result.
5. If particles are present, centrifuge at 2.000 rpm for 20 min or filter using 0.2-0.8u filters to clean up the sample for testing.
6. Samples whose anti-HBsAg antibody concentration is expected to be higher than 250 mIU/ml should be diluted before use either 1:10 or 1:100 in the Calibrator 0 mIU/ml. Dilutions have to be done in clean disposable tubes by diluting 50 ul of each specimen with 450 ul of Cal 0 (1:10). Then 50 ul of the 1:10 dilution are diluted with 450 ul of the Cal 0 (1:100). Mix tubes thoroughly on vortex when preparing the diluted samples.

H. PREPARATION OF COMPONENTS AND WARNINGS

1. Microplate:
Allow the microplate to reach room temperature (about 1 hr) before opening the container. Check that the desiccant has not turned green, indicating a defect in conservation.
In this case, call Dia.Pro's customer service.
Unused strips have to be placed back into the aluminum pouch, with the desiccant supplied, firmly zipped and stored at +2°-8°C. After first opening, remaining strips are stable until the humidity indicator inside the desiccant bag turns from yellow to green.

2. Calibration Curve
Ready to use. Mix well on vortex before use.

3. Control Serum
Add the volume of ELISA grade water, reported on the label, to the lyophilised powder; let fully dissolve and then gently mix on vortex.
Note: *The control after dissolution is not stable. Store frozen in aliquots at –20°C.*

4. Wash buffer concentrate:
The whole content of the concentrated solution has to be diluted 20x with bidistilled water and mixed gently end-over-end before use. During preparation avoid foaming as the presence of bubbles could impact on the efficiency of the washing cycles.
Note: Once diluted, the wash solution is stable for 1 week at +2..8° C.

5. Enzyme conjugate:
Ready to use. Mix well on vortex before use.
Avoid contamination of the liquid with oxidising chemicals, dust or microbes. If this component has to be transferred, use only plastic, and if possible, sterile disposable containers.

6. Specimen Diluent:
Ready to use. Mix well on vortex before use.

7. Chromogen/Substrate:
Ready to use. Mix well on vortex before use.
Avoid contamination of the liquid with oxidising chemicals, air-driven dust or microbes. Do not expose to strong light, oxidising agents and metallic surfaces.
If this component has to be transferred use only plastic, and if possible, sterile disposable container

8. Sulphuric Acid:
Ready to use. Mix well on vortex before use.
Attention: Irritant (H315, H319; P280, P302+P352, P332+P313, P305+P351+P338, P337+P313, P362+P363).

Legenda:

Warning **H statements:**
H315 – Causes skin irritation.
H319 – Causes serious eye irritation.

Precautionary **P statements:**
P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P302 + P352 – IF ON SKIN: Wash with plenty of soap and water.
P332 + P313 – If skin irritation occurs: Get medical advice/attention.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337 + P313 – If eye irritation persists: Get medical advice/attention.
P362 + P363 – Take off contaminated clothing and wash it before reuse.

I. INSTRUMENTS AND TOOLS USED IN COMBINATION WITH THE KIT

1. Micropipettes have to be calibrated to deliver the correct volume required by the assay and must be submitted to regular decontamination (70% ethanol, 10% solution of bleach, hospital grade disinfectants) of those parts that could accidentally come in contact with the sample or the components of the kit. They should also be regularly maintained in order to show a precision of 1% and a trueness of ±2%.
2. The ELISA incubator has to be set at +37°C (tolerance of ±1°C) and regularly checked to ensure the correct temperature is maintained. Both dry incubators and water baths are suitable for the incubations, provided that the instrument is validated for the incubation of ELISA tests.
3. The ELISA washer is extremely important to the overall performances of the assay. The washer must be carefully validated and correctly optimized using the kit controls/calibrator and reference panels, before using the kit for routine laboratory tests. Usually 4-5 washing cycles (aspiration + dispensation of 350ul/well of washing solution = 1 cycle) are sufficient to ensure that the assay performs as expected. A soaking time of 20-30 seconds between cycles is suggested. In order to set correctly their number, it is recommended to run an assay with the kit controls/calibrator and well-characterized negative and positive reference samples, and check to match the values reported below in the sections "Validation of Test" and "Assay Performances". Regular calibration of the volumes delivered and maintenance (decontamination and cleaning of needles) of the washer has to be carried out according to the instructions of the manufacturer.
4. Incubation times have a tolerance of ±5%.
5. The ELISA microplate reader has to be equipped with a reading filter of 450nm and with a second filter (620-630nm, strongly recommended) for blanking purposes. Its standard performances should be (a) bandwidth ≤ 10 nm; (b) absorbance range from 0 to ≥ 2.0; (c) linearity to ≥ 2.0; repeatability ≥ 1%. Blanking is carried out on the well identified in the section "Assay Procedure". The optical system of the reader has to be calibrated regularly to ensure that the correct optical density is measured. It should be regularly maintained according to the manufacturer 's instructions.
6. When using an ELISA automated workstation, all critical steps (dispensation, incubation, washing, reading, shaking, data handling) have to be carefully set, calibrated, controlled and regularly serviced in order to match the

values reported in the sections "Validation of Test" and "Assay Performances". The assay protocol has to be installed in the operating system of the unit and validated as for the washer and the reader. In addition, the liquid handling part of the station (dispensation and washing) has to be validated and correctly set. Particular attention must be paid to avoid carry over by the needles used for dispensing samples and for washing. This must be studied and controlled to minimize the possibility of contamination of adjacent wells due to strongly reactive samples, leading to false positive results. The use of ELISA automated work stations is recommended for blood screening and when the number of samples to be tested exceed 20-30 units per run.

7. Dia.Pro's customer service offers support to the user in the setting and checking of instruments used in combination with the kit, in order to assure full compliance with the requirements described. Support is also provided for the installation of new instruments to be used with the kit.

L. PRE ASSAY CONTROLS AND OPERATIONS

1. Check the expiration date of the kit printed on the external label of the kit box. Do not use if expired.
2. Check that the liquid components are not contaminated by naked-eye visible particles or aggregates. Check that the Chromogen/Substrate is colorless or pale blue by aspirating a small volume of it with a sterile transparent plastic pipette. Check that no breakage occurred in transportation and no spillage of liquid is present inside the box. Check that the aluminum pouch, containing the microplate, is not punctured or damaged.
3. Dilute all the content of the 20x concentrated Wash Solution as described above.
4. Dissolve the Control Serum as described above.
5. Allow all the other components to reach room temperature (about 1 hr) and then mix as described.
6. Set the ELISA incubator at +37°C and prepare the ELISA washer by priming with the diluted washing solution, according to the manufacturers instructions. Set the right number of washing cycles as found in the validation of the instrument for its use with the kit.
7. Check that the ELISA reader has been turned on at least 20 minutes before reading.
8. If using an automated workstation, turn it on, check settings and be sure to use the right assay protocol.
9. Check that the micropipettes are set to the required volume.
10. Check that all the other equipments are available and ready to use.

In case of problems, do not proceed further with the test and advise the supervisor.

M. ASSAY PROCEDURE

The assay has to be carried out according to what reported below, taking care to maintain the same incubation time for all the samples in testing.

Two procedures can be carried out with the device according to the request of the clinician.

M.1 Quantitative analysis

1. Place the required number of strips in the microplate holder. Leave A1 and B1 wells empty for the operation of blanking.
Store the other strips into the bag in presence of the desiccant at 2..8°C, sealed.
Then Dispense in all the wells to be used for the test, except for A1 and B1, 50µl of the Specimen Diluent.

Important note: *This additive is added before distributing samples and controls into specific wells and is particularly intended for blocking some substances present in people undergoing vaccination and capable to mask antibodies.*

2. Pipette 100µl of all the Calibrators, 100µl of Control Serum in duplicate and then 100ul of samples. The Control Serum is used to verify that the whole analytical system works as expected. Check that Calibrators, Control Serum and samples have been correctly added. Then incubate the microplate at **+37°C for 60 min**.

Important note: *Strips have to be sealed with the adhesive sealing foil only when the test is performed manually. Do not cover strips when using ELISA automatic instruments.*

3. Wash the microplate as reported in section I.3.

4. In all the wells except A1 and B1, pipette 100 µl Enzyme Conjugate. Check that the reagent has been correctly added. Incubate the microplate at **+37°C for 60 minutes.**

Important note:

1) *Be careful not to touch the inner surface of the well with the pipette tip when dispensing the Enzyme Conjugate. Contamination might occur.*
2) *Mix thoroughly the Enzyme Conjugate on vortex before use.*

5. Wash the microplate as described.
6. Pipette 100µl TMB/H_2O_2 mixture in each well, the blank wells included. Check that the reagent has been correctly added. Then incubate the microplate at **room temperature for 20 minutes**.

Important note: *Do not expose to strong direct light as a high background might be generated.*

7. Stop the enzymatic reaction by pipette 100µl Sulphuric Acid into each well and using the same pipetting sequence as in step 6. Then measure the colour intensity with a microplate reader at 450nm (reading) and at 620-630nm (blanking, strongly recommended), blanking the instrument on A1 and B1 wells.

M.2 Qualitative analysis

1. Place the required number of strips in the microplate holder. Leave A1 well empty for the operation of blanking.
Store the other strips into the bag in presence of the desiccant at 2..8°C, sealed.
2. Dispense 50 ul Specimen Diluent in all the wells, except for the blank A1. Then pipette 100µl of the Calibrator 0 mIU/ml in duplicate, 100µl of the Calibrator 10 mIU/ml in duplicate, 100µl of the Calibrator 250 mIU/ml in single, and then 100ul of samples. Check that Calibrators and samples have been correctly added. Then incubate the microplate at **+37°C for 60 min**.
3. Wash the microplate as reported in section I.3.
4. In all the wells except A1, pipette 100 µl Enzyme Conjugate. Check that the reagent has been correctly added. Incubate the microplate at **+37°C for 60 minutes.**

Important note:

3) *Be careful not to touch the inner surface of the well with the pipette tip when dispensing the Enzyme Conjugate. Contamination might occur.*
4) *Mix thoroughly the Enzyme Conjugate on vortex before use.*

5. Wash the microplate as described.
6. Pipette 100µl TMB/H_2O_2 mixture in each well, the blank wells included. Check that the reagent has been correctly added. Then incubate the microplate at **room temperature for 20 minutes**.

Important note: *Do not expose to strong direct light as a high background might be generated.*

7. Stop the enzymatic reaction by pipette 100µl Sulphuric Acid into each well and using the same pipetting sequence as in step 6. Then measure the colour intensity with a microplate reader at 450nm (reading) and at 620-630nm (blanking, strongly recommended), blanking the instrument on A1 and B1 wells.

Important general notes:

1. *If the second filter is not available, ensure that no finger prints are present on the bottom of the microwell before reading at 450nm. Finger prints could generate false positive results on reading.*
2. *Reading has should ideally be performed immediately after the addition of the Stop Solution but definitely no longer than 20 minutes afterwards. Some self oxidation of the chromogen can occur leading to a higher background.*
3. *The Control Serum (CS) does not affect the cut-off calculation and therefore the test results calculation. The Control Serum may be used only when a laboratory internal quality control is required by the management.*

N. ASSAY SCHEME (standard procedure)

Specimen Diluent Calibrators Control Serum Samples	50 ul 100 ul 100 ul 100 ul
1st incubation	**60 min**
Temperature	+37°C
Wash step	*4-5 cycles*
Enzyme Conjugate	100 ul
2nd incubation	**60 min**
Temperature	+37°C
Wash step	*4-5 cycles*
TMB/H2O2 mix	100 ul
3rd incubation	**20 min**
Temperature	r.t.
Sulphuric Acid	100 ul
Reading OD	450nm & 620nm

An example of dispensation scheme in quantitative assays is reported below:

Microplate

	1	2	3	4	5	6	7	8	9	10	11	12
A	BLK	CAL4	S3									
B	BLK	CAL4	S4									
C	CAL1	CAL5	S5									
D	CAL1	CAL5	S6									
E	CAL2	CS	S7									
F	CAL2	CS	S8									
G	CAL3	S1	S9									
H	CAL3	S2	S10									

Legenda: BLK = Blank // CAL = Calibrators // CS = Control Serum // S = Sample

An example of dispensation scheme in qualitative assays is reported below:

Microplate

	1	2	3	4	5	6	7	8	9	10	11	12
A	BLK	S 3	S 11									
B	CAL1	S 4	S 12									
C	CAL1	S 5	S 13									
D	CAL2	S 6	S 14									
E	CAL2	S 7	S 15									
F	CAL5	S 8	S 16									
G	S1	S 9	S 17									
H	S2	S 10	S 18									

Legenda: BLK = Blank // CAL = Calibrators // S = Sample

O. INTERNAL QUALITY CONTROL

A validation check is carried out on the controls any time the kit is used in order to verify whether the performances of the assay are as qualified.
Control that the following data are matched:

Parameters	Requirements
Blank well	< 0.100 OD450nm
Calibrator 0 WHO mIU/ml	< 0.200 OD450nm after blanking
Calibrator 10 WHO mIU/ml	OD450nm higher than the OD450nm of the Calibrator 0 mIU/ml + 0.100
Calibrator 250 WHO mIU/ml	> 1.500 OD450nm
Control Serum	OD450nm = OD450nm CAL 50 mIU/ml ± 10%
Coefficient of variation	< 30% for the Calibrator 0 mIU/ml

If the results of the test match the requirements stated above, proceed to the next section.
If they do not, do not proceed any further and perform the following checks:

Problem	Check
Blank well > 0.100 OD450nm	1. that the Chromogen/Substrate solution has not become contaminated during the assay
Calibrator 0 mIU/ml > 0.200 coefficient of variation > 30%	1. that the washing procedure and the washer settings are as validated in the pre qualification study; 2. that the proper washing solution has been used and the washer has been primed with it before use; 3. that no mistake has been done in the assay procedure when the dispensation of standards is carried out; 4. that no contamination of the Cal 0 mIU/ml or of the wells where it was dispensed has occurred due to positive samples, to spills or to the enzyme conjugate; 5. that micropipettes have not become contaminated with positive samples or with the enzyme conjugate 6. that the washer needles are not blocked or partially obstructed.

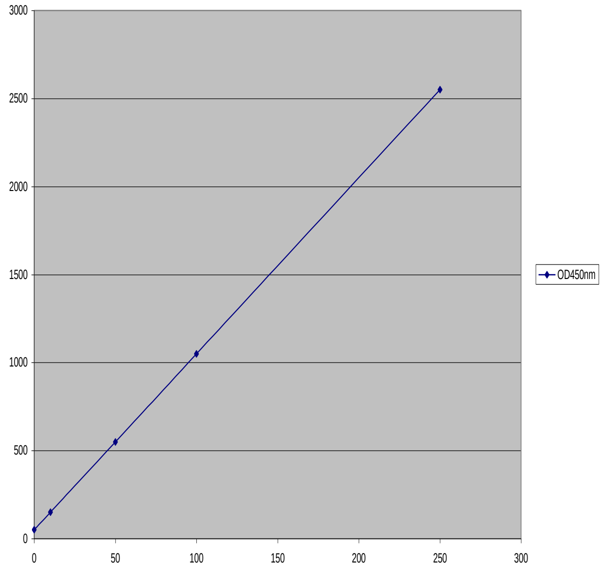
Calibrator 10 mIU/ml OD450nm < Cal 0 + 0.100	1. that the procedure has been correctly performed; 2. that no mistake has occurred during its distribution (ex.: dispensation of a wrong calibrator); 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the standard has occurred.
Calibrator 250 mIU/ml < 1.500 OD450nm	1. that the procedure has been correctly performed; 2. that no mistake has occurred during its distribution; 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the standard has occurred.
Control Serum Different from expected value	First verify that: 1. the procedure has been correctly performed; 2. no mistake has occurred during its distribution (ex.: dispensation of a wrong sample); 3. the washing procedure and the washer settings are correct; 4. no external contamination of the standard has occurred. 5. the Control Serum has been dissolved with the right volume reported on the label. If a mistake has been pointed out, the assay has to be repeated after eliminating the reason of this error. If no mistake has been found, proceed as follows: **a**) a value up to +/-20% is obtained: the overall Precision of the laboratory might not enable the test to match the expected value +/-10%. Report the problem to the Supervisor for acceptance or refusal of this result. **b**) a value higher than +/-20% is obtained: in this case the test is invalid and the DiaPro's customer service has to be called.

P. RESULTS

P.1 Quantitative method

If the test turns out to be valid, use for the quantitative method an approved curve fitting program to draw the calibration curve from the values obtained by reading at 450nm (4-parameters interpolation is suggested).
Then on the calibration curve calculate the concentration of anti HBsAg antibody in samples.
An example of Calibration curve is reported in the next page.

Example of Calibration Curve :



Important Note:
Do not use the calibration curve above to make calculations.

P.2 Qualitative method

In the qualitative method, calculate the mean OD450nm values for the Calibrators 0 and 10 mIU/ml and then check that the assay is valid.

Example of calculation:

The following data must not be used instead or real figures obtained by the user.

Calibrator 0 mIU/ml: 0.020 – 0.024 OD450nm
Mean Value: 0.022 OD450nm
Lower than 0.200 – Accepted

Calibrator 10 mIU/ml: 0.250 – 0.270 OD450nm
Mean Value: 0.260 OD450nm
Higher than Cal 0 + 0.100 – Accepted

Calibrator 250 mIU/ml: 2.845 OD450nm
Higher than 1.500 – Accepted

Q. INTERPRETATION OF RESULTS

Samples with a concentration lower than 10 WHO mIU/ml are considered negative for anti HBsAg antibody by most of the international medical literature.
Samples with a concentration higher than 10 WHO mIU/ml are considered positive for anti HBsAg antibody.
In the follow up of vaccination recipients, however, the value of 20 WHO mIU/ml is usually accepted by the medical literature as the minimum concentration at which the patient is considered clinically protected against HBV infection.

Important notes:

1. *Interpretation of results should be done under the supervision of the laboratory supervisor to reduce the risk of judgement errors and misinterpretations.*
2. *When test results are transmitted from the laboratory to another facility, attention must be paid to avoid erroneous data transfer.*
3. *Diagnosis has to be done and released to the patient by a suitably qualified medical doctor.*

R. PERFORMANCES

Evaluation of Performances has been conducted in accordance to what reported in the Common Technical Specifications or CTS (art. 5, Chapter 3 of IVD Directive 98/79/EC).

1. LIMIT OF DETECTION:

The limit of detection of the assay has been calculated by means of the HBsAb international preparation supplied by CLB on behalf of WHO (1st reference preparation 1977, lot 17-2-77), on which Calibration Curve has been calibrated. HBV negative serum was used as diluent, as recommended by the supplier. Results of Quality Control are given in the following table:

WHO mIU/ml	SAB.CE Lot # 1002	SAB.CE Lot # 1001	SAB.CE Lot # 1002/2
50	0.933	0.812	0.846
10	0.219	0.192	0.194
5	0.110	0.096	0.104
2.5	0.057	0.058	0.067
Std 0	0.021	0.015	0.023

2. DIAGNOSTIC SPECIFICITY AND SENSITIVITY

A Performance Evaluation has been conducted on a total number of more than 700 samples.

2.1 Diagnostic Specificity

It is defined as the probability of the assay of scoring negative in the absence of specific analyte.
More than 500 negative specimens were tested, internally and externally, against a European company.
A diagnostic specificity of 98.8% was assessed. .
Moreover, diagnostic specificity was assessed by testing 113 potentially interfering specimens (other infectious diseases, patients affected by non viral hepatic diseases, dialysis patients, pregnant women, hemolized, lipemic, etc.) against the European company. A value of specificity of 100% was assessed.
Finally, both human plasma, derived with different standard techniques of preparation (citrate, EDTA and heparin), and human sera have been used to determine the specificity.
No false reactivity due to the method of specimen preparation has been observed.

2.2 Diagnostic Sensitivity

It defined as the probability of the assay of scoring positive in the presence of specific analyte.
106 vaccinated patients were evaluated providing a diagnostic sensitivity of 100%.
More than 100 HBV naturally infected patients were tested, internally and externally, against the European company; a diagnostic sensitivity of 100% was found.

3. PRECISION:

The mean values obtained from a study conducted on three samples of different anti-HBsAg reactivity, examined in 16 replicates in three separate runs is reported below:

SAB.CE: lot # 1202

Calibrator 0 mIU/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.038	0.038	0.039	0.039
Std.Deviation	0.003	0.004	0.005	0.004
CV %	8.8	9.5	11.8	10.0

Calibrator 10 mIU/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.250	0.243	0.244	0.246
Std.Deviation	0.020	0.023	0.017	0.020
CV %	8.0	9.3	7.0	8.1

Calibrator 250 mIU/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	2.998	3.000	3.259	3.085
Std.Deviation	0.152	0.151	0.158	0.153
CV %	5.1	5.0	4.8	5.0

SAB.CE: lot # 1002

Calibrator 0 mIU/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.048	0.048	0.050	0.049
Std.Deviation	0.005	0.004	0.006	0.005
CV %	9.4	8.4	11.5	9.8

Calibrator 10 mIU/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.249	0.252	0.242	0.248
Std.Deviation	0.021	0.020	0.023	0.021
CV %	8.3	7.9	9.6	8.6

Calibrator 250 mIU/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	3.544	3.653	3.612	3.603
Std.Deviation	0.153	0.176	0.138	0.156
CV %	4.3	4.8	3.8	4.3

SAB.CE: lot # 1002/2

Calibrator 0 mIU/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.050	0.051	0.050	0.050
Std.Deviation	0.005	0.006	0.006	0.005
CV %	10.0	10.9	11.9	10.9

Calibrator 10 mIU/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.226	0.238	0.239	0.234
Std.Deviation	0.015	0.017	0.018	0.016
CV %	6.5	7.0	7.5	7.0

Calibrator 250 mIU/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	3.526	3.457	3.499	3.494
Std.Deviation	0.137	0.143	0.162	0.147
CV %	3.9	4.1	4.6	4.2

The variability shown in the tables did not result in sample misclassification.

4. ACCURACY

The assay accuracy has been checked by the dilution and recovery tests. Any "hook effect", underestimation likely to happen at high doses of analyte, was ruled out up to 10.000 mIU/ml.

S. LIMITATIONS OF THE PROCEDURE

Bacterial contamination or heat inactivation of the specimen may affect the absorbance values of the samples with consequent alteration of the level of the analyte.
This test is suitable only for testing single samples and not pooled ones.
Diagnosis of an infectious disease should not be established on the basis of a single test result. The patient's clinical history, symptomatology, as well as other diagnostic data should be considered.

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All the IVD Products manufactured by the company are under the control of a certified Quality Management System approved by an EC Notified Body. Each lot is submitted to a quality control and released into the market only if conforming with the EC technical specifications and acceptance criteria.

Manufacturer:
Dia.Pro Diagnostic Bioprobes Srl
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CE
0318

HDV Ab

Competitive Enzyme Immunoassay for the qualitative determination of antibodies to Hepatitis Delta Virus in human serum and plasma

- for "in vitro" diagnostic use only -

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REF DAB.CE
96 Tests

HDV Ab

A. INTENDED USE
Competitive Enzyme ImmunoAssay (ELISA) for the qualitative determination of antibodies to Hepatitis Delta Virus or HDV in human plasma and sera with a “two-steps” methodology.
The kit is used for the follow-up of patients infected by HDV.
For “in vitro” diagnostic use only.

B. INTRODUCTION
The Hepatitis Delta Virus or HDV is a RNA defective virus composed of a core presenting the delta-specific antigen, encapsulated by HBsAg, that requires the helper function of HBV to support its replication.
Infection by HDV occurs in the presence of acute or chronic HBV infection. When acute delta and acute HBV simultaneously occur, the illness becomes severe and clinical and biochemical features may be indistinguishable from those of HBV infection alone. In contrast, a patient with chronic HBV infection can support HDV replication indefinitely, usually with a less severe illness appearing as a clinical exacerbation.
The determination of HDV specific serological markers (HDV Ag, HDV Ab, HDV IgM and HDV IgG) represents in these cases an important tool to the clinician for the classification of the etiological agent, for the follow up of infected patients and their treatment. The detection of HDV total antibodies allows the classification of the illness and the monitoring of the seroconversion event.

C. PRINCIPLE OF THE TEST
Anti-HDV antibodies, if present in the sample, compete with a virus-specific polyclonal IgG, labeled with peroxidase (HRP), for a fixed amount of rec-HDV coated on the microplate. The test is carried out with a two steps incubation competitive system. First the sample is added to the plate and specific anti HDV antibodies bind to the adsorbed antigen. After washing, an enzyme conjugated antibody to HDV is added and binds to the free portion of the antigen coated. After washing a chromogen/substrate mixture is dispensed. The concentration of the bound enzyme on the solid phase becomes inversely proportional to the amount of anti-HDV antibodies in the sample and its activity is detected by the added chromogen/substrate. The concentration of HDV-specific antibodies in the sample is determined by means of a cut-off value that allows for the semi quantitative detection of anti-HDV antibodies.

D. COMPONENTS
Each kit contains sufficient reagents to perform 96 tests.

1. Microplate: MICROPLATE
8x12 microwell strips coated with recombinant HDV-specific antigen and sealed into a bag with desiccant. Allow the microplate to reach room temperature before opening; reseal unused strips in the bag with desiccant and store at 4°C.

2. Negative Control: CONTROL -
1x2.0ml/vial. Ready to use. Contains goat serum proteins, 100 mM Tris-HCl buffer pH 7.4 +/-0.1, 0.09% Sodium Azide and 0.045% ProClin 300 as preservatives. The negative control is colour coded pale yellow.

3. Positive Control: CONTROL +
1x2.0ml/vial. Ready to use. Contains goat serum proteins, high titer anti HDV antibodies, 100 mM Tris-HCl buffer pH 7.4 +/-0.1, 0.09% Sodium Azide and 0.045% ProClin 300 as preservatives. The positive control is colour coded green.

4. Calibrator: CAL ….
n° 1 vial. Lyophilised. To be dissolved with EIA grade water as reported in the label. Contains bovine serum proteins, low titer human antibodies to HDV, 0.2 mg/ml gentamicine sulphate and 0.045% ProClin 300 as preservatives.
Note: The volume necessary to dissolve the content of the vial may vary from lot to lot. Please use the right volume reported on the label.

5. Wash buffer concentrate: WASHBUF 20X
1x60ml/bottle. 20x concentrated solution.
Once diluted, the wash solution contains 10 mM phosphate buffer pH 7.0+/-0.2, 0.05% Tween 20 and 0.045% ProClin 300.

6. Enzyme conjugate: CONJ
1x16ml/vial. Ready-to-use solution. Contains 5% bovine serum albumine, 10 mM tris buffer pH 6.8 +/-0.1, Horseradish peroxidase conjugated antibody to HDV in presence of 0.2 mg/ml gentamicine sulphate and 0.045% ProClin 300 as preservatives. The component is colour coded red.

7. Chromogen/Substrate: SUBS TMB
1x16ml/vial. Contains a 50 mM citrate-phosphate buffered solution at pH 3.5-3.8, 4% DMSO, 0.03% tetra-methyl-benzidine or TMB and 0.02% hydrogen peroxide of H_2O_2.
Note: To be stored protected from light as sensitive to strong illumination.

8. Sulphuric Acid: H_2SO_4 0.3 M
1x15ml/vial. Contains 0.3 M H_2SO_4 solution.
Attention: Irritant (H315, H319; P280, P302+P352, P332+P313, P305+P351+P338, P337+P313, P362+P363).

Plate sealers n° 2

Instructions for Use n° 1

E. MATERIALS REQUIRED BUT NOT PROVIDED
1. Calibrated Micropipettes in the range 10-1000 ul and disposable plastic tips.
2. EIA grade water (double distilled or deionized, charcoal treated to remove oxidizing chemicals used as disinfectants).
3. Timer with 60 minute range or higher.
4. Absorbent paper tissues.
5. Calibrated ELISA microplate thermostatic incubator (dry or wet) set at +37°C.
6. Calibrated ELISA microwell reader with 450nm (reading) and with 620-630nm (blanking) filters.
7. Calibrated ELISA microplate washer.
8. Vortex or similar mixing tools.

F. WARNINGS AND PRECAUTIONS
1. The kit has to be used by skilled and properly trained technical personnel only, under the supervision of a medical doctor responsible of the laboratory.
2. All the personnel involved in performing the assay have to wear protective laboratory clothes, talc-free gloves and glasses. The use of any sharp (needles) or cutting (blades) devices should be avoided. All the personnel involved should be trained in biosafety procedures, as recommended by the Center for Disease Control, Atlanta, U.S. and reported in the National Institute of Health’s publication: “Biosafety in Microbiological and Biomedical Laboratories”, ed. 1984.
3. All the personnel involved in sample handling should be vaccinated for HBV and HAV, for which vaccines are available, safe and effective.

4. The laboratory environment should be controlled so as to avoid contaminants such as dust or air-born microbial agents, when opening kit vials and microplates and when performing the test. Protect the Chromogen/Substrate (TMB/H_2O_2) from strong light and avoid vibration of the bench surface where the test is undertaken.
5. Upon receipt, store the kit at +2..8°C into a temperature controlled refrigerator or cold room.
6. Do not interchange components between different lots of the kits. It is recommended that components between two kits of the same lot should not be interchanged.
7. Check that the reagents are clear and do not contain visible heavy particles or aggregates. If not, advise the laboratory supervisor to initiate the necessary procedures.
8. Avoid cross-contamination between serum/plasma samples by using disposable tips and changing them after each sample. Do not reuse disposable tips.
9. Avoid cross-contamination between kit reagents by using disposable tips and changing them between the use of each one. Do not reuse disposable tips.
10. Do not use the kit after the expiration date stated on external (primary container) and internal (vials) labels.
11. Treat all specimens as potentially infective. All human serum specimens should be handled at Biosafety Level 2, as recommended by the Center for Disease Control, Atlanta, U.S. in compliance with what reported in the Institutes of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
12. The use of disposable plastic labware is recommended in the preparation of the washing solution or in transferring components into other containers of automated workstations, in order to avoid contamination.
13. Waste produced during the use of the kit has to be discarded in compliance with national directives and laws concerning laboratory waste of chemical and biological substances. In particular, liquid waste generated from the washing procedure, from residuals of controls and from samples has to be treated as potentially infective material and inactivated. Suggested procedures of inactivation are treatment with a 10% final concentration of household bleach for 16-18 hrs or heat inactivation by autoclave at 121°C for 20 min..
14. Accidental spills have to be adsorbed with paper tissues soaked with household bleach and then with water. Tissues should then be discarded in proper containers designated for laboratory/hospital waste.
15. The Sulphuric Acid is an irritant. In case of spills, wash the surface with plenty of water.
16. Other waste materials generated from the use of the kit (example: tips used for samples and controls, used microplates) should be handled as potentially infective and disposed according to national directives and laws concerning laboratory wastes.

G. SPECIMEN: PREPARATION AND RECOMMANDATIONS

1. Blood is drawn aseptically by venepuncture and plasma or serum is prepared using standard techniques of preparation of samples for clinical laboratory analysis. No influence has been observed in the preparation of the sample with citrate, EDTA and heparin.
2. Avoid any addition of preservatives to samples; especially sodium azide as this chemical would affect the enzymatic activity of the conjugate.
3. Samples have to be clearly identified with codes or names in order to avoid misinterpretation of results. When the kit is used for the screening of blood units, bar code labeling and electronic reading is strongly recommended.
4. Haemolysed (red) and visibly hyperlipemic ("milky") samples have to be discarded as they could generate false results. Samples containing residues of fibrin or heavy particles or microbial filaments and bodies should be discarded as they could give rise to false results.
5. Sera and plasma can be stored at +2°…+8°C in primary collection tubes for up to five days after collection.
   Do not freeze primary tubes of collection. For longer storage periods, sera and plasma samples, carefully removed from the primary collection tube, can be stored frozen at –20°C for at least 12 months. Any frozen samples should not be frozen/thawed more than once as this may generate particles that could affect the test result.
6. If particles are present, centrifuge at 2.000 rpm for 20 min or filter using 0.2-0.8u filters to clean up the sample for testing.

H. PREPARATION OF COMPONENTS AND WARNINGS

A study conducted on an opened kit has not pointed out any relevant loss of activity up to 6 re-uses of the device and up to 3 months.

1. Antigen coated microwells:
Allow the microplate to reach room temperature (about 1 hr) before opening the container. Check that the desiccant has not turned dark green, indicating a defect in manufacturing.
In this case, call Dia.Pro's customer service.
Unused strips have to be placed back into the aluminium pouch, with the desiccant supplied, firmly zipped and stored at +2°-8°C. When opened the first time, unused strips are stable until the humidity indicator inside the desiccant bag turns from yellow to green.

2. Negative Control:
Ready to use. Mix well on vortex before use.

3. Positive Control:
Ready to use. Mix well on vortex before use.

4. Calibrator:
Low positive control. Add precisely the volume of EIA grade water, reported on its label, to the lyophilized powder; let fully dissolve and then gently mix on vortex.
Note: *The dissolved calibrator is not stable. Store it frozen in aliquots at –20°C. When thawed do not freeze again; discard it.*

5. Wash buffer concentrate:
The whole content of the 20x concentrated solution has to be diluted with EIA grade water up to 1200 ml and mixed gently end-over-end before use. During preparation avoid foaming as the presence of bubbles could impact on the efficiency of the washing cycles.
Note: *Once diluted, the wash solution is stable for 1 week at +2..8° C.*

6. Enzyme conjugate:
Ready to use. Mix well on vortex before use.
Avoid contamination of the liquid with oxidizing chemicals, dust or microbes. If this component has to be transferred, use only plastic, and if possible, sterile disposable containers.

7. Chromogen/Substrate:
Ready to use. Mix well on vortex before use.
Avoid contamination of the liquid with oxidizing chemicals, air-driven dust or microbes. Do not expose to strong light, oxidizing agents and metallic surfaces.
If this component has to be transferred use only plastic, and if possible, sterile disposable container

8. Sulphuric Acid:
Ready to use. Mix well on vortex before use.
Attention: Irritant (H315, H319; P280, P302+P352, P332+P313, P305+P351+P338, P337+P313, P362+P363).

Legenda:
Warning **H statements:**
H315 – Causes skin irritation.
H319 – Causes serious eye irritation.

Precautionary **P statements:**
P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P302 + P352 – IF ON SKIN: Wash with plenty of soap and water.
P332 + P313 – If skin irritation occurs: Get medical advice/attention.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337 + P313 – If eye irritation persists: Get medical advice/attention.
P362 + P363 – Take off contaminated clothing and wash it before reuse.

I. INSTRUMENTS AND TOOLS USED IN COMBINATION WITH THE KIT

1. Micropipettes have to be calibrated to deliver the correct volume required by the assay and must be submitted to regular decontamination (70% ethanol, 10% solution of bleach, hospital grade disinfectants) of those parts that could accidentally come in contact with the sample or the components of the kit. They should also be regularly maintained in order to show a precision of 1% and a trueness of ±2%.
2. The ELISA incubator has to be set at +37°C (tolerance of ±0.5°C) and regularly checked to ensure the correct temperature is maintained. Both dry incubators and water baths are suitable for the incubations, provided that the instrument is validated for the incubation of ELISA tests.
3. The **ELISA washer** is extremely important to the overall performances of the assay. The washer must be carefully validated in advance, checked for the delivery of the right dispensation volume and regularly submitted to maintenance according to the manufacturer's instructions for use. In particular the washer, at the end of the daily workload, has to be extensively cleaned out of salts with deionized water. Before use, the washer has to be extensively primed with the diluted Washing Solution.
   The instrument weekly has to be submitted to decontamination according to its manual (NaOH 0.1 M decontamination suggested).
   5 washing cycles (aspiration + dispensation of 350ul/well of washing solution + 20 sec soaking = 1 cycle) are sufficient to ensure the assay with the declared performances. If soaking is not possible add one more cycle of washing.
   An incorrect washing cycle or salt-blocked needles are the major cause of false positive reactions.
4. Incubation times have a tolerance of ±5%.
5. The ELISA microplate reader has to be equipped with a reading filter of 450nm and with a second filter of 620-630nm, mandatory for blanking purposes. Its standard performances should be (a) bandwidth ≤ 10 nm; (b) absorbance range from 0 to 4; (c) linearity to 4; repeatability ≥ 1%. Blanking is carried out on the well identified in the section "Assay Procedure". The optical system of the reader has to be calibrated regularly to ensure that the correct optical density is measured. It should be regularly maintained according to the manufacturer 's instructions.
6. When using an ELISA automated work station, all critical steps (dispensation, incubation, washing, reading, shaking, data handling) have to be carefully set, calibrated, controlled and regularly serviced in order to match the values reported in the sections "Validation of Test" and "Assay Performances". The assay protocol has to be installed in the operating system of the unit and validated as for the washer and the reader. In addition, the liquid handling part of the station (dispensation and washing) has to be validated and correctly set. Particular attention must be paid to avoid carry over by the needles used for dispensing samples and for washing. This must be studied and controlled to minimize the possibility of contamination of adjacent wells due to strongly reactive samples, leading to false positive results. The use of ELISA automated work stations is recommended for blood screening and when the number of samples to be tested exceed 20-30 units per run.
7. Dia.Pro's customer service offers support to the user in the setting and checking of instruments used in combination with the kit, in order to assure full compliance with the requirements described. Support is also provided for the installation of new instruments to be used with the kit.

L. PRE ASSAY CONTROLS AND OPERATIONS

1. Check the expiration date of the kit printed on the external label (primary container). Do not use if expired.
2. Check that the liquid components are not contaminated by visible particles or aggregates. Check that the Chromogen/Substrate is colorless or pale blue by aspirating a small volume of it with a sterile plastic pipette. Check that no breakage occurred in transportation and no spillage of liquid is present inside the box (primary container). Check that the aluminum pouch, containing the microplate, is not punctured or damaged.
3. Dilute all the content of the 20x concentrated Wash Solution as described above.
4. Dissolve the Calibrator as described above and gently mix.
5. Allow all the other components to reach room temperature (about 1 hr) and then mix gently on vortex all liquid reagents.
6. Set the ELISA incubator at +37°C and prepare the ELISA washer by priming with the diluted washing solution, according to the manufacturers instructions. Set the right number of washing cycles as reported in the specific section.
7. Check that the ELISA reader is turned on or ensure it will be turned on at least 20 minutes before reading.
8. If using an automated work station, turn on, check settings and be sure to use the right assay protocol.
9. Check that the micropipettes are set to the required volume.
10. Check that all the other equipment is available and ready to use.
11. In case of problems, do not proceed further with the test and advise the supervisor.

M. ASSAY PROCEDURE

The assay has to be carried out according to what reported below, taking care to maintain the same incubation time for all the samples in testing.

1. Place the required number of strips in the microplate holder. Leave A1 well empty for the operation of blanking.
Store the other strips into the bag in presence of the desiccant at +2..8°C, sealed.

2. Pipette 100 µl of Negative Control in triplicate, 100 µl Positive Control in single and then 100 µl of samples. Check that controls and samples have been correctly added.
Then incubate the microplate at **+37°C for 60 min**.

3. Wash the microplate as reported in section I.3.

4. In all the wells except A1, pipette 100 µl Enzyme Conjugate. Check that the reagent has been correctly added.
Then incubate the microplate at **+37°C for 60 min.**

Important note: *Be careful not to touch the inner surface of the well with the pipette tip when dispensing the Enzyme Conjugate. Contamination might occur.*

5. Wash the microplate as described.

6. Pipette 100 µl TMB/H_2O_2 mixture in each well, the blank wells included. Check that the reagent has been correctly added. Then incubate the microplate at **room temperature for 20 min**.

Important note: *Do not expose to strong direct light as a high background might be generated.*

7. Pipette 100 µl Sulphuric Acid into all the wells using the same pipetting sequence as in step n° 6 to stop the enzymatic reaction. Addition of the stop solution will turn the negative control and negative samples from blue to yellow.

8. Measure the colour intensity of the solution in each well, as described in section I.5 using a 450nm filter (reading) and a 620-630nm filter (background subtraction, mandatory), blanking the instrument on A1.

Important notes:

1. *Ensure that no finger prints are present on the bottom of the microwell before reading. Finger prints could generate false positive results on reading.*
2. *Reading has should ideally be performed immediately after the addition of the Stop Solution but definitely no longer than 20 minutes afterwards. Some self oxidation of the chromogen can occur leading to a higher background.*
3. *The use of the Calibrator, a low positive control, is not mandatory for the assay as the CAL does not enter into the cut-off calculation. The CAL may be used as a low titer positive control when a laboratory internal quality verification is required by the management. When used for such purpose, dispense 100 ul of it, possibly in duplicate.*

N. ASSAY SCHEME

Controls/Calibrator Samples	100 ul 100 ul
1st incubation	**60 min**
Temperature	+37°C
Washing step	n° 5 cycles with 20'' of soaking OR n° 6 cycles without soaking
Enzyme Conjugate	100 ul
2nd incubation	**60 min**
Temperature	+37°C
Washing step	n° 5 cycles with 20'' of soaking OR n° 6 cycles without soaking
TMB/H2O2 mix	100 ul
3rd incubation	**20 min**
Temperature	r.t.
Sulphuric Acid	100 ul
Reading OD	450nm / 620-630nm

An example of dispensation scheme (including CAL) is reported in the table below:

Microplate

	1	2	3	4	5	6	7	8	9	10	11	12
A	BLK	S2										
B	NC	S3										
C	NC	S4										
D	NC	S5										
E	CAL	S6										
F	CAL	S7										
G	PC	S8										
H	S1	S9										

Legenda: BLK = Blank NC = Negative Control
CAL = Calibrator PC = Positive Control S = Sample

O. INTERNAL QUALITY CONTROL

A check is performed on the negative and positive controls any time, and on the Calibrator in addition when the kit is used for the first time, in order to verify whether the expected OD450nm / 620-630nm or Co/S values have been matched in the analysis.
Ensure that the following parameters are met:

Parameter	Requirements
Blank well	< 0.100 OD450nm value
Negative Control (NC)	> 1.000 OD450nm after blanking If lower carefully control the washing procedure and decrease the number of cycles or the soaking time coefficient of variation < 30%
Positive Control (PC)	OD450 nm < NC/10
Calibrator (CAL)	PC $\leq$ OD450nm < (NC+PC)/5

If the results of the test match the requirements stated above, proceed to the next section.
If they don't, do not proceed any further and perform the following checks:

Problem	Check
Blank well > 0.100 OD450nm	that the Chromogen/Substrate solution has not become contaminated during the assay
Negative Control (NC) < 1.000 OD450nm after blanking coefficient of variation > 30%	1. that the washing procedure and the washer settings are as validated in the pre qualification study; 2. that the proper washing solution has been used and the washer has been primed with it before use; 3. that no mistake has been done in the assay procedure (dispensation of positive control instead of negative control); 4. that no contamination of the negative control or of the wells where the control was dispensed has occurred due to positive samples, to spills or to the enzyme conjugate; 5. that micropipettes have not become contaminated with positive samples or with the enzyme conjugate; 6. that the washer needles are not blocked or partially obstructed.

Calibrator OD450nm Outside the range	1. that the procedure has been correctly performed; 2. that no mistake has occurred during its distribution (ex.: dispensation of negative control instead of Calibrator); 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the calibrator has occurred.
Positive Control OD450nm > NC/10	1. that the procedure has been correctly performed; 2. that no mistake has occurred during the distribution of the control (dispensation of negative control instead of positive control). 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the positive control has occurred.

If any of the above problems have occurred, report the problem to the supervisor for further actions.

Important note:
The analysis must be done proceeding as the reading step described in the section M, point 8.

P. RESULTS
The results are calculated by means of a cut-off value determined with the following formula:

Cut-Off = (NC + PC) / 5

***Important note**: When the calculation of results is performed by the operating system of an ELISA automated work station, ensure that the proper formulation is used to calculate the cut-off value and generate the correct interpretation of results.*

Q. INTERPRETATION OF RESULTS
Results are interpreted as ratio between the cut-off value and the sample OD450nm / 620-630nm or Co/S. Results are interpreted according to the following table:

Co/S	Interpretation
< 0.9	Negative
0.9 – 1.1	Equivocal
> 1.1	Positive

A negative result indicates that the patient has not been infected by HDV.
Any patient showing an equivocal result should be re-tested on a second sample taken 1-2 weeks after the initial sample.
A positive result is indicative of HDV infection and therefore the patient should be treated accordingly.

Important notes:
1. *Interpretation of results should be done under the supervision of the laboratory supervisor to reduce the risk of judgement errors and misinterpretations.*
2. *When test results are transmitted from the laboratory to another facility, attention must be paid to avoid erroneous data transfer.*
3. *Diagnosis of viral hepatitis infection has to be taken by and released to the patient by a suitably qualified medical doctor.*

An example of calculation is reported below (data obtained proceeding as the the reading step described in the section M, point 8).

The following data must not be used instead of real figures obtained by the user.

Negative Control: 2.100 – 2.200 – 2.000 OD450nm
Mean Value: 2.100 OD450nm
Higher than 1.000 – Accepted

Positive Control: 0.100 OD450nm
Lower than NC/10 – Accepted

Cut-Off = (2.100 + 0.100) / 5 = 0.440

Calibrator: 0.300-0.260 OD450nm
Mean value: 0.280 OD450nm
Within the range PC ≤ OD450nm < (NC+PC)/5 – *Accepted*

Sample 1: 0.020 OD450nm
Sample 2: 1.900 OD450nm
Sample 1 Co/S > 1.1 positive
Sample 2 Co/S < 0.9 negative

R. PERFORMANCES
Evaluation of Performances has been conducted in accordance to what reported in the Common Technical Specifications or CTS (art. 5, Chapter 3 of IVD Directive 98/79/EC)

1. LIMIT OF DETECTION:
In absence of an international standard, the sensitivity of the assay has been calculated by means of the product named Accurun n° 127 supplied by Boston Biomedica Inc. – USA .
The table below reports the OD450nm shown by this preparation when diluted in Fetal Calf Serum to prepare a limiting dilution curve, in three different lots.

Co/S values

	DAB.CE	Lot # 1102	DAB.CE	Lot # 0103	DAB.CE	Lot # 0403
Accurun # 127	**OD450 nm**	**Co/S value**	**OD450 nm**	**Co/S value**	**OD450 nm**	**Co/S value**
1x	0.171	**3.0**	0.163	**2.9**	0.156	**2.8**
2x	0.187	**2.7**	0.176	**2.6**	0.179	**2.5**
4x	0.230	**2.2**	0.220	**2.1**	0.202	**2.2**
8x	0.298	**1.7**	0.285	**1.6**	0.271	**1.6**
16x	0.417	**1.2**	0.405	**1.1**	0.402	**1.1**
32x	0.514	**1.0**	0.490	***0.9***	0.482	***0.9***
64x	0.717	0.7	0.700	0.7	0.705	0.6
128x	1.063	0.5	1.006	0.5	1.015	0.4
CTRL (-)	2.484	//////////	2.261	//////////	2.114	//////////

2. DIAGNOSTIC SPECIFICITY AND SENSITIVITY
The diagnostic performances were evaluated in a clinical trial conducted by the Department of Gastro-Hepatology, Prof. M.Rizzetto, S.Giovanni Battista hospital, Torino, Italy, on more than 400 samples against a reference kit.
Negative, positive and potentially interfering samples were examined in the trial.
Both plasma, derived with different standard techniques of preparation (citrate, EDTA and heparin), and sera have been used to determine the specificity. No false reactivity due to the method of specimen preparation has been observed.
Results are briefly reported in the tables below:

Sensitivity	> 98 %
Specificity	> 98 %

3. PRECISION

The mean values obtained from a study conducted on two samples of different anti-HDV antibody reactivity, examined in 16 replicates in three separate runs for three lots of product, is reported below:

DAB.CE: lot #1102

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	2.342	2.428	2.433	2.401
Std.Deviation	0.113	0.106	0.122	0.114
CV %	4.8	4.4	5.0	4.7

Calibrator (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.298	0.289	0.286	0.291
Std.Deviation	0.023	0.027	0.026	0.025
CV %	7.7	9.3	9.1	8.7
Co/S	1.6	1.7	1.7	1.7

DAB.CE: lot #0103

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	2.208	2.237	2.246	2.230
Std.Deviation	0.105	0.108	0.108	0.107
CV %	4.7	4.8	4.8	4.8

Calibrator (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.269	0.277	0.266	0.271
Std.Deviation	0.026	0.024	0.025	0.025
CV %	9.8	8.5	9.5	9.3
Co/ S	1.7	1.7	1.7	1.7

DAB.CE: lot # 0403

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	2.246	2.221	2.182	2.216
Std.Deviation	0.097	0.103	0.118	0.106
CV %	4.3	4.6	5.4	4.8

Calibrator (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.286	0.273	0.280	0.280
Std.Deviation	0.027	0.023	0.026	0.025
CV %	9.3	8.5	9.1	9.0
Co/S	1.6	1.7	1.6	1.6

The variability shown in the tables did not result in sample misclassification.

Important note:

The performance data have been obtained proceeding as the reading step described in the section M, point 8.

S. LIMITATIONS

Bacterial contamination or heat inactivation of the specimen may affect the absorbance values of the samples with consequent alteration of the level of the analyte.

This test is suitable only for testing single samples and not pooled ones.

Diagnosis of an infectious disease should not be established on the basis of a single test result. The patient's clinical history, symptomatology, as well as other diagnostic data should be considered.

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All the IVD Products manufactured by the company are under the control of a certified Quality Management System approved by an EC Notified Body. Each lot is submitted to a quality control and released into the market only if conforming with the EC technical specifications and acceptance criteria.

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CE
0318

HDV Ab

Ensayo inmunoenzimático competitivo para la determinación cualitativa de anticuerpos frente al Virus de la Hepatitis Delta en plasma y suero humanos

Uso exclusivo para diagnóstico “in vitro”

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REF DAB.CE
96 pruebas

HDV Ab

A. OBJETIVO DEL EQUIPO.
Ensayo inmunoenzimático competitivo (ELISA) para la determinación cualitativa de anticuerpos frente al Virus de la Hepatitis Delta (HDV) en plasma y suero humanos con una metodología de "dos pasos".
El equipo ha sido desarrollado para el seguimiento de pacientes infectados con HDV.
Uso exclusivo para diagnóstico "in vitro".

B. INTRODUCCIÓN.
El Virus de la Hepatitis Delta es un virus ARN defectivo. Se compone de un núcleo con los antígenos delta específicos, y está encapsulado por el HBsAg. Para su replicación necesita ayuda funcional de HBV.
La infección por HDV ocurre en presencia de una infección aguda o crónica por HBV. Cuando se presenta simultáneamente la infección aguda por los dos virus, la enfermedad es grave y el cuadro clínico, así como las características bioquímicas son practicamente indistinguibles de una infección por HBV. Sin embargo, una persona infectada por HBV de forma crónica puede soportar indefinidamente la replicación por HDV, normalmente la enfermedad es menos severa y aparece como exacerbación clínica.
La determinación de los marcadores serológicos específicos de HDV (HDV Ag, HDV Ab, HDV IgM y HDV IgG) representa una herramienta importante para los clínicos en la clasificación del agente etiológico, en el seguimiento de los pacientes así como en el tratamiento.
La detección de anticuerpos totales permite la clasificación de la enfermedad y el seguimiento de la seroconversión.

C. PRINCIPIOS DEL ENSAYO.
El ensayo es de tipo competitivo, donde los anticuerpos anti-HDV de la muestra compiten con un anticuerpo policlonal (IgG) específico para el virus y conjugado con peroxidasa (HRP), por el antígeno recombinate-HDV de la fase sólida.
El ensayo se realiza mediante un sistema de dos pasos con incubación competitiva. La muestra se añade a la placa y los anticuerpos específicos anti-HDV se combinan con el antígeno de la fase sólida. Después del lavado, se añade un anticuerpo conjugado con peroxidasa (HRP) que se une al antígeno libre en la placa. Previo lavado, se añade el substrato cromogénico.
La concentración de la enzima conjugada, unida a la fase sólida es inversamente proporcional a la cantidad de anticuerpos al HDV presentes en la muestra y su actividad se detecta por la adición del substrato cromogénico.
La concentración de anticuerpos específicos al HDV en la muestra se determina de manera semicuantitativa a través del cálculo de un valor de corte.

D. COMPONENTES.
Cada equipo contiene reactivos suficientes para realizar 96 pruebas.

1. Microplaca: MICROPLATE
12 tiras de 8 pocillos recubiertos con antígeno recombinante específico de HDV, en bolsas selladas con desecante. Se deben poner las placas a temperatura ambiente antes de abrirlas, sellar las tiras sobrantes en la bolsa con el desecante y almacenar a 4ºC.

2. Control Negativo: CONTROL -
1x2.0ml/vial. Listo para el uso. Contiene proteinas del suero de cabra, tampón Tris-HCl 100 mM pH 7.4 +/-0.1, además de azida sódica 0.09% y ProClin 300 0.045% como conservantes. El control negativo está codificado con el color amarillo pálido.

3. Control Positivo: CONTROL +
1x2.0ml/vial. Listo para el uso. Contiene proteinas del suero de cabra, alto título de anticuerpos anti-HDV, tampón Tris-HCl 100 mM pH 7.4 +/-0.1, además de azida sódica 0.09% y ProClin 300 0.045% como conservantes. El control positivo está codificado con el color verde.

4. Calibrador: CAL ….
n° 1 vial. Liofilizado. Para disolver en agua calidad EIA como se indica en la etiqueta. Contiene suero bovino fetal, bajo título de anticuerpos humanos al HDV, además de sulfato de gentamicina 0.02 mg/ml y ProClin 300 0.045% como conservantes.
Nota: El volumen necesario para disolver el contenido del frasco, varía en cada lote. Se recomienda usar el volumen indicado en la etiqueta.

5. Tampón de Lavado Concentrado: WASHBUF 20X
1x60ml/botella. Solución concentrada 20x.
Una vez diluida, la solución de lavado contiene tampón fosfato 10 mM a pH 7.0 +/- 0.2, Tween 20 al 0.05% y ProClin 300 al 0.045%

6. Conjugado CONJ
1x16ml/vial. Solución lista para el uso. Contiene 5% de albúmina de suero bovino, tampón Tris 10mM a pH 6.8 +/- 0.1, anticuerpo anti-HDV conjugado con peroxidasa (HPR) en presencia de 0.2 mg/ml de sulfato de gentamicina y ProClin 300 0.045% como conservante. El conjugado está codificado con el color rojo.

7. Cromógeno/Substrato SUBS TMB
1x16ml/vial. Contiene una solución tamponada citrato-fosfato 50mM pH 3.5-3.8, tetra-metil-benzidina (TMB) 0.03% y peróxido de hidrógeno (H_2O_2) 0.02% así como dimetilsulfóxido 4%.
Nota: Evitar la exposición a la luz, ya que la sustancia es fotosensible.

8. Ácido Sulfúrico: H_2SO_4 O.3 M
1x15ml/vial. Contiene solución de H_2SO_4 0.3M
Atención: Irritante (H315, H319; P280, P302+P352, P332+P313, P305+P351+P338, P337+P313, P362+P363).

Sellador adhesivo, n° 2

Manual de instrucciones, n° 1

E. MATERIALES NECESARIOS NO SUMINISTRADOS.
1. Micropipetas calibradas (10-1000 µl) y puntas plásticas desechables.
2. Agua de calidad EIA (Bidestilada o desionizada, tratada con carbón para remover químicos oxidantes usados como desinfectantes).
3. *Timer* con un rango de 60 minutos como mínimo.
4. Papel absorbente.
5. Incubador termostático de microplacas ELISA, calibrado (en seco o húmedo) fijo a 37ºC.
6. Lector calibrado de microplacas de ELISA con filtros de 450nm (lectura) y de 620-630 nm.
7. Lavador calibrado de microplacas ELISA.
8. Vórtex o similar.

F. ADVERTENCIAS Y PRECAUCIONES.
1. El equipo debe ser usado por personal técnico adecuadamente entrenado, bajo la supervisión de un doctor responsable del laboratorio.
2. Todas las personas encargadas de la realización de las pruebas deben llevar las ropas protectoras adecuadas de laboratorio, guantes y gafas. Evitar el uso de objetos cortantes (cuchillas) o punzantes (agujas). El personal

debe ser adiestrado en procedimientos de bioseguridad, según ha sido recomendado por el Centro de Control de Enfermedades de Atlanta, Estados Unidos, y publicado por el Instituto Nacional de Salud: "Biosafety in Microbiological and Biomedical Laboratories", ed.1984.

3. Todo el personal involucrado en el manejo de muestras debe estar vacunado contra HBV y HAV, para lo cual existen vacunas disponibles, seguras y eficaces.
4. Se debe controlar el ambiente del laboratorio para evitar la contaminación de los componentes con polvo o agentes microbianos cuando se abran los equipos, así como durante la realización del ensayo. Evitar la exposición del substrato (TMB/H_2O_2) a la luz y las vibraciones de la mesa de trabajo durante el ensayo.
5. Conservar el equipo a temperaturas entre 2-8 ºC, en un refrigerador con temperatura regulada o en cámara fría.
6. No intercambiar reactivos de diferentes lotes ni tampoco de diferentes equipos.
7. Comprobar que los reactivos no contienen precipitados ni agregados en el momento del uso. De darse el caso, informar al responsable para realizar el procedimiento pertinente.
8. Evitar contaminación cruzada entre muestras de suero/ plasma usando puntas desechables y cambiándolas después de cada uso. No reutilizar puntas desechables.
9. Evitar contaminación cruzada entre los reactivos del equipo usando puntas desechables y cambiándolas después de cada uso. No reutilizar puntas desechables.
10. No usar el producto después de la fecha de caducidad indicada en el equipo e internamente en los reactivos.
11. Tratar todas las muestras como potencialmente infecciosas. Las muestras de suero humano deben ser manipuladas al nivel 2 de bioseguridad, según ha sido recomendado por el Centro de Control de Enfermedades de Atlanta, Estados Unidos y publicado por el Instituto Nacional de Salud: "Biosafety in Microbiological and Biomedical Laboratories", ed.1984.
12. Se recomienda el uso de material plástico desechable para la preparación de las soluciones de lavado y para la transferencia de los reactivos a los diferentes equipos automatizados a fin de evitar contaminaciones.
13. Los desechos producidos durante el uso del equipo deben de ser eliminados según lo establecido por las directivas nacionales y las leyes relacionadas con el tratamiento de los residuos químicos y biológicos de laboratorio. En particular, los desechos líquidos provenientes del proceso de lavado deben ser tratados como potencialmente infecciosos y deben ser inactivados. Se recomienda la inactivación con lejía al 10% de 16 a 18 horas o el uso de la autoclave a 121°C por 20 minutos.
14. En caso de derrame accidental de algún producto, se debe utilizar papel absorbente embebido en lejía y posteriormente en agua. El papel debe eliminarse en contenedores designados para este fin en hospitales y laboratorios.
15. El ácido sulfúrico es irritante. En caso de derrame, se debe lavar la superficie con abundante agua.
16. Otros materiales de desecho generados durante la utilización del equipo (por ejemplo: puntas usadas en la manipulación de las muestras y controles, microplacas usadas) deben ser manipuladas como fuentes potenciales de infección de acuerdo a las directivas nacionales y leyes para el tratamiento de residuos de laboratorio.

G. MUESTRA: PREPARACIÓN Y RECOMENDACIONES.

1. Extraer la sangre asépticamente por punción venosa y preparar el suero o plasma según las técnicas estándar de los laboratorios de análisis clínico. No se ha detectado que el tratamiento con citrato, EDTA o heparina afecte las muestras.
2. Evitar el uso de conservantes, en particular azida sódica, ya que pudiera afectar la actividad enzimática del conjugado.
3. Las muestras deben estar identificadas claramente mediante código de barras o nombres, a fin de evitar errores en los resultados. Cuando el equipo se emplea para el pesquisaje en unidades de sangre, se recomienda el uso del código de barras.
4. Las muestras hemolizadas (color rojo) o hiperlipémicas (aspecto lechoso) deben ser descartadas para evitar falsos resultados, al igual que aquellas donde se observe la presencia de precipitados, restos de fibrina o filamentos microbianos.
5. El suero y el plasma pueden conservarse a una temperatura entre +2° y +8°C en tubos de recolección principales hasta cinco días después de la extracción. No congelar tubos de recolección principales. Para periodos de almacenamiento más prolongados, las muestras de plasma o suero, retiradas cuidadosamente del tubo de extracción principal, pueden almacenarse congeladas a –20°C durante al menos 12 meses. Evitar congelar/descongelar cada muestra más de una vez, ya que pueden generarse partículas que podrían afectar al resultado de la prueba.
6. Si hay presencia de agregados, la muestra se puede aclarar mediante centrifugación a 2000 rpm durante 20 minutos o por filtración con un filtro de 0,2-0,8 micras.

H. PREPARACIÓN DE LOS COMPONENTES Y PRECAUCIONES.

Según estudios realizados, no se ha detectado pérdida relevante de actividad en equipos abiertos, en uso por un período de hasta 3 meses.

1. Microplacas:
Dejar la microplaca a temperatura ambiente (aprox. 1 hora) antes de abrir el envase. Compruebe que el desecante no esté de un color verde oscuro, lo que indicaría un defecto de fabricación. De ser así, debe solicitar el servicio de Dia.Pro: atención al cliente.
Las tiras de pocillos no utilizadas, deben guardarse herméticamente cerradas en la bolsa de aluminio con el desecante a 2-8ºC. Una vez abierto el envase, las tiras sobrantes, se mantienen estables hasta que el indicador de humedad dentro de la bolsa del desecante cambie de amarillo a verde.

2. Control Negativo:
Listo para el uso. Mezclar bien con la ayuda de un vórtex, antes de usar.

3. Control Positivo:
Listo para el uso. Mezclar bien con la ayuda de un vórtex, antes de usar.

4. Calibrador:
Control positivo bajo. Añadir de manera precisa al polvo liofilizado el volumen de agua de calidad EIA indicado en la etiqueta. Dejar disolver totalmente y mezclar suavemente en el vórtex.
Note: *Una vez reconstituida, la solución no es estable. Se recomienda mantenerla congelada en alícuotas a –20ºC. Cuando se descongele, descartar el agua en lugar de congelarla nuevamente.*

5. Solución de Lavado Concentrada:
Todo el contenido de la solución concentrada 20x debe diluirse con agua bidestilada hasta 1200ml y mezclarse suavemente antes de usarse. Durante la preparación evitar la formación de espuma y burbujas, lo que podría influir en la eficiencia de los ciclos de lavado.
Nota: *Una vez diluida, la solución es estable por una semana a temperaturas entre +2 y 8ºC.*

6. Conjugado:
Listo para el uso. Mezclar bien con un vórtex antes de usar. Evitar posible contaminación del líquido con oxidantes químicos, polvo o microbios. En caso de que deba transferirse el reactivo, usar contenedores de plástico, estériles y desechables, siempre que sea posible.

7. Cromógeno/ Substrato:
Listo para el uso. Mezclar bien con un vórtex antes de usar. Evitar posible contaminación del líquido con oxidantes químicos, polvo o microbios. Evitar la exposición a la luz, agentes oxidantes y superficies metálicas. En caso de que deba transferirse el reactivo, usar contenedores de plástico, estériles y desechables, siempre que sea posible.

8. Ácido Sulfúrico:
Listo para el uso. Mezclar bien con un vórtex antes de usar.
Atención: Irritante (H315, H319; P280, P302+P352, P332+P313, P305+P351+P338, P337+P313, P362+P363).

Leyenda:

Indicación de peligro, **Frases H**
H315 – Provoca irritación cutánea.
H319 – Provoca irritación ocular grave.

Consejo de prudencia, **Frases P**
P280 – Llevar guantes/prendas/gafas/máscara de protección.
P302 + P352 – EN CASO DE CONTACTO CON LA PIEL: Lavar con agua y jabón abundantes.
P332 + P313 – En caso de irritación cutánea: Consultar a un médico.
P305 + P351 + P338 – EN CASO DE CONTACTO CON LOS OJOS: Aclarar cuidadosamente con agua durante varios minutos. Quitar las lentes de contacto, si lleva y resulta fácil. Seguir aclarando.
P337 + P313 – Si persiste la irritación ocular: Consultar a un médico.
P362 + P363 – Quitarse las prendas contaminadas y lavarlas antes de volver a usarlas.

I. INSTRUMENTOS Y EQUIPAMIENTO UTILIZADOS EN COMBINACIÓN CON EL EQUIPO.

1. Las micropipetas deben ser calibradas para dispensar correctamente el volumen requerido en el ensayo y sometidas a una descontaminación periódica de las partes que pudieran entrar accidentalmente en contacto con la muestra o los reactivos (etanol 70%, lejía 10%, de calidad de los desinfectantes hospitalarios). Deben además, ser regularmente revisadas para mantener una precisión del 1% y una confiabilidad de +/- 2%.
2. La incubadora de ELISA debe ser ajustada a 37ºC (+/- 0.5ºC) y controlada periódicamente para mantener la temperatura correcta. Pueden emplearse incubadoras secas o baños de agua siempre que estén validados para la incubación de pruebas de ELISA.
3. El **lavador ELISA** es extremadamente importante para el rendimiento global del ensayo. El lavador debe ser validado de forma minuciosa previamente, revisado para comprobar que suministra el volumen de dispensación correcto y enviado regularmente a mantenimiento de acuerdo con las instrucciones de uso del fabricante. En particular, deben lavarse minuciosamente las sales con agua desionizada del lavador al final de la carga de trabajo diaria. Antes del uso, debe suministrarse extensivamente solución de lavado diluida al lavador. Debe enviarse el instrumento semanalmente a descontaminación según se indica en su manual (se recomienda descontaminación con NaOH 0.1 M). Para asegurar que el ensayo se realiza conforme a los rendimientos declarados, basta con 5 ciclos de lavado (aspiración + dispensado de 350 µl/pocillo de solución de lavado + 20 segundos de remojo = 1 ciclo). Si no es posible remojar, añadir un ciclo de lavado adicional. Un ciclo de lavado incorrecto o agujas obstruidas con sal son las principales causas de falsas reacciones positivas.
4. Los tiempos de incubación deben tener un margen de $\pm$5%.
5. El lector de microplaca ELISA debe estar provisto de un filtro de lectura de 450nm y de un segundo filtro de 620-630 nm, obligatorio para reducir interferencias en la lectura. El procedimiento estándar debe contemplar: a) Ancho de banda $\leq$10nm b) Rango de absorbancia de 0 a 4, c) Linealidad a 4, reproducibilidad $\geq$1%. El blanco se prueba en el pocillo indicado en la sección “Procedimiento del ensayo”. El sistema óptico del lector debe ser calibrado periódicamente para garantizar que se mide la densidad óptica correcta. Periódicamente debe procederse al mantenimiento según las instrucciones del fabricante.
6. En caso de usar un sistema automatizado de ELISA, los pasos críticos (dispensado, incubación, lavado, lectura, agitación y procesamiento de datos) deben ser cuidadosamente fijados, calibrados, controlados y periódicamente ajustados, para garantizar los valores indicados en las secciones “Control interno de calidad” y “Procedimiento del ensayo”. El protocolo del ensayo debe ser instalado en el sistema operativo de la unidad y validado tanto para el lavador como para el lector. Por otro lado, la parte del sistema que maneja los líquidos (dispensado y lavado) debe ser validada y fijada correctamente. Debe prestarse particular atención a evitar el arrastre por las agujas de dispensación y las de lavado, a fin de minimizar la posibilidad de ocurrencia de falsos positivos por contaminación de los pocillos adyacentes por muestras fuertemente reactivas. Se recomienda el uso de sistemas automatizados para el pesquisaje en unidades de sangre y cuando la cantidad de muestras supera las 20-30 unidades por ensayo.
7. El servicio de atención al cliente en Dia.Pro, ofrece apoyo al usuario para calibrar, ajustar e instalar los equipos a usar en combinación con el equipo, con el propósito de asegurar el cumplimiento de los requerimientos descritos.

L. OPERACIONES Y CONTROLES PREVIOS AL ENSAYO.

1. Compruebe la fecha de caducidad indicada en la parte externa del equipo (envase primario). No usar si ha caducado.
2. Compruebe que los componentes líquidos no están contaminados con partículas o agregados visibles. Asegúrese de que el cromógeno (TMB) es incoloro o azul pálido, aspirando un pequeño volumen de este con una pipeta estéril de plástico. Compruebe que no han ocurrido rupturas ni derrames de líquido dentro de la caja (envase primario) durante el transporte. Asegurarse de que la bolsa de aluminio que contiene la microplaca no esté rota o dañada.
3. Diluir totalmente la solución de lavado 20x concentrada, como se ha descrito anteriormente.
4. Disolver el Calibrador como se ha descrito anteriormente y mezclar suavemente usando un vórtex.
5. Dejar los componentes restantes alcanzar la temperatura ambiente (aprox. 1 hora), mezclar luego suavemente en el vórtex todos los reactivos líquidos.
6. Ajustar la incubadora de ELISA a 37ºC y cebar el lavador de ELISA utilizando la solución de lavado, según las instrucciones del fabricante. Fijar el número de ciclos de lavado según se indica en la sección específica.
7. Comprobar que el lector de ELISA esté conectado al menos 20 minutos antes de realizar la lectura.
8. En caso de trabajar automáticamente, conectar el equipo y comprobar que los protocolos estén correctamente programados.
9. Comprobar que las micropipetas estén fijadas en el volumen requerido.
10. Asegurarse de que el equipamiento a usar esté en perfecto estado, disponible y listo para el uso.

11. En caso de surgir algún problema, se debe detener el ensayo y avisar al responsable.

M. PROCEDIMIENTO DEL ENSAYO.
El ensayo debe realizarse según las instrucciones que siguen a continuación, es importante mantener en todas las muestras el mismo tiempo de incubación.
1. Poner el número necesario de tiras en el soporte plástico. Dejar el pocillo A1 vacío para el blanco.
Almacenar las tiras restantes en la bolsa con el desecante a temperaturas entre 2 y 8°C.
2. Dispensar 100µl del Control Negativo, por triplicado, 100µl del Control Positivo una vez y, posteriormente, añadir 100µl de muestras. Comprobar que los controles y muestras se han añadido correctamente.
Después incubar la microplaca durante **60 minutos a +37ºC.**
3. Lavar la microplaca según lo descrito previamente (sección I.3).
4. Dispensar 100µl de Conjugado en todos los pocillos, excepto A1; comprobar que los reactivos se han añadido correctamente.
Incubar la microplaca durante **60 minutos a +37°C.**

***Nota importante**: Tener cuidado de no tocar la pared interna del pocillo con la punta de la pipeta al dispensar el conjugado. Podría producirse contaminación.*

5. Lavar la microplaca según lo descrito previamente (sección I.3).
6. Dispensar 100µl del Cromógeno/Substrato en todos los pocillos, incluido el A1.
Incubar la microplaca protegida de la luz a **temperatura ambiente (18-24°C) durante 20 minutos**.

***Nota importante**: No exponer directamente a fuerte iluminación, de lo contrario se generan interferencias.*

7. Dispensar 100µl de ácido sulfúrico en todos los pocillos para detener la reacción enzimática, usar la misma secuencia que en el paso 6. La adición de la solución de parada cambia el color del Control Negativo y las muestras negativas de azul a amarillo.
8. Medir la intensidad del color de la solución en cada pocillo, según se indica en la sección I.5, con un filtro de 450 nm (lectura) y otro de 620-630 nm (substracción del fondo, obligatorio), calibrando el instrumento con el pocillo A1 (blanco).

Notas importantes:
1. *Asegurarse de que no hay impresiones digitales en el fondo de los pocillos antes de leer. Podrían generarse falsos positivos en la lectura.*
2. *La lectura debe hacerse inmediatamente después de añadir la solución de parada y, en cualquier caso, nunca transcurridos 20 minutos después de su adición. Se podría producir auto oxidación del cromógeno causando un elevado fondo.*
3. *El uso del calibrador (CAL), un control negativo bajo, no es obligatorio para el ensayo ya que el calibrador (CAL) no afecta al cálculo del valor de corte. El calibrador (CAL) puede usarse como un control interno de calidad del laboratorio. Dispensar 100µl del calibrador (CAL), posiblemente por duplicado, cuando se utilice para este propósito.*

N. ESQUEMA DEL ENSAYO.

Controles/Calibrador Muestras	100 µl 100 µl
1ra incubación	**60 min**
Temperatura	+37°C
Lavado	5 ciclos con 20''de remojo o 6 ciclos sin remojo
Conjugado	100 µl
2da incubación	**60 min**
Temperatura	+37°C
Lavado	5 ciclos con 20''de remojo o 6 ciclos sin remojo
Mezcla TMB/H2O2	100 µl
3ra incubación	**20 min**
Temperatura	t.a.*
Ácido Sulfúrico	100 µl
Lectura D.O.	450nm / 620-630nm

t.a. temperatura ambiente*

A continuación se describe un ejemplo del esquema de dispensado (incluido el calibrador (CAL):

Microplaca

	1	2	3	4	5	6	7	8	9	10	11	12
A	BL	M2										
B	CN	M3										
C	CN	M4										
D	CN	M5										
E	CAL	M6										
F	CAL	M7										
G	CP	M8										
H	M1	M9										

Leyenda: BL = Blanco CN = Control Negativo
CAL = Calibrador CP = Control Positivo M = Muestra

O. CONTROL DE CALIDAD INTERNO.
Se realiza un grupo de pruebas con los controles negativo y positivo cada vez que se usa el equipo, y con el calibrador la primera vez que se usa el equipo, para verificar si los valores DO450nm o Co/M son los esperados.

Asegurar el cumplimiento de los siguientes parámetros:

Parámetro	Exigencia
Pocillo Blanco	valor < 0.100 DO450nm
Control Negativo (CN)	> 1.000 DO450nm después de leer el blanco Si es menor, controle cuidadosamente el proceso de lavado y disminuya los ciclos o el tiempo entre los mismos. Coeficiente de variación < 30%
Control Positivo (CP)	DO450 nm < CN/10
Calibrador (CAL)	CP ≤ DO450nm < (CN+CP)/5

Si los resultados del ensayo coinciden con lo establecido anteriormente, pase a la siguiente sección.

En caso contrario, no siga adelante y compruebe:

Problema	Compruebe que
Pocillo blanco > 0.100DO450nm	la solución cromógeno/substrato no se ha contaminado durante el ensayo.
Control	1. el proceso de lavado y los parámetros

Negativo (CN) < 1.000DO450nm después de leer el blanco Coeficiente de variación > 20%	del lavador estén validados según los estudios previos de calificación. 2. se ha usado la solución de lavado apropiada y que el lavador ha sido cebado con la misma antes del uso. 3. no se han cometido errores en el procedimiento (dispensar el control positivo en lugar del negativo). 4. no ha existido contaminación del control negativo o de sus pocillos debido a muestras positivas derramadas, o al conjugado. 5. las micropipetas no se han contaminado con muestras positivas o con el conjugado. 6. las agujas del lavador no estén parcial o totalmente obstruidas.
Calibrador DO450nm Fuera de rango	1. el procedimiento ha sido realizado correctamente. 2. no ha habido errores durante su distribución (dispensar el control negativo en lugar del calibrador). 3. el proceso de lavado y los parámetros del lavador estén validados según los estudios previos de calificación. 4. no ha ocurrido contaminación externa del calibrador.
Control Positivo DO450nm > CN/10	1. el procedimiento ha sido realizado correctamente. 2. no se han cometido errores en el procedimiento (dispensar el control negativo en lugar del positivo). 3. el proceso de lavado y los parámetros del lavador estén validados según los estudios previos de calificación. 4. no ha ocurrido contaminación externa del control positivo.

Si ocurre alguno de los problemas anteriores, informe al responsable para tomar las medidas pertinentes.

Nota importante:
El análisis debe seguir el paso de lectura descrito en la sección M, punto 8.

P. RESULTADOS.
Los resultados se calculan por medio de un valor de corte (cut-off) hallado con la siguiente fórmula:

Valor de corte = (CN + CP) / 5

Nota Importante*: Cuando el cálculo de los resultados se halla mediante el sistema operativo de un equipo de ELISA automático, asegurarse de que la formulación usada para el cálculo del valor de corte, y para la interpretación de los resultados sea correcta.*

Q. INTERPRETACIÓN DE LOS RESULTADOS.
La interpretación de los resultados se realiza mediante la razón entre las DO a 450nm / 620-630nm de las muestras y el Valor de corte Co/M.
Los resultados se interpretan según la siguiente tabla:

Co/M	Interpretación
< 0.9	Negativo
0.9 - 1.1	Equívoco
> 1.1	Positivo

Un resultado negativo indica que el paciente no está infectado por HDV.
Cualquier paciente, cuya muestra resulte equívoca debe someterse a una nueva prueba con una segunda muestra de sangre colectada 1 ó 2 semanas después de la inicial.
Un resultado positivo es indicativo de infección por HDV y por consiguiente el paciente debe ser tratado adecuadamente.

Notas importantes:
1. *La interpretación de los resultados debe hacerse bajo la vigilancia del responsable del laboratorio para reducir el riesgo de errores de juicio y de interpretación.*
2. *Cuando se transmiten los resultados de la prueba, del laboratorio a otras instalaciones, debe ponerse mucha atención para evitar el traslado de datos erróneos.*
3. *El diagnóstico de infección con un virus de la hepatitis debe ser evaluado y comunicado al paciente por un médico calificado.*

A continuación se incluye un ejemplo de los cálculos (datos obtenidos siguiendo el paso de lectura descrito en la sección M, punto 8).

Los siguientes datos no deben usarse en lugar de los valores reales obtenidos en el laboratorio.

Control Negativo: 2.100 – 2.200 – 2.000 DO450nm
Valor medio: 2.100 DO450nm
Mayor de 1.000 – Válido

Control Positivo: 0.100 DO450nm
Menor de CN/10 – Válido

Valor de corte = (2.100 + 0.100) / 5 = 0.440

Calibrador: 0.300-0.260 DO450nm
Valor medio: 0.280 DO450nm
Dentro del rango CP ≤ DO450nm < (CN+CP)/5 – Válido

Muestra 1: 0.020 DO450nm
Muestra 2: 1.900 DO450nm
Muestra 1 Co/M > 1.1 positiva
Muestra 2 Co/M < 0.9 negativa

R. FUNCIONAMIENTO.
La evaluación del funcionamiento ha sido realizada según lo reportado en las Especificaciones Técnicas Comunes (ETC) (art. 5, Capítulo 3 de las Directivas IVD 98/79/EC).

1. LÍMITE DE DETECCIÓN.
En ausencia de un estándar internacional, la sensibilidad del ensayo ha sido calculada por medio de un producto denominado Accurun n° 127 suministrado por Boston Biomedical Inc., Estados Unidos.
La siguiente tabla muestra los valores de DO450nm para esta preparación, diluido en suero bovino fetal (SFB), para construir la curva de dilución límite en tres lotes diferentes:

Valores Co/M

	DAB.CE	Lote # 1102	DAB.CE	Lote # 0103	DAB.CE	Lote # 0403
Accurun # 127	**DO450 nm**	**Co/M valor**	**DO450 nm**	**Co/M valor**	**DO450 nm**	**Co/M valor**
1x	0.171	**3.0**	0.163	**2.9**	0.156	**2.8**
2x	0.187	**2.7**	0.176	**2.6**	0.179	**2.5**
4x	0.230	**2.2**	0.220	**2.1**	0.202	**2.2**
8x	0.298	**1.7**	0.285	**1.6**	0.271	**1.6**
16x	0.417	**1.2**	0.405	**1.1**	0.402	**1.1**
32x	0.514	**1.0**	0.490	***0.9***	0.482	***0.9***
64x	0.717	0.7	0.700	0.7	0.705	0.6
128x	1.063	0.5	1.006	0.5	1.015	0.4
CTRL (-)	2.484	//////////	2.261	//////////	2.114	//////////

2. ESPECIFICIDAD Y SENSIBILIDAD DIAGNÓSTICA.
La evaluación del procedimiento diagnóstica se realizó mediante un ensayo con más de 400 muestras frente a un equipo de referencia. Este ensayo clínico fue conducido por el Prof. M. Rizzetto, Departamento de Gastro-Hepatología del hospital S. Giovanni Battista de Turín, Italia.
Se examinaron muestras negativas, positivas y otras que pudieran provocar interferencia.
Se emplearon además plasma sometido a métodos de tratamiento estándar (citrato, EDTA y heparina) y suero humanos. No se ha observado falsa reactividad debida a los métodos de tratamiento de muestras.
A continuación se muestran brevemente los resultados obtenidos:

Sensibilidad	> 98 %
Especificidad	> 98 %

3. PRECISIÓN.
Se realizó un estudio con 3 lotes y dos muestras de diferente reactividad anti-HDV, examinadas en 16 réplicas, en tres tandas separadas. Los valores medios obtenidos se reportan a continuación:

DAB.CE: lote #1102

Control Negativo (N = 16)

Valores medios	1ra tanda	2da tanda	3ra tanda	Valor Promedio
DO 450nm	2.342	2.428	2.433	2.401
Desviación estándar	0.113	0.106	0.122	0.114
CV %	4.8	4.4	5.0	4.7

Calibrador (N = 16)

Valores medios	1ra tanda	2da tanda	3ra tanda	Valor Promedio
DO 450nm	0.298	0.289	0.286	0.291
Desviación estándar	0.023	0.027	0.026	0.025
CV %	7.7	9.3	9.1	8.7
Co/M	1.6	1.7	1.7	1.7

DAB.CE: lote #0103
Control Negativo (N = 16)

Valores medios	1ra tanda	2da tanda	3ra tanda	Valor Promedio
DO 450nm	2.208	2.237	2.246	2.230
Desviación estándar	0.105	0.108	0.108	0.107
CV %	4.7	4.8	4.8	4.8

Calibrador (N = 16)

Valores medios	1ra tanda	2da tanda	3ra tanda	Valor Promedio
DO 450nm	0.269	0.277	0.266	0.271
Desviación estándar	0.026	0.024	0.025	0.025
CV %	9.8	8.5	9.5	9.3
Co/M	1.7	1.7	1.7	1.7

DAB.CE: lote # 0403

Control Negativo (N = 16)

Valores medios	1ra tanda	2da tanda	3ra tanda	Valor Promedio
DO 450nm	2.246	2.221	2.182	2.216
Desviación estándar	0.097	0.103	0.118	0.106
CV %	4.3	4.6	5.4	4.8

Calibrador (N = 16)

Valores medios	1ra tanda	2da tanda	3ra tanda	Valor Promedio
DO 450nm	0.286	0.273	0.280	0.280
Desviación estándar	0.027	0.023	0.026	0.025
CV %	9.3	8.5	9.1	9.0
Co/M	1.6	1.7	1.6	1.6

La variabilidad mostrada en las tablas no dió como resultado una clasificación errónea de las muestras.

Nota importante:
Los datos de rendimiento se obtuvieron siguiendo el paso de lectura descrito en la sección M, punto 8.

S. LIMITACIONES.
La contaminación bacteriana de las muestras o la inactivación por calor pueden modificar los valores de absorbancia con la consiguiente alteración de los niveles del analito. Este ensayo es adecuado solo para el análisis de muestras individuales y no para mezclas.
El diagnóstico de una enfermedad infecciosa no se debe formular en base al resultado de un solo ensayo, sino que es necesario tomar en consideraciòn la historia clínica y la sintomatología del paciente así como otros datos diagnósticos.

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Todos los productos de diagnóstico in vitro fabricados por la empresa son controlados por un sistema certificado de control de calidad aprobado por un organismo notificado para el marcado CE. Cada lote se somete a un control de calidad y se libera al mercado únicamente si se ajusta a las especificaciones técnicas y criterios de aceptación de la CE.

Fabricante:
Dia.Pro Diagnostic Bioprobes S.r.l.
Via G. Carducci n° 27 – Sesto San Giovanni (Mi) – Italia

CE
0318

HBcAb

Competitive Enzyme Immunoassay for the determination of antibodies to Hepatitis B core Antigen in human serum and plasma

- for “in vitro” diagnostic use only -

DIA.PRO
Diagnostic Bioprobes Srl
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REF. BCAB.CE
96 Tests

HBcAb

A. INTENDED USE

Competitive Enzyme ImmunoAssay (ELISA) for the determination of antibodies to Hepatitis B core Antigen in human plasma and sera.
The kit is intended for the screening of blood units and the follow-up of HBV-infected patients.
For "in vitro" diagnostic use only.

B. INTRODUCTION

The World Health Organization (WHO) defines Hepatitis B as follows:

"Hepatitis B is one of the major diseases of mankind and is a serious global public health problem. Hepatitis means inflammation of the liver, and the most common cause is infection with one of 5 viruses, called hepatitis A,B,C,D, and E. All of these viruses can cause an acute disease with symptoms lasting several weeks including yellowing of the skin and eyes (jaundice); dark urine; extreme fatigue; nausea; vomiting and abdominal pain. It can take several months to a year to feel fit again. Hepatitis B virus can cause chronic infection in which the patient never gets rid of the virus and many years later develops cirrhosis of the liver or liver cancer.

HBV is the most serious type of viral hepatitis and the only type causing chronic hepatitis for which a vaccine is available. Hepatitis B virus is transmitted by contact with blood or body fluids of an infected person in the same way as human immunodeficiency virus (HIV), the virus that causes AIDS. However, HBV is 50 to 100 times more infectious than HIV. The main ways of getting infected with HBV are: (a) perinatal (from mother to baby at the birth); (b) child- to-child transmission; (c) unsafe injections and transfusions; (d) sexual contact.

Worldwide, most infections occur from infected mother to child, from child to child contact in household settings, and from reuse of un-sterilized needles and syringes. In many developing countries, almost all children become infected with the virus. In many industrialized countries (e.g. Western Europe and North America), the pattern of transmission is different. In these countries, mother-to-infant and child-to-child transmission accounted for up to one third of chronic infections before childhood hepatitis B vaccination programmes were implemented. However, the majority of infections in these countries are acquired during young adulthood by sexual activity, and injecting drug use. In addition, hepatitis B virus is the major infectious occupational hazard of health workers, and most health care workers have received hepatitis B vaccine.

Hepatitis B virus is not spread by contaminated food or water, and cannot be spread casually in the workplace. High rates of chronic HBV infection are also found in the southern parts of Eastern and Central Europe. In the Middle East and Indian sub-continent, about 5% are chronically infected. Infection is less common in Western Europe and North America, where less than 1% are chronically infected.

Young children who become infected with HBV are the most likely to develop chronic infection. About 90% of infants infected during the first year of life and 30% to 50% of children infected between 1 to 4 years of age develop chronic infection. The risk of death from HBV-related liver cancer or cirrhosis is approximately 25% for persons who become chronically infected during childhood.

Chronic hepatitis B in some patients is treated with drugs called *interferon or lamivudine*, which can help some patients. Patients with cirrhosis are sometimes given liver transplants, with varying success. It is preferable to prevent this disease with vaccine than to try and cure it.

Hepatitis B vaccine has an outstanding record of safety and effectiveness. Since 1982, over one billion doses of hepatitis B vaccine have been used worldwide. The vaccine is given as a series of three intramuscular doses. Studies have shown that the vaccine is 95% effective in preventing children and adults from developing chronic infection if they have not yet been infected. In many countries where 8% to 15% of children used to become chronically infected with HBV, the rate of chronic infection has been reduced to less than 1% in immunized groups of children. Since 1991, WHO has called for all countries to add hepatitis B vaccine into their national immunization programmes."

Hepatitis B core Antigen (or HBcAg) is the major component of the core particles of HBV.
HBcAg is composed of a single polypeptide of about 17 kD that is released upon disaggregating the core particles; the antigen contains at least one immunological determinant.
Upon primary infection, anti HBcAg antibodies are one of the first markers of HBV hepatitis appearing in the serum of the patient, slightly later than HBsAg, the viral surface antigen.
Anti HBcAg antibodies are produced usually at high titers and their presence is detectable even years after infection. Isolated HBcAb, in absence of other HBV markers, have been observed in infected blood units, suggesting the use of this test for screening HBV, in addition of HBsAg.
The determination of HBcAb has become important for the classification of the viral agent, together with the detection of the other markers of HBV infection, in sera and plasma.

C. PRINCIPLE OF THE TEST

The assay is based on the principle of competition where the antibodies in the sample compete with a monoclonal antibody for a fixed amount of antigen on the solid phase.
A purified recombinant HBcAg is coated to the microwells.
The patient's serum/plasma is added to the microwell together with an additive able to block interferences present in the sample.
In the second incubation after washing, a monoclonal antibody, conjugated with Horseradish Peroxidase (HRP) and specific for HBcAg is added and binds to the free rec-HBcAg coated on the plastic.
After incubation, microwells are washed to remove any unbound conjugate and then the chromogen/substrate is added. In the presence of peroxidase enzyme the colorless substrate is hydrolyzed to a colored end-product.
The color intensity is inversely proportional to the amount of antibodies to HBcAg present in the sample.

D. COMPONENTS

Each kit contains sufficient reagents to perform 96 tests.

1. Microplate MICROPLATE

8x12 microwell strips coated with recombinant HBcAg and sealed into a bag with desiccant. Allow the microplate to reach room temperature before opening; reseal unused strips in the bag with desiccant and store at 2..8℃.

2. Negative Control CONTROL -
1x1.0ml/vial. Ready to use. Contains 5% bovine serum albumin, 10 mM phosphate buffer pH 7.4 +/-0.1, 0.09% sodium azide and 0.1% Kathon GC as preservatives. The negative control is pale yellow color coded.

3. Positive Control CONTROL +
1x1.0ml/vial. Ready to use. Contains 5% bovine serum albumin, anti HBcAg antibodies at a concentration of about 10 PEI U/ml, (calibrated on PEI HBc Reference Material 82), 10 mM phosphate buffer pH 7.4 +/-0.1, 0.09% sodium azide and 0.1% Kathon GC as preservatives. The positive control is green color coded.

4. Calibrator CAL ….
n° 1 vial. Lyophilised. To be dissolved with EIA gr ade water as reported in the label. Contains fetal bovine serum, human antibodies to HBcAg at a concentration of 2 PEI U/ml +/-10% (calibrated on PEI HBc Reference Material 82) and 0.1% Kathon GC as preservative.
Note: The volume necessary to dissolve the content of the vial may vary from lot to lot. Please use the right volume reported on the label .

5. Wash buffer concentrate WASHBUF 20X
1x60ml/bottle. 20x concentrated solution.
Once diluted, the wash solution contains 10 mM phosphate buffer pH 7.0+/-0.2, 0.05% Tween 20 and 0.1% Kathon GC.

6. Enzyme Conjugate CONJ
1x16ml/vial. Ready-to-use solution. Contains 5% bovine serum albumine, 10 mM tris buffer pH 6.8 +/-0.1, Horseradish peroxidase conjugated mouse monoclonal antibody to HBcAg in presence of 0.3 mg/ml gentamicine sulphate and 0.1% Kathon GC as preservatives. The component is red colour coded .

7. Chromogen/Substrate SUBS TMB
1x16ml/vial. Contains a 50 mM citrate-phosphate buffered solution at pH 3.6 +/-0.1, 0.03% tetra-methyl-benzidine (TMB), 0.02% hydrogen peroxide (H_2O_2) and 4% dimethylsulphoxide
Note: To be stored protected from light as sensitive to strong illumination.

8. Specimen Diluent DILSPE
4x3ml/vial. 10 mM tris buffered solution pH 8.0 +/-0.1 containing 0.1% Kathon GC for the pre-treatment of samples and controls in the plate, blocking interference.
Note: Use all the content of one vial before opening a second one. The reagent is sensitive to oxidation.

9. Sulphuric Acid H_2SO_4 O.3 M
1x15ml/vial. Contains 0.3 M H_2SO_4 solution.
Attention: Irritant (Xi R36/38; S2/26/30)

10. Plate sealing foil n°2

11. Instruction manual n°1

E. MATERIALS REQUIRED BUT NOT PROVIDED

1. Calibrated Micropipettes (100ul and 50ul) and disposable plastic tips.
2. EIA grade water (double distilled or deionised, charcoal treated to remove oxidizing chemicals used as disinfectants).
3. Timer with 60 minute range or higher.
4. Absorbent paper tissues.
5. Calibrated ELISA microplate thermostatic incubator (dry or wet) set at +37℃.
6. Calibrated ELISA microwell reader with 450nm (reading) and with 620-630nm (blanking) filters.
7. Calibrated ELISA microplate washer.
8. Vortex or similar mixing tools.

F. WARNINGS AND PRECAUTIONS

1. The kit has to be used by skilled and properly trained technical personnel only, under the supervision of a medical doctor responsible of the laboratory.
2. When the kit is used for the screening of blood units and blood components, it has to be used in a laboratory certified and qualified by the national authority in that field (Ministry of Health or similar entity) to carry out this type of analysis.
3. All the personnel involved in performing the assay have to wear protective laboratory clothes, talc-free gloves and glasses. The use of any sharp (needles) or cutting (blades) devices should be avoided. All the personnel involved should be trained in biosafety procedures, as recommended by the Center for Disease Control, Atlanta, U.S. and reported in the National Institute of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
4. All the personnel involved in sample handling should be vaccinated for HBV and HAV, for which vaccines are available, safe and effective.
5. The laboratory environment should be controlled so as to avoid contaminants such as dust or air-born microbial agents, when opening kit vials and microplates and when performing the test. Protect the Chromogen (TMB) from strong light and avoid vibration of the bench surface where the test is undertaken.
6. Upon receipt, store the kit at 2-8℃ into a temp erature controlled refrigerator or cold room.
7. Do not interchange components between different lots of the kits. It is recommended that components between two kits of the same lot should not be interchanged.
8. Check that the reagents are clear and do not contain visible heavy particles or aggregates. If not, advise the laboratory supervisor to initiate the necessary procedures.
9. Avoid cross-contamination between serum/plasma samples by using disposable tips and changing them after each sample.
10. Avoid cross-contamination between kit reagents by using disposable tips and changing them between the use of each one.
11. Do not use the kit after the expiration date stated on external (primary container) and internal (vials) labels.
12. Treat all specimens as potentially infective. All human serum specimens should be handled at Biosafety Level 2, as recommended by the Center for Disease Control, Atlanta, U.S. in compliance with what reported in the Institutes of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
13. The use of disposable plastic-ware is recommended in the preparation of the washing solution or in transferring components into other containers of automated workstations, in order to avoid contamination.
14. Waste produced during the use of the kit has to be discarded in compliance with national directives and laws concerning laboratory waste of chemical and biological substances. In particular, liquid waste generated from the washing procedure, from residuals of controls and from samples has to be treated as potentially infective material and inactivated. Suggested procedures of inactivation are treatment with a 10% final concentration of household bleach for 16-18 hrs or heat inactivation by autoclave at 121℃ for 20 min..
15. Accidental spills have to be adsorbed with paper tissues soaked with household bleach and then with water. Tissues should then be discarded in proper containers designated for laboratory/hospital waste.
16. The Sulphuric Acid is an irritant. In case of spills, wash the surface with plenty of water.
17. Other waste materials generated from the use of the kit (example: tips used for samples and controls, used microplates) should be handled as potentially infective and

disposed according to national directives and laws concerning laboratory wastes.

G. SPECIMEN: PREPARATION AND RECOMMANDATIONS

1. Blood is drawn aseptically by venepuncture and plasma or serum is prepared using standard techniques of preparation of samples for clinical laboratory analysis. No influence has been observed in the preparation of the sample with citrate, EDTA and heparin.
2. Avoid any addition of preservatives to samples; especially sodium azide as this chemical would affect the enzymatic activity of the conjugate.
3. Samples have to be clearly identified with codes or names in order to avoid misinterpretation of results. When the kit is used for the screening of blood units, bar code labeling and electronic reading is strongly recommended.
4. Haemolysed (red) and visibly hyperlipemic ("milky") samples have to be discarded as they could generate false results. Samples containing residues of fibrin or heavy particles or microbial filaments and bodies should be discarded as they could give rise to false results.
5. Sera and plasma can be stored at +2°..8°C for up to five days after collection. For longer storage periods, samples can be stored frozen at –20°C for several months. Any frozen samples should not be frozen/thawed more than once as this may generate particles that could affect the test result.
6. If particles are present, centrifuge at 2.000 rpm for 20 min or filter using 0.2-0.8u filters to clean up the sample for testing.

H. PREPARATION OF COMPONENTS AND WARNINGS

A study conducted on an opened kit has not pointed out any relevant loss of activity up to 6 re-uses of the device and up to 6 months.

1. Microplates:
Allow the microplate to reach room temperature (about 1 hr) before opening the container. Check that the desiccant has not turned dark green, indicating a defect in storage.
In this case, call Dia.Pro's customer service.
Unused strips have to be placed back inside the aluminum pouch, with the desiccant supplied, firmly zipped and stored at +2°..8°C. After first opening, remaining strips are stable until the humidity indicator inside the desiccant bag turns from yellow to green.

2. Negative Control:
Ready to use. Mix well on vortex before use.

3. Positive Control:
Ready to use. Mix well on vortex before use.

4. Calibrator:
Add the volume of ELISA grade water, reported on the label, to the lyophilised powder; let fully dissolve and then gently mix on vortex.
Note: *The dissolved calibrator is not stable. Store it frozen in aliquots at –20°C.*

5. Wash buffer concentrate:
The whole content of the concentrated solution has to be diluted 20x with bidistilled water and mixed gently end-over-end before use. During preparation avoid foaming as the presence of bubbles could impact on the efficiency of the washing cycles.
Note: *Once diluted, the wash solution is stable for 1 week at +2..8°C.*

6. Enzyme conjugate:
Ready to use. Mix well on vortex before use.
Avoid contamination of the liquid with oxidizing chemicals, dust or microbes. If this component has to be transferred, use only plastic, and if possible, sterile disposable containers.

7. Chromogen/Substrate:
Ready to use. Mix well on vortex before use.
Avoid contamination of the liquid with oxidizing chemicals, air-driven dust or microbes. Do not expose to strong light, oxidizing agents and metallic surfaces.
If this component has to be transferred use only plastic, and if possible, sterile disposable container.

8. Specimen Diluent
Ready to use solution. Mix gently on vortex before use. Use all the content of one vial before opening a second one. The reagent is sensitive to oxidation.

9. Sulphuric Acid:
Ready to use. Mix well on vortex before use.
Attention: Irritant (Xi R36/38; S2/26/30)
Legenda: R 36/38 = Irritating to eyes and skin.
S 2/26/30 = In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

I. INSTRUMENTS AND TOOLS USED IN COMBINATION WITH THE KIT

1. Micropipettes have to be calibrated to deliver the correct volume required by the assay and must be submitted to regular decontamination (70% ethanol, 10% solution of bleach, hospital grade disinfectants) of those parts that could accidentally come in contact with the sample or the components of the kit. They should also be regularly maintained in order to show a precision of 1% and a trueness of ±2%.
2. The ELISA incubator has to be set at +37°C (tolerance of ±0.5°C) and regularly checked to ensure the correct temperature is maintained. Both dry incubators and water baths are suitable for the incubations, provided that the instrument is validated for the incubation of ELISA tests.
3. The ELISA washer is extremely important to the overall performances of the assay. The washer must be carefully validated and correctly optimized using the kit controls/calibrator and reference panels, before using the kit for routine laboratory tests. Usually 4-5 washing cycles (aspiration + dispensation of 350 ul/well of washing solution = 1 cycle) are sufficient to ensure that the assay performs as expected. A soaking time of 20-30 seconds between cycles is suggested. In order to set correctly their number, it is recommended to run an assay with the kit controls/calibrator and well characterized negative and positive reference samples, and check to match the values reported below in the sections "Validation of Test" and "Assay Performances". Regular calibration of the volumes delivered and maintenance (decontamination and cleaning of needles) of the washer has to be carried out according to the instructions of the manufacturer.
4. Incubation times have a tolerance of ±5%.
5. The ELISA microplate reader has to be equipped with a reading filter of 450nm and with a second filter (620-630nm, strongly recommended) for blanking purposes. Its standard performances should be (a) bandwidth $\leq$ 10 nm; (b) absorbance range from 0 to $\geq$ 2.0; (c) linearity to $\geq$ 2.0; repeatability $\geq$ 1%. Blanking is carried out on the well identified in the section "Assay Procedure". The optical system of the reader has to be calibrated regularly to ensure that the correct optical density is measured. It should be regularly maintained according to the manufacturer 's instructions.

6. When using an ELISA automated work station, all critical steps (dispensation, incubation, washing, reading, shaking, data handling) have to be carefully set, calibrated, controlled and regularly serviced in order to match the values reported in the sections “Validation of Test” and “Assay Performances”. The assay protocol has to be installed in the operating system of the unit and validated as for the washer and the reader. In addition, the liquid handling part of the station (dispensation and washing) has to be validated and correctly set. Particular attention must be paid to avoid carry over by the needles used for dispensing samples and for washing. This must be studied and controlled to minimize the possibility of contamination of adjacent wells due to strongly reactive samples, leading to false positive results. The use of ELISA automated work stations is recommended for blood screening and when the number of samples to be tested exceed 20-30 units per run.
7. Dia.Pro’s customer service offers support to the user in the setting and checking of instruments used in combination with the kit, in order to assure full compliance with the requirements described. Support is also provided for the installation of new instruments to be used with the kit.

L. PRE ASSAY CONTROLS AND OPERATIONS

1. Check the expiration date of the kit printed on the external label (primary container). Do not use if expired.
2. Check that the liquid components are not contaminated by visible particles or aggregates. Check that the Chromogen (TMB) is colourless or pale blue by aspirating a small volume of it with a sterile plastic pipette. Check that no breakage occurred in transportation and no spillage of liquid is present inside the box (primary container). Check that the aluminium pouch, containing the microplate, is not punctured or damaged.
3. Dilute all the content of the 20x concentrated Wash Solution as described above.
4. Dissolve the Calibrator as described above and gently mix.
5. Allow all the other components to reach room temperature (about 1 hr) and then mix gently on vortex all liquid reagents.
6. Set the ELISA incubator at +37°C and prepare the ELISA washer by priming with the diluted washing solution, according to the manufacturers instructions. Set the right number of washing cycles as found in the validation of the instrument for its use with the kit.
7. Check that the ELISA reader is turned on or ensure it will be turned on at least 20 minutes before reading.
8. If using an automated work station, turn on, check settings and be sure to use the right assay protocol.
9. Check that the micropipettes are set to the required volume.
10. Check that all the other equipment is available and ready to use.
11. In case of problems, do not proceed further with the test and advise the supervisor.

M. ASSAY PROCEDURE

The assay has to be performed according to the procedure given below, taking care to maintain the same incubation time for all the samples being tested.

1. Place the required number of strips in the plastic holder and carefully identify the wells for controls, calibrator and samples.
2. Leave the A1 well empty for blanking purposes.
3. Dispense 50 ul Specimen Diluent into all the control and sample wells.
4. Pipette 50 µl of the Negative Control in triplicate, 50 ul of the Calibrator in duplicate and then 50 ul of the Positive Control in single. Then dispense 50 ul of each of the samples.
5. Incubate the microplate for **60 min at +37°C.**

Important note: *Strips have to be sealed with the adhesive sealing foil, only when the test is performed manually. Do not cover strips when using ELISA automatic instruments.*

6. When the first incubation is finished, wash the microwells as previously described (section I.3)
7. Pipette 100 µl Enzyme Conjugate in all the wells, except A1; incubate the microplate for **60 min at +37°C.**

Important note: *Be careful not to touch the plastic inner surface of the well with the tip filled with the Enzyme Conjugate. Contamination might occur.*

8. When the second incubation is finished, wash the microwells as previously described (section I.3)
9. Pipette 100 µl Chromogen/Substrate into all the wells, A1 included.

Important note: *Do not expose to strong direct light. as a high background might be generated.*

10. Incubate the microplate protected from light at **room temperature (18-24°C) for 20 minutes**. Wells dispensed with negative control and negative samples will turn from clear to blue (competitive method).
11. Pipette 100 µl Sulphuric Acid into all the wells using the same pipetting sequence as in step 9 to stop the enzymatic reaction. Addition of the stop solution will turn the negative control and negative samples from blue to yellow.
12. Measure the colour intensity of the solution in each well, as described in section I.5 using a 450nm filter (reading) and a 620-630nm filter (background subtraction, strongly recommended), blanking the instrument on A1.

Important notes:

1. *If the second filter is not available, ensure that no finger prints are present on the bottom of the microwell before reading at 450nm. Finger prints could generate false positive results on reading.*
2. *Reading has should ideally be performed immediately after the addition of the Stop Solution but definitely no longer than 20 minutes afterwards. Some self oxidation of the chromogen can occur leading to a higher background.*

N. ASSAY SCHEME

Specimen Diluent	50 ul
Controls&calibrator and samples	50 ul
1st incubation	**60 min**
Temperature	+37°C
Wash	n°4-5
Enzyme Conjugate	100 ul
2nd incubation	**60 min**
Temperature	+37°C
Wash	n°4-5
TMB/H2O2 mix	100 ul
3rd incubation	**20 min**
Temperature	r.t.
Sulphuric Acid	100 ul
Reading OD	450nm

An example of dispensation scheme is reported below:

Microplate

	1	2	3	4	5	6	7	8	9	10	11	12
A	BLK	S2										
B	NC	S3										
C	NC	S4										
D	NC	S5										
E	CAL	S6										
F	CAL	S7										
G	PC	S8										
H	S1	S9										

Legenda: BLK = Blank NC = Negative Control
CAL = Calibrator PC = Positive Control S = Sample

O. INTERNAL QUALITY CONTROL

A check is performed on the controls/calibrator any time the kit is used in order to verify whether the expected OD450nm or Co/S values have been matched in the analysis.
Ensure that the following parameters are met:

Parameter	Requirements
Blank well	< 0.050 OD450nm value
Negative Control (NC)	> 1.000 OD450nm after blanking coefficient of variation < 20%
Calibrator (about 2 PEI U/ml)	Co/S > 1
Positive Control	< 0.200 OD450nm

If the results of the test match the requirements stated above, proceed to the next section.

If they do not, do not proceed any further and perform the following checks:

Problem	Check
Blank well > 0.050 OD450nm	that the Chromogen/Substrate solution has not become contaminated during the assay
Negative Control (NC) < 1.000 OD450nm after blanking coefficient of variation > 20%	1. that the washing procedure and the washer settings are as validated in the pre qualification study; 2. that the proper washing solution has been used and the washer has been primed with it before use; 3. that no mistake has been done in the assay procedure (dispensation of positive control instead of negative control; 4. that no contamination of the negative control or of the wells where the control was dispensed has occurred due to positive samples, to spills or to the enzyme conjugate; 5. that micropipettes have not become contaminated with positive samples or with the enzyme conjugate 6. that the washer needles are not blocked or partially obstructed.
Calibrator Co/S < 1	1. that the procedure has been correctly performed; 2. that no mistake has occurred during its distribution (ex.: dispensation of negative control instead 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the calibrator has occurred.
Positive Control > 0.200 OD450nm	1. that the procedure has been correctly performed; 2. that no mistake has occurred during the distribution of the control (dispensation of negative control instead of positive control). 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the positive control has occurred.

If any of the above problems have occurred, report the problem to the supervisor for further actions.

P. RESULTS

The results are calculated by means of a cut-off value determined with the following formula:

Cut-Off = (NC + PC) / 5

Important note*: When the calculation of results is performed by the operating system of an ELISA automated work station, ensure that the proper formulation is used to calculate the cut-off value and generate the correct interpretation of results.*

Q. INTERPRETATION OF RESULTS

Results are interpreted as ratio between the cut-off value and the sample OD450nm or Co/S.

Results are interpreted according to the following table:

Co/S	Interpretation
< 0.9	Negative
0.9 - 1.1	Equivocal
> 1.1	Positive

A negative result indicates that the patient has not been infected by HBV.
Any patient showing an equivocal result should be re-tested on a second sample taken 1-2 weeks after the initial sample.
The blood unit should not be transfused.
A positive result is indicative of HBV infection and therefore the patient should be treated accordingly or the blood unit should be discarded.

Important notes:

1. *Interpretation of results should be done under the supervision of the laboratory supervisor to reduce the risk of judgement errors and misinterpretations.*
2. *When test results are transmitted from the laboratory to another facility, attention must be paid to avoid erroneous data transfer.*
3. *Diagnosis of viral hepatitis infection has to be taken by and released to the patient by a suitably qualified medical doctor.*

An example of calculation is reported below.

The following data must not be used instead or real figures obtained by the user.

Negative Control: 2.000 – 2.200 – 2.000 OD450nm
Mean Value: 2.100 OD450nm
Higher than 1.000 – Accepted

Positive Control: 0.100 OD450nm
Lower than 0.200 – Accepted

Cut-Off = (2.100 + 0.100) / 5 = 0.440

Calibrator: 0.400-0.360 OD450nm
Mean value: 0.380 OD450nm
Co/S>1 – Accepted

Sample 1: 0.028 OD450nm
Sample 2: 1.890 OD450nm
Sample 1 Co/S > 1.1 positive
Sample 2 Co/S < 0.9 negative

R. PERFORMANCES

Evaluation of Performances has been conducted in accordance to what reported in the Common Technical Specifications or CTS (art. 5, Chapter 3 of IVD Directive 98/79/EC).

1. LIMIT OF DETECTION:

The sensitivity of the assay has been calculated by means of the reference preparation for HBcAb supplied by Paul Erlich Institute (PEI HBc Reference Material 82). The assay shows a sensitivity of about 1.25 PEI U/ml.
The table below reports the Co/S values shown by the PEI standard diluted as suggested by the manufacturer to prepare a limiting dilution curve in Fetal Calf Serum (FCS).

PEI U/ml	Lot 1001	Lot 0702	Lot 0702/2	Lot 1202
5	**22.6**	**18.0**	**19.0**	**17.7**
2.5	**8.0**	**5.5**	**5.4**	**5.0**
1.25	**1.1**	**1.3**	**1.0**	**1.0**
0.625	0.4	0.4	0.4	0.4

In addition Accurun 1 – series 3000 – supplied by Boston Biomedica Inc., USA, was tested to determine its Co/S value. Results are reported in the table below:

Accurun 1 – series 3000

Value	Lot 1001	Lot 0702	Lot 1202
Co/S	2.9	2.3	2.2

2. DIAGNOSTIC SPECIFICITY AND SENSITIVITY

The Performance Evaluation of the device was carried out in a trial conducted on more than total 6000 samples.

2.1 Diagnostic Specificity

It is defined as the probability of the assay of scoring negative in the absence of specific analyte. A total of more 5000 unselected donors, including 1st time donors, were examined.
In a first study 2023 samples were tested against a US company as reference. A specificity of 99.5% was found. In a second study 1588 samples were examined against a European company. A specificity of 99.7% was found. In the last study 1565 samples were assayed against the same US company; a value of 99.8% was found.
In addition to the above population, 206 samples from hospitalized patients were tested against the European company. A value of 99.3% specificity was found.
Moreover, diagnostic specificity was assessed by testing 164 potentially interfering specimens (other infectious diseases, patients affected by non viral hepatic diseases, dialysis patients, pregnant women, hemolized, lipemic, etc.) against the European company. A value of specificity of 100% was assessed.
Finally, both human plasma, derived with different standard techniques of preparation (citrate, EDTA and heparin), and human sera have been used to determine the specificity.
No false reactivity due to the method of specimen preparation has been observed.

2.2 Diagnostic Sensitivity

It defined as the probability of the assay of scoring positive in the presence of specific analyte.
373 positive specimens were tested against the European company; a diagnostic sensitivity of 99.7 was found.

3. PRECISION

The mean values obtained from a study conducted on three lots and on two samples of different anti-HBcAg reactivity, examined in 16 replicates in three separate runs is reported below:

BCAB.CE: lot # 1202

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	1.943	1.939	1.924	1.935
Std.Deviation	0.081	0.078	0.103	0.087
CV %	4.2	4.0	5.3	4.5

Calibrator (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.143	0.147	0.148	0.146
Std.Deviation	0.014	0.017	0.018	0.016
CV %	9.8	11.4	12.1	11.1
Co/S	2.8	2.7	2.6	2.7

BCAB.CE: lot # 0702

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	2.163	2.110	2.106	2.126
Std.Deviation	0.105	0.088	0.139	0.111
CV %	4.9	4.2	6.6	5.2

Calibrator (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.182	0.193	0.195	0.190
Std.Deviation	0.018	0.023	0.019	0.020
CV %	10.0	12.0	9.9	10.6
Co/S	2.5	2.2	2.3	2.3

BCAB.CE: lot # 0702/2

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	2.278	2.098	2.130	2.169
Std.Deviation	0.135	0.126	0.159	0.140
CV %	5.9	6.0	7.5	6.5

Calibrator (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.193	0.190	0.199	0.134
Std.Deviation	0.023	0.023	0.027	0.025
CV %	12.1	12.3	13.5	12.6
Co/S	2.4	2.2	2.2	2.3

The variability shown in the tables did not result in sample misclassification.

S. LIMITATIONS OF THE PROCEDURE

Bacterial contamination or heat inactivation of the specimen may affect the absorbance values of the samples with consequent alteration of the level of the analyte. This test is suitable only for testing single samples and not pooled ones.
Diagnosis of an infectious disease should not be established on the basis of a single test result. The patient's clinical history, symptomatology, as well as other diagnostic data should be considered.

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All the IVD Products manufactured by the company are under the control of a certified Quality Management System approved by an EC Notified Body. Each lot is submitted to a quality control and released into the market only if conforming with the EC technical specifications and acceptance criteria.

Produced by
Dia.Pro Diagnostic Bioprobes Srl
Via G. Carducci n° 27 – Sesto San Giovanni (MI) – Italy

CE
0318

HBe Ag&Ab

Enzyme Immunoassay (ELISA) for the determination of Hepatitis B Virus "e" Antigen and Antibody in human plasma and sera.

- for "in vitro" diagnostic use only -

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REF. HBE.CE
96 Tests

HBe Ag&Ab

A. INTENDED USE
Enzyme ImmunoAssay (ELISA) for the determination of Hepatitis B Virus "e" Antigen and Antibody in human plasma and sera.
The kit is intended for the follow-up of acute infection and of chronic patients under therapy.
For "in vitro" diagnostic use only.

B. INTRODUCTION
Hepatitis B "e" Antigen or HBeAg is known to be intimately associated with Hepatitis B Virus or HBV replication and the presence of infectious Dane particles in the blood.
Recently, it has been found that HBeAg is a product of proteolytic degradation of Hepatitis B core Antigen or HBcAg, occurring in hepatocites, whose expression is under the control of the precore region of HBV genome.
If HBeAg is considered a specific marker of infectivity, the presence of anti HBeAg antibodies in blood is recognised to be a clinical sign of recovery from infection to convalescence.
The determination of these two analytes in samples from HBV patients has become important for the classification of the phase of illness and as a prognostic value in the follow up of infected patients.

C. PRINCIPLE OF THE TEST
HBeAg:
HBeAg, if present in the sample, is captured by a specific monoclonal antibody, in the 1st incubation.
In the 2nd incubation, after washing, a tracer, composed of a mix of two specific anti HBeAg monoclonal antibodies, labeled with peroxidase (HRP), is added to the microplate and binds to the captured HBeAg.
The concentration of the bound enzyme on the solid phase is proportional to the amount of HBeAg in the sample and its activity is detected by adding the chromogen/substrate in the 3rd incubation.
The presence of HBeAg in the sample is determined by means of a cut-off value that allows for the semiquantitative detection of the antigen.

HBeAb
Anti HBeAg antibodies, if present in the sample, compete with a recombinant HBeAg preparation for a fixed amount of an anti HBeAg antibody, coated on the microplate wells.
The competitive assay is carried out in two incubations, the first with the sample and recHBeAg, and the second with a tracer, composed of two anti HBeAg monoclonal antibodies, labeled with peroxidase (HRP).
The concentration of the bound enzyme on the solid phase becomes inversely proportional to the amount of anti HBeAg antibodies in the sample and its activity is detected by adding the chromogen/substrate in the third incubation.
The concentration of HBeAg specific antibodies in the sample is determined by means of a cut-off value that allows for the semi quantitative detection of anti HBeAg antibodies.

D. COMPONENTS
The kit contains reagents for total 96 tests.

1. Microplate: MICROPLATE
n° 1 coated microplate
12 strips of 8 breakable wells coated with anti HBeAg specific monoclonal antibody, postcoated with bovine serum proteins and sealed into a bag with desiccant. Allow the microplate to reach room temperature before opening; reseal unused strips in the bag with desiccant and store at 2..8°C.

2. Negative Control: CONTROL -
1x2.0ml/vial. Ready to use control. It contains bovine serum, 0.09% sodium azide and 0.045% ProClin 300 as preservatives.
The negative control is colorless.

3. Antigen Positive Control: CONTROL + Ag
1x1.0ml/vial. Ready to use control. It contains 2% bovine serum albumin, non infectious recombinant HBeAg, 100 mM tris buffer pH 7.4+/-0.1, 0.09% sodium azide and 0.045% ProClin 300 as preservatives.
The positive control is green color coded.

4. Antibody Positive Control: **:** CONTROL + Ab
1x1.0ml/vial. Ready to use control. It contains 2% bovine serum albumin, human anti HbeAg positive plasma at about 10 PEI U/ml, 100 mM tris buffer pH 7.4+/-0.1, 0.09% sodium azide and 0.045% ProClin 300 as preservatives. The label is red colored.
The positive control is yellow color coded.

5. Antigen Calibrator: CALAG …ml
n° 1 vial. Lyophilised calibrator for HBeAg. To be dissolved with EIA grade water as reported in the label. It contains fetal bovine serum, non infectious recombinant HBeAg at 1 PEI U/ml +/-10%, 0.02% gentamicine sulphate and 0.045% ProClin 300 as preservatives.
Important Note: The volume necessary to dissolve the content of the vial may vary from lot to lot. Please use the right volume reported on the label.

6. Antibody Calibrator: CALAB …ml
n° 1 vial. Lyophilized calibrator for anti HBeAg antibody. To be dissolved with EIA grade water as reported in the label. It contains fetal bovine serum, positive plasma at 0.25 PEI U/ml +/-10%, 0.02% gentamicine sulphate and 0.045% ProClin 300 as preservatives. The label is red colored.
Important Note: The volume necessary to dissolve the content of the vial may vary from lot to lot. Please use the right volume reported on the label.

7. Wash buffer concentrate: WASHBUF 20X
1x60ml/bottle. 20x concentrated solution.
Once diluted, the wash solution contains 10 mM phosphate buffer pH 7.0+/-0.2, 0.05% Tween 20 and 0.045% ProClin 300.

8. Enzyme conjugate: CONJ
1x16ml/vial. Ready to use conjugate. It contains Horseradish peroxidase conjugated with a mix of monoclonal antibodies to HBeAg, 10 mM Tris buffer pH 6.8+/-0.1, 2% BSA, 0.045% ProClin 300 and 0.02% gentamicine sulphate as preservatives.
The reagent is red color coded.

9. HBe Antigen: Ag-HBe
1x10ml/vial. Ready to use reagent. It contains recombinant HBeAg, fetal bovine serum, buffered solution pH 8.0+/-0.1, 0.045% ProClin 300 and 0.09% sodium azide as preservatives.
The reagent is blue color coded.

10. Chromogen/Substrate: SUBS TMB
1x16ml/vial. Ready-to-use component. It contains a 50 mM citrate-phosphate buffered solution at pH 3.5-3.8, 4% dimethylsulphoxide, 0.03% tetra-methyl-benzidine or TMB and 0.02% hydrogen peroxide or H_2O_2.
Note: To be stored protected from light as sensitive to strong illumination.

11. Sulphuric Acid: H_2SO_4 O.3 M
1x15ml/vial. It contains 0.3 M H2SO4 solution.
Attention: Irritant (H315, H319; P280, P302+P352, P332+P313, P305+P351+P338, P337+P313, P362+P363).

12. Plate sealing foils n°2

13. Package insert n°1

E. MATERIALS REQUIRED BUT NOT PROVIDED
1. Calibrated Micropipettes (150ul, 100ul and 50ul) and disposable plastic tips.
2. EIA grade water (double distilled or deionised, charcoal treated to remove oxidizing chemicals used as disinfectants).
3. Timer with 60 minute range or higher.
4. Absorbent paper tissues.
5. Calibrated ELISA microplate thermostatic incubator (dry or wet) set at +37°C.
6. Calibrated ELISA microwell reader with 450nm (reading) and with 620-630nm (blanking) filters.
7. Calibrated ELISA microplate washer.
8. Vortex or similar mixing tools.

F. WARNINGS AND PRECAUTIONS
1. The kit has to be used by skilled and properly trained technical personnel only, under the supervision of a medical doctor responsible of the laboratory.
2. All the personnel involved in performing the assay have to wear protective laboratory clothes, talc-free gloves and glasses. The use of any sharp (needles) or cutting (blades) devices should be avoided. All the personnel involved should be trained in biosafety procedures, as recommended by the Center for Disease Control, Atlanta, U.S. and reported in the National Institute of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
3. All the personnel involved in sample handling should be vaccinated for HBV and HAV, for which vaccines are available, safe and effective.
4. The laboratory environment should be controlled so as to avoid contaminants such as dust or air-born microbial agents, when opening kit vials and microplates and when performing the test. Protect the Chromogen/Substrate (TMB) from strong light and avoid vibration of the bench surface where the test is undertaken.
5. Upon receipt, store the kit at 2-8°C into a temperature controlled refrigerator or cold room.
6. Do not interchange components between different lots of the kits. It is recommended that components between two kits of the same lot should not be interchanged.
7. Check that the reagents are clear and do not contain visible heavy particles or aggregates. If not, advise the laboratory supervisor to initiate the necessary procedures.
8. Avoid cross-contamination between serum/plasma samples by using disposable tips and changing them after each sample. Do not reuse disposable tips.
9. Avoid cross-contamination between kit reagents by using disposable tips and changing them between the use of each one. Do not reuse disposable tips.
10. Do not use the kit after the expiration date stated on external (primary container) and internal (vials) labels.
11. Treat all specimens as potentially infective. All human serum specimens should be handled at Biosafety Level 2, as recommended by the Center for Disease Control, Atlanta, U.S. in compliance with what reported in the Institutes of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
12. The use of disposable plastic-ware is recommended in the preparation of the washing solution or in transferring components into other containers of automated workstations, in order to avoid contamination.
13. Waste produced during the use of the kit has to be discarded in compliance with national directives and laws concerning laboratory waste of chemical and biological substances. In particular, liquid waste generated from the washing procedure, from residuals of controls and from samples has to be treated as potentially infective material and inactivated. Suggested procedures of inactivation are treatment with a 10% final concentration of household bleach for 16-18 hrs or heat inactivation by autoclave at 121°C for 20 min..
14. Accidental spills have to be adsorbed with paper tissues soaked with household bleach and then with water. Tissues should then be discarded in proper containers designated for laboratory/hospital waste.
15. The Stop Solution is an irritant. In case of spills, wash the surface with plenty of water
16. Other waste materials generated from the use of the kit (example: tips used for samples and controls, used microplates) should be handled as potentially infective and disposed according to national directives and laws concerning laboratory wastes.

G. SPECIMEN: PREPARATION AND RECOMMANDATIONS
1. Blood is drawn aseptically by venepuncture and plasma or serum is prepared using standard techniques of preparation of samples for clinical laboratory analysis. No influence has been observed in the preparation of the sample with citrate, EDTA and heparin.
2. Avoid any addition of preservatives; especially sodium azide as this chemical would affect the enzymatic activity of the conjugate, generating false negative results.
3. Samples have to be clearly identified with codes or names in order to avoid misinterpretation of results.
4. Haemolysed and visibly hyperlipemic ("milky") samples have to be discarded as they could generate false results. Samples containing residues of fibrin or heavy particles or microbial filaments and bodies should be discarded as they could give rise to false results.
5. Sera and plasma can be stored at +2°…+8°C in primary collection tubes for up to five days after collection.
Do not freeze primary tubes of collection. For longer storage periods, sera and plasma samples, carefully removed from the primary collection tube, can be stored frozen at –20°C for at least 12 months. Any frozen samples should not be frozen/thawed more than once as this may generate particles that could affect the test result.
6. If particles are present, centrifuge at 2.000 rpm for 20 min or filter using 0.2-0.8u filters to clean up the sample for testing.

H. PREPARATION OF COMPONENTS AND WARNINGS
A study conducted on an opened kit has not pointed out any relevant loss of activity up to 6 re-uses of the device and up to 3 months.

1. Microplate:
Allow the microplate to reach room temperature (about 1 hr) before opening the container. Check that the desiccant has not turned dark green, indicating a defect in manufacturing.
In this case, call Dia.Pro's customer service.
Unused strips have to be placed back into the aluminum pouch, with the desiccant supplied, firmly zipped and stored at +2°-8°C.
When opened the first time, unused strips are stable until the humidity indicator inside the desiccant bag turns from yellow to green.

2. Negative Control:
Ready to use. Mix well on vortex before use.

3. Antigen Positive Control:
Ready to use. Mix well on vortex before use.

4. Antibody Positive Control:
Ready to use. Mix well on vortex before use.

5. Antigen Calibrator:
Add the volume of ELISA grade water, reported on the label, to the lyophilized powder; let fully dissolve and then gently mix on vortex.

Note: The dissolved calibrator is not stable. Store it frozen in aliquots at –20°C.

6. Antibody Calibrator:
Add the volume of ELISA grade water, reported on the label, to the lyophilized powder; let fully dissolve and then gently mix on vortex.
Note: The dissolved calibrator is not stable. Store it frozen in aliquots at –20°C.

7. Wash buffer concentrate:
The whole content of the 20x concentrated solution has to be diluted with bidistilled water up to 1200 ml and mixed gently end-over-end before use.
During preparation avoid foaming as the presence of bubbles could impact on the efficiency of the washing cycles.
Note: Once diluted, the wash solution is stable for 1 week at +2..8° C.

8. Enzyme conjugate:
Ready to use. Mix well on vortex before use.
Avoid contamination of the liquid with oxidizing chemicals, air-driven dust or microbes. If this component has to be transferred, use only plastic, and if possible, sterile disposable containers.

9. HBe Antigen:
Ready to use. Mix well on vortex before use.
Avoid contamination of the liquid with oxidizing chemicals, air-driven dust or microbes. If this component has to be transferred, use only plastic, and if possible, sterile disposable containers.

10. Chromogen/Substrate:
Ready to use. Mix well on vortex before use.
Avoid contamination of the liquid with oxidizing chemicals, air-driven dust or microbes. Do not expose to strong light, oxidizing agents and metallic surfaces.
If this component has to be transferred use only plastic, and if possible, sterile disposable container.

11. Sulphuric Acid:
Ready to use. Mix well on vortex before use.
Attention: Irritant (H315, H319; P280, P302+P352, P332+P313, P305+P351+P338, P337+P313, P362+P363).

Legenda:

Warning **H statements:**
H315 – Causes skin irritation.
H319 – Causes serious eye irritation.

Precautionary **P statements:**
P280 – Wear protective gloves/protective clothing/eye protection/face protection.

P302 + P352 – IF ON SKIN: Wash with plenty of soap and water.
P332 + P313 – If skin irritation occurs: Get medical advice/attention.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337 + P313 – If eye irritation persists: Get medical advice/attention.
P362 + P363 – Take off contaminated clothing and wash it before reuse.

I. INSTRUMENTS AND TOOLS USED IN COMBINATION WITH THE KIT

1. Micropipettes have to be calibrated to deliver the correct volume required by the assay and must be submitted to regular decontamination (household alcohol, 10% solution of bleach, hospital grade disinfectants) of those parts that could accidentally come in contact with the sample. Decontamination of spills or residues of kit components should also be carried out regularly. They should also be regularly maintained in order to show a precision of 1% and a trueness of ±2%.
2. The ELISA incubator has to be set at +37°C (tolerance of +/-0.5°C) and regularly checked to ensure the correct temperature is maintained. Both dry incubators and water baths are suitable for the incubations, provided that the instrument is validated for the incubation of ELISA tests.
3. The **ELISA washer** is extremely important to the overall performances of the assay. The washer must be carefully validated in advance, checked for the delivery of the right dispensation volume and regularly submitted to maintenance according to the manufacturer's instructions for use. In particular the washer, at the end of the daily workload, has to be extensively cleaned out of salts with deionized water. Before use, the washer has to be extensively primed with the diluted Washing Solution.
   The instrument weekly has to be submitted to decontamination according to its manual (NaOH 0.1 M decontamination suggested).
   5 washing cycles (aspiration + dispensation of 350ul/well of washing solution + 20 sec soaking = 1 cycle) are sufficient to ensure the assay with the declared performances. If soaking is not possible add one more cycle of washing.
   An incorrect washing cycle or salt-blocked needles are the major cause of false positive reactions.
4. Incubation times have a tolerance of ±5%.
5. The ELISA reader has to be equipped with a reading filter of 450nm and with a second filter of 620-630nm, mandatory for blanking purposes. Blanking is carried out on the well identified in the section "Assay Procedure". The optical system of the reader has to be calibrated regularly to ensure the correct optical density is measured. It should be regularly maintained according to the manufacturer 's instructions.
6. When using an ELISA automated work station, all critical steps (dispensation, incubation, washing, reading, data handling) have to be carefully set, calibrated, controlled and regularly serviced in order to match the values reported in the section "Internal Quality Control''. The assay protocol has to be installed in the operating system of the unit and validated as for the washer and the reader. In addition, the liquid handling part of the station (dispensation and washing) has to be validated and correctly set. Particular attention must be paid to avoid carry over by the needles used for dispensing and for washing. This must be studied and controlled to minimize the possibility of contamination of adjacent wells. The use of ELISA automated work stations is recommended when the number of samples to be tested exceed 20-30 units per run.
7. Dia.Pro's customer service offers support to the user in the setting and checking of instruments used in combination with the kit, in order to assure compliance with the requirements described. Support is also provided for the installation of new instruments to be used with the kit.

L. PRE ASSAY CONTROLS AND OPERATIONS

1. Check the expiration date of the kit printed on the external label (primary container). Do not use if expired.
2. Check that the liquid components are not contaminated by visible particles or aggregates. Check that the Chromogen/Substrate (TMB+H_2O_2) is colourless or pale blue by aspirating a small volume of it with a sterile plastic pipette. Check that no breakage occurred in transportation

and no spillage of liquid is present inside the box (primary container). Check that the aluminium pouch, containing the microplate, is not punctured or damaged.
3. Dilute all the content of the 20x concentrated Wash Solution as described above.
4. Dissolve the Calibrator as described above and gently mix.
5. Allow all the other components to reach room temperature (about 1 hr) and then mix gently on vortex all liquid reagents.
6. Set the ELISA incubator at +37°C and prepare the ELISA washer by priming with the diluted washing solution, according to the manufacturers instructions. Set the right number of washing cycles as reported in the specific section.
7. Check that the ELISA reader is turned on or ensure it will be turned on at least 20 minutes before reading.
8. If using an automated work station, turn on, check settings and be sure to use the right assay protocol.
9. Check that the micropipettes are set to the required volume.
10. Check that all the other equipment is available and ready to use.

In case of problems, do not proceed further with the test and advise the supervisor.

M. ASSAY PROCEDURE
The assay has to be performed according to the procedure given below, taking care to maintain the same incubation time for all the samples being tested.

A) HBe Antigen:

1. Place the required number of strips in the plastic holder and carefully identify the wells for controls, calibrator and samples.
2. Leave the A1 well empty for blanking purposes.
3. Pipette 100 µl of the Negative Control in triplicate, 100 µl of the Antigen Calibrator in duplicate and then 100 µl of the Antigen Positive Control in single.
4. Then dispense 100 µl of samples in the proper wells.
5. Check for the presence of samples in wells by naked eye (there is a marked colour difference between empty and full wells) or by reading at 450/620nm (samples show OD values higher than 0.100).
6. Incubate the microplate for **60 min at +37°C**.

Important note: *Strips have to be sealed with the adhesive sealing foil, only when the test is performed manually. Do not cover strips when using ELISA automatic instruments.*

7. When the first incubation is finished, wash the microwells as previously described (section I.3)
8. Dispense 100 µl Enzyme Conjugate in all wells, except for A1, used for blanking operations.

Important note: *Be careful not to touch the inner surface of the well with the pipette tip and not to immerse the top of it into samples or controls. Contamination might occur.*

9. Check that the reagent has been dispensed properly and then incubate the microplate for **60 min at +37°C**.
10. When the second incubation is finished, wash the microwells as previously described (section I.3)
11. Pipette 100 µl Chromogen/Substrate into all the wells, A1 included.

Important note: *Do not expose to strong direct light as a high background might be generated.*

12. Incubate the microplate protected from light at **room temperature (18-24°C) for 20 minutes**. Wells dispensed with positive control and positive samples will turn from clear to blue.
13. Pipette 100 µl Sulphuric Acid into all the wells using the same pipetting sequence as in step 11. Addition of the stop solution will turn the positive control and positive samples from blue to yellow.
14. Measure the color intensity of the solution in each well, as described in section I.5 using a 450nm filter (reading) and a 620-630nm filter (background subtraction, mandatory), blanking the instrument on A1.

B) HBe Antibody:

1. Place the required number of strips in the plastic holder and carefully identify the wells for controls, calibrator and samples.
2. Leave the A1 well empty for blanking purposes.
3. Pipette 50 µl of the Negative Control in triplicate, 50 µl of the Antibody Calibrator in duplicate and then 50 µl of the Antibody Positive Control in single.
4. Then dispense 50 µl of samples in the proper wells.
5. Check for the presence of samples in wells by naked eye (there is a marked color difference between empty and full wells) or by reading at 450/620nm (samples show OD values higher than 0.100).
6. Dispense then 50 µl of HBe Antigen in all the wells, except for A1.
7. Incubate the microplate for **60 min at +37°C**.

Important note: *Strips have to be sealed with the adhesive sealing foil, only when the test is performed manually. Do not cover strips when using ELISA automatic instruments.*

8. When the first incubation is finished, wash the microwells as previously described (section I.3)
9. Finally proceed as described for the HBeAg assay from point 8 to the last one.

Important notes:
1. *Ensure that no finger prints are present on the bottom of the microwell before reading. Finger prints could generate false positive results on reading.*
2. *Reading should ideally be performed immediately after the addition of the Stop Solution but definitely no longer than 20 minutes afterwards. Some self oxidation of the chromogen can occur leading to a higher background.*
3. *The Calibrator (CAL) does not affect the cut-off calculation and therefore the test results calculation. The Calibrator may be used only when a laboratory internal quality control is required by the management.*

N. ASSAY SCHEME

HBe antigen test

Controls and calibrator Samples	100 ul 100 ul
1st incubation	**60 min**
Temperature	+37°C
Wash step	n° 5 cycles with 20'' of soaking OR n° 6 cycles without soaking
Enzyme Conjugate	100 ul
2nd incubation	**60 min**
Temperature	+37°C
Wash step	n° 5 cycles with 20'' of soaking OR n° 6 cycles without soaking
TMB/H2O2 mix	100 ul
3rd incubation	**20 min**
Temperature	r.t.
Sulphuric Acid	100 ul
Reading OD	450nm/620-630nm

HBe antibody test

Controls and calibrator Samples	50 ul 50 ul
Neutralising antigen	50 ul
1st incubation	**60 min**
Temperature	+37°C
Wash step	n° 5 cycles with 20" of soaking OR n° 6 cycles without soaking
Enzymatic conjugate	100 ul
2nd incubation	**60 min**
Temperature	+37°C
Wash step	n° 5 cycles with 20" of soaking OR n° 6 cycles without soaking
TMB/H2O2 mixture	100 ul
3rd incubation	**20 min**
Temperature	r.t.
Sulphuric Acid	100 ul
Reading OD	450nm/620-630nm

An example of dispensation scheme is reported below:

Microplate

	1	2	3	4	5	6	7	8	9	10	11	12
A	BLK	S2										
B	NC	S3										
C	NC	S4										
D	NC	S5										
E	CAL	S6										
F	CAL	S7										
G	PC	S8										
H	S1	S9										

Legenda: BLK = Blank // NC = Negative Control
PC = Positive Control // CAL = Calibrators // S = Sample

O. INTERNAL QUALITY CONTROL

A validation check is carried out on the controls any time the kit is used in order to verify whether the performances of the assay are as qualified.

Control that the following data are matched:

HBe Antigen

Check	OD450nm
Blank well	< 0.100 OD450nm
Negative Control (NC)	< 0.150 OD450nm after blanking coefficient of variation < 30%
Antigen Calibrator	S/Co > 2.0
Positive Control (PC)	> 1.500 OD450nm

HBe Antibody

Check	OD450nm
Blank well	< 0.100 OD450nm
Negative Control (NC)	> 1.000 OD450nm after blanking coefficient of variation < 10%
Antibody Calibrator	OD450nm < NC/1.5
Positive Control (PC)	OD450nm < NC/10

If the results of the test match the requirements stated above, proceed to the next section.

If they do not, don't proceed any further and perform the following checks:

HBeAg

Problem	Check
Blank well > 0.100 OD450nm	1. that the Chromogen/Substrate solution has not become contaminated during the assay
Negative Control (NC) > 0.150 OD450nm after blanking coefficient of variation > 30%	1. that the washing procedure and the washer settings are as validated in the pre qualification study; 2. that the proper washing solution has been used and the washer has been primed with it before use; 3. that no mistake has been done in the assay procedure (dispensation of positive control instead of negative control); 4. that no contamination of the negative control or of the wells where the control was dispensed has occurred due to positive samples, to spills or to the enzyme conjugate; 5. that micropipettes have not become contaminated with positive samples or with the enzyme conjugate 6. that the washer needles are not blocked or partially obstructed.
Calibrator S/Co < 2	1. that the procedure has been correctly performed; 2. that no mistake has occurred during its distribution (ex.: dispensation of negative control instead); 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the calibrator has occurred.
Positive Control < 1.500 OD450nm	1. that the procedure has been correctly performed; 2. that no mistake has occurred during the distribution of the control (dispensation of negative control instead of positive control); 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the positive control has occurred.

HBe antibody

Problem	Check
Blank well > 0.100 OD450nm	1. that the Chromogen/Substrate solution has not become contaminated during the assay
Negative Control (NC) < 1.000 OD450nm after blanking coefficient of variation > 10%	1. that the washing procedure and the washer settings are as validated in the pre qualification study; 2. that the proper washing solution has been used and the washer has been primed with it before use; 3. that no mistake has been done in the assay procedure (e.g.: dispensation of positive control instead of negative control; no dispensation of the Neutralizing Antigen; no dispensation of the Enzyme Conjugate); 4. that no contamination of the negative control or of the wells where the control was dispensed has occurred; 5. that micropipettes have not become contaminated with positive samples; 6. that the washer needles are not blocked or partially obstructed.

Calibrator OD450nm > NC/1.5	1. that the procedure has been correctly performed; 2. that no mistake has occurred during its distribution (ex.: dispensation of negative control instead; no dispensation of the Neutralizing Antigen; no dispensation of the Enzyme Conjugate); 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the calibrator has occurred.
Positive Control OD450nm > NC/10	1. that the procedure has been correctly performed; 2. that no mistake has occurred during the distribution of the control; 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the positive control has occurred.

If any of the above problems have occurred, report the problem to the supervisor for further actions.

Important note:
The analysis must be done proceeding as the reading step described in the section M, point 14.

P. CALCULATION OF THE CUT-OFF
The results are calculated by means of a cut-off value determined with the following formula:

HBeAg:

NC + 0.100 = Cut-Off (Co)

The value found for the test is used for the interpretation of results as described in the next paragraph.

HBeAb:

(NC + PC) / 3 = Cut-Off (Co)

Important note*: When the calculation of results is performed by the operating system of an ELISA automated work station, ensure that the proper formulation is used to calculate the cut-off value and generate the correct interpretation of results.*

Q. INTERPRETATION OF RESULTS
Results are interpreted as follows:

HBeAg:

S/Co	Interpretation
< 0.9	Negative
0.9 - 1.1	Equivocal
> 1.1	Positive

HBeAb:

Co/S	Interpretation
< 0.9	Negative
0.9 - 1.1	Equivocal
> 1.1	Positive

Note:
S = OD450nm/620-630nm of the sample
Co = cut-off value

An example of calculation for HBeAg assay is reported below (data obtained proceeding as the the reading step described in the section M, point 14):

The following data must not be used instead or real figures obtained by the user.

Negative Control: 0.020 – 0.030 – 0.025 OD450nm
Mean Value: 0.025 OD450nm
Lower than 0.150 – Accepted

Positive Control: 2.489 OD450nm
Higher than 1.500 – Accepted
Cut-Off = 0.025+0.100 = 0.125
Calibrator: 0.520 - 0.540 OD450nm
Mean value: 0.530 OD450nm S/Co = 4.2
S/Co higher than 2.0 – Accepted

Sample 1: 0.030 OD450nm
Sample 2: 1.800 OD450nm
Sample 1 S/Co < 0.9 = negative
Sample 2 S/Co > 1.1 = positive

An example of calculation for HBeAb is reported below (data obtained proceeding as the the reading step described in the section M, point 14):

The following data must not be used instead or real figures obtained by the user.

Negative Control: 2.100 – 2.200 – 2.000 OD450nm
Mean Value: 2.100 OD450nm
Higher than 1.000 – Accepted

Positive Control: 0.100 OD450nm
Lower than NC/10 – Accepted

Cut-Off = (2.100 + 0.100) / 3 = 0.733
Calibrator: 0.720-0.760 OD450nm
Mean value: 0.740 OD450nm
OD450nm < NC/1.5 – Accepted

Sample 1: 0.020 OD450nm
Sample 2: 1.900 OD450nm
Sample 1 Co/S > 1.1 positive
Sample 2 Co/S < 0.9 negative

Important notes:
1. *Interpretation of results should be done under the supervision of the laboratory director to reduce the risk of judgment errors and misinterpretations.*
2. *The Identification of the clinical status of a HBV patient (acute, chronic, asymptomatic hepatitis) has to be done on the basis also of the other markers of HBV infection (HBsAg, HBsAb, HBcAb, HBcIgM);*
3. *When test results are transmitted from the laboratory to another facility, attention must be paid to avoid erroneous data transfer.*
4. *Diagnosis of viral hepatitis infection has to be taken by and released to the patient by a suitably qualified medical doctor.*

R. PERFORMANCE CHARACTERISTICS

A) HBeAg

1. Limit of detection

The limit of detection of the assay has been calculated by means of the International Standard for HBeAg, supplied by Paul Erlich Institute (PEI).

The data obtained by examining the limit of detection on three lots is reported in the table below.

HBE.CE Lot ID	PEI U/ml HBeAg
0103	0.25
0103/2	0.25
0303	0.25

In addition the preparation Accurun # 51, produced by Boston Biomedica Inc., USA, has been tested, upon dilution in FCS. Results are reported for three lots of products.

BBI's Accurun 51 (S/Co)

HBE.CE Lot ID	1 x	2 x	4 x	8 x	16x
0103	**4.1**	**1.6**	0.9	0.6	0.4
0103/2	**4.1**	**1.7**	0.9	0.6	0.4
0303	**4.0**	**1.6**	0.9	0.5	0.4

2. Diagnostic Sensitivity:

The diagnostic sensitivity has been tested on panels of samples classified positive by a US FDA approved kit.

Positive samples were collected from different HBV pathologies (acute, chronic) bearing HBeAg reactivity.

An overall value > 98% has been found in the study conducted on a total number of more than 200 samples.

Moreover the Panel of Seroconversion code PHM 935B, produced by BBI, was examined.

Data are reported below and compared with those reported by BBI for two other commercial products.

Sample ID	HBE.CE S/Co	Abbott EIA S/Co	Sorin EIA S/Co
21	5.4	4.5	6.3
22	3.7	4.3	5.4
23	1.9	3.2	3.1
24	1.1	2.4	1.5
25	1.0	2.1	1.2
26	0.6	1.7	0.7
27	0.2	0.8	0.3
28	0.2	0.6	0.2
29	0.2	0.4	0.2
30	0.2	0.3	0.2
31	0.1	0.3	0.2
32	0.1	0.3	0.2

Finally the Performance Panel code PHJ 201, produced by BBI, was tested. Data are reported below and compared with those reported by BBI for an other commercial product.

Member	PEI U/ml	HBE.CE	Sorin EIA
1	3	3.3	7.0
2	6	17.5	21.9
3	26	30.1	37.1
4	31	29.4	23.5
5	1	1.1	2.2
6	2	2.3	6.9
7	35	30.1	24.6
8	38	29.2	31.9
9	4	16.6	10.8
10	-	0.3	0.2
11	1	3.4	3.6
12	< 1	0.2	1.2
13	< 1	0.9	1.4
14	-	0.2	0.2
15	-	0.4	0.1
16	-	0.5	0.1
17	-	0.3	0.2
18	-	0.2	0.2
19	-	0.2	0.1
20	-	0.2	0.1
21	-	0.3	1.0
22	-	0.3	0.1
23	-	0.4	0.1
24	-	0.2	0.2
25	-	0.3	0.2

3. Diagnostic Specificity:

The diagnostic specificity has been determined on panels of negative samples from normal individuals and blood donors, classified negative with a FDA approved kit.

Both plasma, derived with different standard techniques of preparation (citrate, EDTA and heparin), and sera have been used to determine the specificity.

No false reactivity due to the method of specimen preparation has been observed.

Frozen specimens have also been tested to check whether this interferes with the performance of the test. No interference was observed on clean and particle free samples.

Samples derived from patients with different viral (HCV and HAV) and non viral pathologies of the liver that may interfere with the test were examined.

No cross reaction were observed.

The Performance Evaluation study conducted in a qualified external reference center on more than 500 samples has provided a value > 98% .

4. Precision

It has been calculated on two samples examined in 16 replicate in three different runs on three lots.

The values found were as follows:

HBE.CE: lot # 0103

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.030	0.027	0.032	0.029
Std.Deviation	0.002	0.002	0.003	0.002
CV %	7.4	8.2	7.9	7.8

PEI 1 U/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.569	0.559	0.575	0.568
Std.Deviation	0.027	0.029	0.028	0.028
CV %	4.7	5.3	4.9	4.9
S/Co	4.4	4.4	4.4	4.4

HBE.CE: lot # 0103/2

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.033	0.031	0.030	0.032
Std.Deviation	0.003	0.003	0.002	0.003
CV %	7.9	8.5	7.4	8.0

PEI 1 U/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.565	0.573	0.568	0.569
Std.Deviation	0.026	0.025	0.024	0.025
CV %	4.7	4.3	4.2	4.4
S/Co	4.2	4.4	4.4	4.3

HBE.CE: lot # 0303

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.029	0.034	0.038	0.034
Std.Deviation	0.003	0.003	0.004	0.003
CV %	9.7	9.8	9.2	9.6

PEI 1 U/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.579	0.573	0.564	0.572
Std.Deviation	0.023	0.028	0.025	0.025
CV %	4.1	4.8	4.5	4.5
S/Co	4.5	4.3	4.1	4.3

B) HBe Antibody

1. Limit of detection

The limit of detection of the assay has been calculated by means of the International Standard for HBeAb, supplied by Paul Erlich Institute (PEI).

The data obtained by examining the limit of detection on three lots is reported in the table below.

HBE.CE Lot ID	PEI U/ml HBeAb
0103	0.25
0103/2	0.25
0303	0.25

In addition the preparation Accurun # 52, produced by Boston Biomedica Inc., USA, has been tested, upon dilution in FCS. Results are reported for three lots of products.

Accurun 52 (Co/S)

HBE.CE Lot ID	1 x	2 x	4 x	8 x	16x
0103	1.0	0.8	0.6	0.4	0.4
0103/2	1.0	0.8	0.6	0.5	0.4
0303	1.0	0.8	0.6	0.4	0.4

2. Diagnostic sensitivity:

The diagnostic sensitivity has been tested on panels of samples classified positive for HBeAb by a US FDA approved kit.

Positive samples were collected from different HBV pathologies bearing anti HBeAg antibody reactivity.

An overall value > 98% has been found in the study conducted on a total number of more than 200 samples.

Moreover the Panel of Seroconversion code PHM 935B, produced by BBI, was examined.

Data are reported below and compared with those reported by BBI for two other commercial products.

Sample ID	HBE.CE Co/S	Abbott EIA Co/S	Sorin EIA Co/S
21	0.4	0.4	0.5
22	0.4	0.5	0.6
23	0.4	0.6	0.5
24	0.4	0.5	0.6
25	0.4	0.6	0.5
26	0.5	0.6	0.6
27	0.6	0.8	0.7
28	0.7	0.9	0.7
29	0.6	0.9	0.7
30	0.8	1.0	0.9
31	1.0	1.3	1.1
32	1.0	1.2	1.0

Finally the Performance Panel code PHJ 201, produced by BBI, was tested. Data are reported below and compared with those reported by BBI for another commercial product.

Member	PEI U/ml	HBE.CE	Sorin EIA
1	-	0.3	0.5
2	-	0.2	0.5
3	-	0.2	0.5
4	-	0.2	0.5
5	-	0.3	0.6
6	-	0.3	0.6
7	-	0.2	0.4
8	-	0.2	0.4
9	-	0.2	0.5
10	-	1.9	0.6
11	-	0.3	0.5
12	-	0.4	0.9
13	2	4.4	9.1
14	1	3.8	2.9
15	< 1	1.0	1.5
16	> 50	4.3	120.9
17	< 1	1.0	1.0
18	5	5.6	21.8
19	1	2.7	6.4
20	11	5.0	47.3
21	2	1.9	10.0
22	26	28.1	90.7
23	-	0.3	0.5
24	< 1	0.8	1.3
25	50	28.1	167.4

3. Diagnostic specificity:

The clinical specificity has been determined as described before for HBeAg.

The Performance Evaluation study conducted in a qualified external reference center on more than 500 samples has provided a value > 98% .

4. Precision:

It has been calculated on two samples examined in 16 replicate in three different runs on three lots.

The values found were as follows:

HBE.CE: lot # 0103

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	2.484	2.420	2.471	2.458
Std.Deviation	0.129	0.160	0.142	0.144
CV %	5.2	6.6	5.7	5.9

PEI 0.25 U/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.867	0.800	0.878	0.848
Std.Deviation	0.043	0.060	0.050	0.051
CV %	5.0	7.5	5.7	6.1
Co/S	1.0	1.0	1.0	1.0

HBE.CE: lot # 0103/2

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	2.316	2.361	2.413	2.363
Std.Deviation	0.127	0.144	0.146	0.139
CV %	5.5	6.1	6.0	5.9

PEI 0.25 U/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.767	0.793	0.785	0.781
Std.Deviation	0.041	0.050	0.046	0.046
CV %	5.4	6.3	5.8	5.8
Co/S	1.0	1.0	1.0	1.0

HBE.CE: lot #0303

Negative Control (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	2.334	2.415	2.437	2.395
Std.Deviation	0.146	0.155	0.158	0.153
CV %	6.3	6.4	6.5	6.4

PEI 0.25 U/ml (N = 16)

Mean values	1st run	2nd run	3rd run	Average value
OD 450nm	0.850	0.867	0.876	0.864
Std.Deviation	0.052	0.051	0.048	0.050
CV %	6.1	5.9	5.5	5.8
Co/S	0.9	1.0	1.0	1.0

Important note:
The performance data have been obtained proceeding as the reading step described in the section M, point 14.

S. LIMITATIONS

Frozen samples containing fibrin particles or aggregates may generate false positive results.
Bacterial contamination or heat inactivation of the specimen may affect the absorbance values of the samples with consequent alteration of the level of the analyte.
This test is suitable only for testing single samples and not pooled ones.
Diagnosis of an infectious disease should not be established on the basis of a single test result. The patient's clinical history, symptomatology, as well as other diagnostic data should be considered.

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All the IVD Products manufactured by the company are under the control of a certified Quality Management System approved by an EC Notified Body. Each lot is submitted to a quality control and released into the market only if conforming with the EC technical specifications and acceptance criteria.

Manufacturer:
Dia.Pro Diagnostic Bioprobes S.r.l.
Via G. Carducci n° 27 – Sesto San Giovanni (MI) – Italy

CE
0318

HCV Ab

Version 4.0 Enzyme Immunoassay for the determination of anti Hepatitis C Virus antibody in human serum and plasma

- for "in vitro" diagnostic use only -

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REF CVAB.CE
96,192,480,960 Tests

HCV Ab

A. INTENDED USE

Version 4.0 Enzyme ImmunoAssay (ELISA) for the determination of antibodies to Hepatitis C Virus in human plasma and sera. The kit is intended for the screening of blood units and the follow-up of HCV-infected patients.
For "in vitro" diagnostic use only.

B. INTRODUCTION

The World Health Organization (WHO) define Hepatitis C infection as follows:

"Hepatitis C is a viral infection of the liver which had been referred to as parenterally transmitted "non A, non B hepatitis" until identification of the causative agent in 1989. The discovery and characterization of the hepatitis C virus (HCV) led to the understanding of its primary role in post-transfusion hepatitis and its tendency to induce persistent infection.

HCV is a major cause of acute hepatitis and chronic liver disease, including cirrhosis and liver cancer. Globally, an estimated 170 million persons are chronically infected with HCV and 3 to 4 million persons are newly infected each year. HCV is spread primarily by direct contact with human blood. The major causes of HCV infection worldwide are use of unscreened blood transfusions, and re-use of needles and syringes that have not been adequately sterilized. No vaccine is currently available to prevent hepatitis C and treatment for chronic hepatitis C is too costly for most persons in developing countries to afford. Thus, from a global perspective, the greatest impact on hepatitis C disease burden will likely be achieved by focusing efforts on reducing the risk of HCV transmission from nosocomial exposures (e.g. blood transfusions, unsafe injection practices) and high-risk behaviours (e.g. injection drug use).

Hepatitis C virus (HCV) is one of the viruses (A, B, C, D, and E), which together account for the vast majority of cases of viral hepatitis. It is an enveloped RNA virus in the *flaviviridae* family which appears to have a narrow host range. Humans and chimpanzees are the only known species susceptible to infection, with both species developing similar disease. An important feature of the virus is the relative mutability of its genome, which in turn is probably related to the high propensity (80%) of inducing chronic infection. HCV is clustered into several distinct genotypes which may be important in determining the severity of the disease and the response to treatment.

The incubation period of HCV infection before the onset of clinical symptoms ranges from 15 to 150 days. In acute infections, the most common symptoms are fatigue and jaundice; however, the majority of cases (between 60% and 70%), even those that develop chronic infection, are a symptomatic. About 80% of newly infected patients progress to develop chronic infection. Cirrhosis develops in about 10% to 20% of persons with chronic infection, and liver cancer develops in 1% to 5% of persons with chronic infection over a period of 20 to 30 years. Most patients suffering from liver cancer who do not have hepatitis B virus infection have evidence of HCV infection. The mechanisms by which HCV infection leads to liver cancer are still unclear. Hepatitis C also exacerbates the severity of underlying liver disease when it coexists with other hepatic conditions. In particular, liver disease progresses more rapidly among persons with alcoholic liver disease and HCV infection. HCV is spread primarily by direct contact with human blood. Transmission through blood transfusions that are not screened for HCV infection, through the reuse of inadequately sterilized needles, syringes or other medical equipment, or through needle-sharing among drug-users, is well documented. Sexual and perinatal transmission may also occur, although less frequently. Other modes of transmission such as social, cultural, and behavioural practices using percutaneous procedures (e.g. ear and body piercing, circumcision, tattooing) can occur if inadequately sterilized equipment is used. HCV is not spread by sneezing, hugging, coughing, food or water, sharing eating utensils, or casual contact.

In both developed and developing countries, high risk groups include injecting drug users, recipients of unscreened blood, haemophiliacs, dialysis patients and persons with multiple sex partners who engage in unprotected sex. In developed countries, it is estimated that 90% of persons with chronic HCV infection are current and former injecting drug users and those with a history of transfusion of unscreened blood or blood products. In many developing countries, where unscreened blood and blood products are still being used, the major means of transmission are unsterilized injection equipment and unscreened blood transfusions. In addition, people who use traditional scarification and circumcision practices are at risk if they use or re-use unsterilized tools.

WHO estimates that about 170 million people, 3% of the world's population, are infected with HCV and are at risk of developing liver cirrhosis and/or liver cancer. The prevalence of HCV infection in some countries in Africa, the Eastern Mediterranean, South-East Asia and the Western Pacific (when prevalence data are available) is high compared to some countries in North America and Europe.

Diagnostic tests for HCV are used to prevent infection through screening of donor blood and plasma, to establish the clinical diagnosis and to make better decisions regarding medical management of a patient. Diagnostic tests commercially available today are based on Enzyme immunosorbent assays (EIA) for the detection of HCV specific antibodies. EIAs can detect more than 95% of chronically infected patients but can detect only 50% to 70% of acute infections. A recombinant immunoblot assay (RIBA) that identifies antibodies which react with individual HCV antigens is often used as a supplemental test for confirmation of a positive EIA result. Testing for HCV circulating by amplification tests RNA (e.g. polymerase chain reaction or PCR, branched DNA assay) is also being utilized for confirmation of serological results as well as for assessing the effectiveness of antiviral therapy. A positive result indicates the presence of active infection and a potential for spread of the infection and or/the development of chronic liver disease.

Antiviral drugs such as interferon taken alone or in combination with ribavirin, can be used for the treatment of persons with chronic hepatitis C, but the cost of treatment is very high. Treatment with interferon alone is effective in about 10% to 20% of patients. Interferon combined with ribavirin is effective in about 30% to 50% of patients. Ribavirin does not appear to be effective when used alone.

There is no vaccine against HCV. Research is in progress but the high mutability of the HCV genome complicates vaccine development. Lack of knowledge of any protective immune response following HCV infection also impedes vaccine research. It is not known whether the immune system is able to eliminate the virus.

Some studies, however, have shown the presence of virus neutralizing antibodies in patients with HCV infection. In the absence of a vaccine, all precautions to prevent infection must be taken including (a) screening and testing of blood and organ donors; (b) Virus inactivation of plasma derived products; (c) implementation and maintenance of infection control practices in health care settings, including appropriate sterilization of medical and dental equipment; (d) promotion of behaviour change among the general public and health care workers to reduce overuse of injections and to use safe injection practices; and (e) Risk reduction counselling for persons with high-risk drug and sexual practices. "

The genome encodes for structural components, a nucleocapsid protein and two envelope glycoproteins, and functional constituents involved in the virus replication and protein processing.
The nucleocapsid-encoding region seems to be the most conservative among the isolates obtained all over the world.

C. PRINCIPLE OF THE TEST
Microplates are coated with HCV-specific antigens derived from "core" and "ns" regions encoding for conservative and immunodominant antigenic determinants (Core peptide, recombinant NS3, NS4 and NS5 peptides).
The solid phase is first treated with the diluted sample and HCV Ab are captured, if present, by the antigens.
After washing out all the other components of the sample, in the 2nd incubation bound HCV antibodies, IgG and IgM as well, are detected by the addition of polyclonal specific anti hIgG&M antibodies, labelled with peroxidase (HRP).
The enzyme captured on the solid phase, acting on the substrate/chromogen mixture, generates an optical signal that is proportional to the amount of anti HCV antibodies present in the sample. A cut-off value let optical densities be interpreted into HCV antibody negative and positive results.

D. COMPONENTS
Code CVAB.CE contains reagents for 192 tests.

1. Microplate MICROPLATE
n° 2 microplates
12 strips of 8 microwells coated with Core peptide, recombinant NS3, NS4 and NS5 peptides. Plates are sealed into a bag with desiccant.

2. Negative Control CONTROL -
1x4.0ml/vial. Ready to use control. It contains 1% goat serum proteins, 10 mM Na-citrate buffer pH 6.0 +/-0.1, 0.5% Tween 20, 0.09% Na-azide and 0.045% ProClin 300 as preservatives. The negative control is olive green colour coded.

3. Positive Control CONTROL +
1x4.0ml/vial. Ready to use control. It contains 1% goat serum proteins, human antibodies positive to HCV, 10 mM Na-citrate buffer pH 6.0 +/-0.1, 0.5% Tween 20, 0.09% Na-azide and 0.045% ProClin 300 as preservatives. The Positive Control is blue colour coded.

4. Calibrator CAL ….
n° 2 vials. Lyophilized calibrator. To be dissolved with the volume of EIA grade water reported on the label. It contains foetal bovine serum proteins, human antibodies to HCV whose content is calibrated on the NIBSC Working Standard code 99/588-003-WI, 10 mM Na-citrate buffer pH 6.0 +/-0.1, 0.3 mg/ml gentamicine sulphate and 0.045% ProClin 300 as preservatives.

Note: The volume necessary to dissolve the content of the vial may vary from lot to lot. Please use the right volume reported on the label .

5. Wash buffer concentrate WASHBUF 20X
2x60ml/bottle. 20x concentrated solution. Once diluted, the wash solution contains 10 mM phosphate buffer pH 7.0+/-0.2, 0.05% Tween 20 and 0.045% ProClin 300.

6. Enzyme Conjugate CONJ
2x16ml/vial. Ready to use and pink/red colour coded reagent. It contains Horseradish Peroxidase conjugated goat polyclonal antibodies to human IgG and IgM, 5% BSA, 10 mM Tris buffer pH 6.8+/-0.1, 0.045% ProClin 300 and 0.02% gentamicine sulphate as preservatives.

7. Chromogen/Substrate SUBS TMB
2x16ml/vial. Ready-to-use component. It contains 50 mM citrate-phosphate buffer pH 3.5-3.8, 4% dimethylsulphoxide, 0.03% tetra-methyl-benzidine or TMB and 0.02% hydrogen peroxide or H2O2.
Note: To be stored protected from light as sensitive to strong illumination.

8. Assay Diluent DILAS
1x15ml/vial. 10 mM tris buffered solution pH 8.0 +/-0.1 containing 0.045% ProClin 300 for the pre-treatment of samples and controls in the plate, blocking interference.

9. Sulphuric Acid H_2SO_4 0.3 M
1x32ml/bottle. It contains 0.3 M H_2SO_4 solution.
Attention: Irritant (H315; H319; P280; P302+P352; P332+P313; P305+P351+P338; P337+P313; P362+P363)

10. Sample Diluent: DILSPE
2x50ml/bottle. It contains 1% goat serum proteins, 10 mM Na-citrate buffer pH 6.0 +/-0.1, 0.5% Tween 20, 0.09% Na-azide and 0.045% ProClin 300 as preservatives. To be used to dilute the sample.
Note: The diluent changes colour from olive green to dark bluish green in the presence of sample.

11. Plate sealing foils **n° 4**

12. Package insert **n° 1**

Important note: Only upon specific request , Dia.Pro can supply reagents for 96, 480, 960 tests , as reported below**:**

1. Microplate	n°1	n°5	n°10
2.NegativeControl	1x2.0ml/vial	1x10ml/vial	1x20.ml/vial
3.PositiveControl	1x2.0ml/vial	1x10ml/vial	1x20.ml/vial
4.Calibrator	n° 1 vial	n° 5 vials	n° 10 vials
5.Wash buff conc	1x60ml/bottle	5x60ml/bottles	4x150ml/bottles
6.Enz. Conjugate	1x16ml/vial	2x40ml/bottles	4x40ml/bottles
7.Chromog/Subs	1x16ml/vial	2x40ml/bottles	4x40ml/bottles
8.Assay Diluent	1x8ml/vial	1x40ml/bottle	1x80ml/bottle
9.Sulphuric Acid	1x15ml/vial	2x40ml/bottle	2x80ml/bottles
10.SampleDiluent	1x50ml/vial	5x50ml/bottles	4x125ml/bottles
11.Plate seal foils	n° 2	n° 10	n° 20
12. Pack. insert	n° 1	n° 1	n° 1
Number of tests	**96**	**480**	**960**
Code	**CVAB.CE.96**	**CVAB.CE.480**	**CVAB.CE.960**

E. MATERIALS REQUIRED BUT NOT PROVIDED

1. Calibrated Micropipettes (200ul and 10ul) and disposable plastic tips.
2. EIA grade water (bidistilled or deionised, charcoal treated to remove oxidizing chemicals used as disinfectants).
3. Timer with 60 minute range or higher.
4. Absorbent paper tissues.
5. Calibrated ELISA microplate thermostatic incubator capable to provide a temperature of +37°C.
6. Calibrated ELISA microwell reader with 450nm (reading) and with 620-630nm (blanking) filters.
7. Calibrated ELISA microplate washer.
8. Vortex or similar mixing tools.

F. WARNINGS AND PRECAUTIONS

1. The kit has to be used by skilled and properly trained technical personnel only, under the supervision of a medical doctor responsible of the laboratory.
2. When the kit is used for the screening of blood units and blood components, it has to be used in a laboratory certified and qualified by the national authority in that field (Ministry of Health or similar entity) to carry out this type of analysis.
3. All the personnel involved in performing the assay have to wear protective laboratory clothes, talc-free gloves and glasses. The use of any sharp (needles) or cutting (blades) devices should be avoided. All the personnel involved should be trained in biosafety procedures, as recommended by the Center for Disease Control, Atlanta, U.S. and reported in the National Institute of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
4. All the personnel involved in sample handling should be vaccinated for HBV and HAV, for which vaccines are available, safe and effective.
5. The laboratory environment should be controlled so as to avoid contaminants such as dust or air-born microbial agents, when opening kit vials and microplates and when performing the test. Protect the Chromogen/Substrate from strong light and avoid vibration of the bench surface where the test is undertaken.
6. Upon receipt, store the kit at 2..8°C into a temperature controlled refrigerator or cold room.
7. Do not interchange components between different lots of the kits. It is recommended that components between two kits of the same lot should not be interchanged.
8. Check that the reagents are clear and do not contain visible heavy particles or aggregates. If not, advise the laboratory supervisor to initiate the necessary procedures for kit replacement.
9. Avoid cross-contamination between serum/plasma samples by using disposable tips and changing them after each sample. Do not reuse disposable tips.
10. Avoid cross-contamination between kit reagents by using disposable tips and changing them between the use of each one. Do not reuse disposable tips.
11. Do not use the kit after the expiration date stated on the external container and internal (vials) labels.
12. Treat all specimens as potentially infective. All human serum specimens should be handled at Biosafety Level 2, as recommended by the Center for Disease Control, Atlanta, U.S. in compliance with what reported in the Institutes of Health's publication: "Biosafety in Microbiological and Biomedical Laboratories", ed. 1984.
13. The use of disposable plastic-ware is recommended in the preparation of the liquid components or in transferring components into automated workstations, in order to avoid cross contamination.
14. Waste produced during the use of the kit has to be discarded in compliance with national directives and laws concerning laboratory waste of chemical and biological substances. In particular, liquid waste generated from the washing procedure, from residuals of controls and from samples has to be treated as potentially infective material and inactivated before waste. Suggested procedures of inactivation are treatment with a 10% final concentration of household bleach for 16-18 hrs or heat inactivation by autoclave at 121°C for 20 min..
15. Accidental spills from samples and operations have to be adsorbed with paper tissues soaked with household bleach and then with water. Tissues should then be discarded in proper containers designated for laboratory/hospital waste.
16. The Sulphuric Acid is an irritant. In case of spills, wash the surface with plenty of water
17. Other waste materials generated from the use of the kit (example: tips used for samples and controls, used microplates) should be handled as potentially infective and disposed according to national directives and laws concerning laboratory wastes.

G. SPECIMEN: PREPARATION AND RECOMMANDATIONS

1. Blood is drawn aseptically by venipuncture and plasma or serum is prepared using standard techniques of preparation of samples for clinical laboratory analysis. No influence has been observed in the preparation of the sample with citrate, EDTA and heparin.
2. Avoid any addition of preservatives to samples; especially sodium azide as this chemical would affect the enzymatic activity of the conjugate, generating false negative results.
3. Samples have to be clearly identified with codes or names in order to avoid misinterpretation of results. When the kit is used for the screening of blood units, bar code labeling and electronic reading is strongly recommended.
4. Haemolysed (red) and visibly hyperlipemic ("milky") samples have to be discarded as they could generate false results. Samples containing residues of fibrin or heavy particles or microbial filaments and bodies should be discarded as they could give rise to false results.
5. Sera and plasma can be stored at +2°…+8°C in primary collection tubes for up to five days after collection.
Do not freeze primary tubes of collection. For longer storage periods, sera and plasma samples, carefully removed from the primary collection tube, can be stored frozen at –20°C for several months. Any frozen samples should not be frozen/thawed more than once as this may generate particles that could affect the test result.
6. If particles are present, centrifuge at 2.000 rpm for 20 min or filter using 0.2-0.8u filters to clean up the sample for testing.

H. PREPARATION OF COMPONENTS AND WARNINGS

A study conducted on an opened kit has not pointed out any relevant loss of activity up to 6 re-use of the device and up to 6 months.

1. Microplates:
Allow the microplate to reach room temperature (about 1 hr) before opening the container. Check that the desiccant is not turned to dark green, indicating a defect of manufacturing.
In this case call Dia.Pro's customer service.
Unused strips have to be placed back into the aluminium pouch, in presence of desiccant supplied, firmly zipped and stored at +2°..8°C.
When opened the first time, residual strips are stable till the indicator of humidity inside the desiccant bag turns from yellow to green.

2. Negative Control:
Ready to use. Mix well on vortex before use.

3. Positive Control:
Ready to use. Mix well on vortex before use. Handle this component as potentially infective, even if HCV, eventually present in the control, has been chemically inactivated.

4. Calibrator:
Dissolve carefully the content of the lyophilised vial with the volume of EIA grade water reported on its label.
Mix well on vortex before use.
Handle this component as potentially infective, even if HCV, eventually present in the control, has been chemically inactivated.
***Note**: When dissolved the Calibrator is not stable. Store in aliquots at –20°C.*

5. Wash buffer concentrate:
The 20x concentrated solution has to be diluted with EIA grade water up to 1200 ml and mixed gently end-over-end before use. As some salt crystals may be present into the vial, take care to dissolve all the content when preparing the solution.
In the preparation avoid foaming as the presence of bubbles could give origin to a bad washing efficiency.
***Note:** Once diluted, the wash solution is stable for 1 week at +2..8° C.*

6. Enzyme conjugate:
Ready to use. Mix well on vortex before use.
Be careful not to contaminate the liquid with oxidizing chemicals, air-driven dust or microbes.
If this component has to be transferred use only plastic, possibly sterile disposable containers.

7. Chromogen/Substrate:
Ready to use. Mix well on vortex before use.
Be careful not to contaminate the liquid with oxidizing chemicals, air-driven dust or microbes.
Do not expose to strong illumination, oxidizing agents and metallic surfaces.
If this component has to be transferred use only plastic, possible sterile disposable container.

8. Assay Diluent:
Ready to use. Mix well on vortex before use.

9. Sulphuric Acid:
Ready to use. Mix well on vortex before use.
Attention: Irritant (H315; H319; P280; P302+P352; P332+P313; P305+P351+P338; P337+P313; P362+P363).

Precautionary **P statements:**
P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P302 + P352 – IF ON SKIN: Wash with plenty of soap and water.
P332 + P313 – If skin irritation occurs: Get medical advice/attention.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337 + P313 – If eye irritation persists: Get medical advice/attention.
P362 + P363 - Take off contaminated clothing and wash it before reuse.

10. Sample Diluent:
Ready to use. Mix well on vortex before use.

I. INSTRUMENTS AND TOOLS USED IN COMBINATION WITH THE KIT

1. Micropipettes have to be calibrated to deliver the correct volume required by the assay and must be submitted to regular decontamination (household alcohol, 10% solution of bleach, hospital grade disinfectants) of those parts that could accidentally come in contact with the sample. They should also be regularly maintained in order to show a precision of 1% and a trueness of +/-2%. Decontamination of spills or residues of kit components should also be carried out regularly.
2. The ELISA incubator has to be set at +37°C (tolerance of +/-0.5°C) and regularly checked to ensure the correct temperature is maintained. Both dry incubators and water baths are suitable for the incubations, provided that the instrument is validated for the incubation of ELISA tests.
3. The **ELISA washer** is extremely important to the overall performances of the assay. The washer must be carefully validated in advance, checked for the delivery of the right dispensation volume and regularly submitted to maintenance according to the manufacturer's instructions for use. In particular the washer, at the end of the daily workload, has to be extensively cleaned out of salts with deionized water. Before use, the washer has to be extensively primed with the diluted Washing Solution.
The instrument weekly has to be submitted to decontamination according to its manual (NaOH 0.1 M decontamination suggested).
5 washing cycles (aspiration + dispensation of 350ul/well of washing solution + 20 sec soaking = 1 cycle) are sufficient to ensure the assay with the declared performances. If soaking is not possible add one more cycle of washing.
An incorrect washing cycle or salt-blocked needles are the major cause of false positive reactions.
4. Incubation times have a tolerance of $\underline{+}$5%.
5. The ELISA microplate reader has to be equipped with a reading filter of 450nm and with a second filter of 620-630nm, mandatory for blanking purposes. Its standard performances should be (a) bandwidth $\leq$ 10 nm; (b) absorbance range from 0 to $\geq$ 2.0; (c) linearity to $\geq$ 2.0; (d) repeatability $\geq$ 1%. Blanking is carried out on the well identified in the section "Assay Procedure". The optical system of the reader has to be calibrated regularly to ensure that the correct optical density is measured. It should be regularly maintained according to the manufacturer 's instructions.
6. When using an ELISA automated work station, all critical steps (dispensation, incubation, washing, reading, data handling) have to be carefully set, calibrated, controlled and regularly serviced in order to match the values reported in the section O "Internal Quality Control". The assay protocol has to be installed in the operating system of the unit and validated as for the washer and the reader. In addition, the liquid handling part of the station (dispensation and washing) has to be validated and correctly set. Particular attention must be paid to avoid carry over by the needles used for dispensing and for washing. This must be studied and controlled to minimize the possibility of contamination of adjacent wells. The use of ELISA automated work stations is recommended for blood screening when the number of samples to be tested exceed 20-30 units per run.
7. When using automatic devices, in case the vial holder of the instrument does not fit with the vials supplied in the kit, transfer the solution into appropriate containers and label them with the same label peeled out from the original vial. This operation is important in order to avoid mismatching contents of vials, when transferring them. When the test is over, return the secondary labeled containers to 2..8°C, firmly capped.
8. Dia.Pro's customer service offers support to the user in the setting and checking of instruments used in combination with the kit, in order to assure compliance with the requirements described. Support is also provided for the installation of new instruments to be used with the kit.

L. PRE ASSAY CONTROLS AND OPERATIONS

1. Check the expiration date of the kit printed on the external label of the kit box. Do not use if expired.
2. Check that the liquid components are not contaminated by naked-eye visible particles or aggregates. Check that the Chromogen/Substrate is colorless or pale blue by aspirating a small volume of it with a sterile transparent plastic pipette. Check that no breakage occurred in transportation and no spillage of liquid is present inside the box. Check that the

aluminum pouch, containing the microplate, is not punctured or damaged.

3. Dilute all the content of the 20x concentrated Wash Solution as described above.
4. Dissolve the Calibrator as described above.
5. Allow all the other components to reach room temperature (about 1 hr) and then mix as described.
6. Set the ELISA incubator at +37°C and prepare the ELISA washer by priming with the diluted washing solution, according to the manufacturers instructions. Set the right number of washing cycles as reported in the specific section.
7. Check that the ELISA reader has been turned on at least 20 minutes before reading.
8. If using an automated workstation, turn it on, check settings and be sure to use the right assay protocol.
9. Check that the micropipettes are set to the required volume.
10. Check that all the other equipment is available and ready to use.
11. In case of problems, do not proceed further with the test and advise the supervisor.

M. ASSAY PROCEDURE

The assay has to be carried out according to what reported below, taking care to maintain the same incubation time for all the samples in testing.

Automated assay:

In case the test is carried out automatically with an ELISA system, we suggest to make the instrument aspirate 200 ul Sample Diluent and then 10 ul sample.

All the mixture is then carefully dispensed directly into the appropriate sample well of the microplate. Before the next sample is aspirated, needles have to be duly washed to avoid any cross-contamination among samples.

Do not dilute controls/calibrator as they are ready to use.

Dispense 200 ul controls/calibrator in the appropriate control/calibration wells.

Important Note: *Visually monitor that samples have been diluted and dispensed into appropriate wells. This is simply achieved by checking that the colour of dispensed samples has turned to dark bluish-green while the colour of the negative control has remained olive green.*

For the next operations follow the operative instructions reported below for the Manual Assay.

It is strongly recommended to check that the time lap between the dispensation of the first and the last sample will be calculated by the instrument and taken into consideration by delaying the first washing operation accordingly.

Manual assay:

1. Place the required number of Microwells in the microwell holder. Leave the 1st well empty for the operation of blanking.
2. Dispense 200 ul of Negative Control in triplicate, 200 ul Calibrator in duplicate and 200 ul Positive Control in single in proper wells. Do not dilute Controls and Calibrator as they are pre-diluted, ready to use !
3. Add 200 ul of Sample Diluent (DILSPE) to all the sample wells; then dispense 10 ul sample in each properly identified well. Mix gently the plate, avoiding overflowing and contaminating adjacent wells, in order to fully disperse the sample into its diluent.

Important note: *Check that the colour of the Sample Diluent, upon addition of the sample, changes from light green to dark bluish green, monitoring that the sample has been really added.*

4. Dispense 50 ul Assay Diluent (DILAS) into all the controls/calibrator and sample wells. Check that the color of samples has turned to dark blue.
5. Incubate the microplate for **45 min at +37°C**.

Important note: *Strips have to be sealed with the adhesive sealing foil, supplied, only when the test is carried out manually. Do not cover strips when using ELISA automatic instruments.*

6. Wash the microplate with an automatic washer by delivering and aspirating 350ul/well of diluted washing solution as reported previously (section I.3).
7. Pipette 100µl Enzyme Conjugate into each well, except the 1st blanking well, and cover with the sealer. Check that this pink/red coloured component has been dispensed in all the wells, except A1.

Important note: *Be careful not to touch the plastic inner surface of the well with the tip filled with the Enzyme Conjugate. Contamination might occur.*

8. Incubate the microplate for **45 min at +37°C**.
9. Wash microwells as in step 6.
10. Pipette 100µl Chromogen/Substrate mixture into each well, the blank well included. Then incubate the microplate at **room temperature (18-24°C) for 15 minutes**.

Important note: *Do not expose to strong direct illumination. High background might be generated.*

11. Pipette 100µl Sulphuric Acid into all the wells using the same pipetting sequence as in step 10 to stop the enzymatic reaction. Addition of acid will turn the positive control and positive samples from blue to yellow/brown.
12. Measure the colour intensity of the solution in each well, as described in section I.5, at 450nm filter (reading) and at 620-630nm (background subtraction), blanking the instrument on A1 (mandatory).

Important notes:

1. *Ensure that no finger prints are present on the bottom of the microwell before reading. Finger prints could generate false positive results on reading.*
2. *Reading has to be carried out just after the addition of the Stop Solution and anyway not any longer than 20 minutes after its addition. Some self oxidation of the chromogen can occur leading to high background.*
3. *Shaking at 350 ±150 rpm during incubation has been proved to increase the sensitivity of the assay of about 20%.*
4. *The Calibrator (CAL) does not affect the cut-off calculation and therefore the test results calculation. The Calibrator may be used only when a laboratory internal quality control is required by the management.*

N. ASSAY SCHEME

Method	Operations
Controls & Calibrator Samples Assay Diluent (DILAS)	200 ul 200ul dil.+10ul 50 ul
1st incubation	**45 min**
Temperature	+37°C
Wash step	n° 5 cycles with 20'' of soaking OR n° 6 cycles without soaking
Enzyme conjugate	100 ul
2nd incubation	**45 min**
Temperature	+37°C
Wash step	n° 5 cycles with 20'' of soaking OR n° 6 cycles without soaking
TMB/H2O2	100 ul
3rd incubation	**15 min**
Temperature	r.t.
Sulphuric Acid	100 ul
Reading OD	450nm / 620-630nm

An example of dispensation scheme is reported below:

Microplate

	1	2	3	4	5	6	7	8	9	10	11	12
A	BLK	S2										
B	NC	S3										
C	NC	S4										
D	NC	S5										
E	CAL	S6										
F	CAL	S7										
G	PC	S8										
H	S1	S9										

Legenda: BLK = Blank NC = Negative Control
CAL = Calibrator PC = Positive Control S = Sample

O. INTERNAL QUALITY CONTROL

A check is carried out on the controls and the calibrator any time the kit is used in order to verify whether their OD450nm values are as expected and reported in the table below.

Check	Requirements
Blank well	< 0.100 OD450nm value
Negative Control (NC)	< 0.050 mean OD450nm value after blanking
Calibrator	S/Co > 1.1
Positive Control	> 1.000 OD450nm value

If the results of the test match the requirements stated above, proceed to the next section.
If they do not, do not proceed any further and operate as follows:

Problem	Check
Blank well > 0.100 OD450nm	1. that the Chromogen/Sustrate solution has not got contaminated during the assay
Negative Control (NC) > 0.050 OD450nm after blanking	1. that the washing procedure and the washer settings are as validated in the pre qualification study; 2. that the proper washing solution has been used and the washer has been primed with it before use; 3. that no mistake has been done in the assay procedure (dispensation of positive control instead of negative control; 4. that no contamination of the negative control or of their wells has occurred due to positive samples, to spills or to the enzyme conjugate; 5. that micropipettes haven't got contaminated with positive samples or with the enzyme conjugate 6. that the washer needles are not blocked or partially obstructed.
Calibrator S/Co < 1.1	1. that the procedure has been correctly executed; 2. that no mistake has been done in its distribution (ex.: dispensation of negative control instead of control serum) 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the calibrator has occurred.
Positive Control < 1.000 OD450nm	1. that the procedure has been correctly executed; 2. that no mistake has been done in the distribution of controls (dispensation of negative control instead of positive control. In this case, the negative control will have an OD450nm value > 0.150, too. 3. that the washing procedure and the washer settings are as validated in the pre qualification study; 4. that no external contamination of the positive control has occurred.

Should these problems happen, after checking, report any residual problem to the supervisor for further actions.

P. CALCULATION OF THE CUT-OFF

The tests results are calculated by means of a cut-off value determined with the following formula on the mean OD450nm value of the Negative Control (NC):

NC + 0.350 = Cut-Off (Co)

The value found for the test is used for the interpretation of results as described in the next paragraph.

***Important note**: When the calculation of results is done by the operative system of an ELISA automated work station be sure that the proper formulation is used to calculate the cut-off value and generate the right interpretations of results.*

Q. INTERPRETATION OF RESULTS

Test results are interpreted as ratio of the sample OD450nm and the Cut-Off value (or S/Co) according to the following table:

S/Co	Interpretation
< 0.9	Negative
0.9 - 1.1	Equivocal
> 1.1	Positive

A negative result indicates that the patient has not been infected by HCV or that the blood unit may be transfused.
Any patient showing an equivocal result should be tested again on a second sample taken 1-2 weeks later from the patient and examined. The blood unit should not be transfused.
A positive result is indicative of HCV infection and therefore the patient should be treated accordingly or the blood unit should be discarded.

Important notes:

1. *Interpretation of results should be done under the supervision of the responsible of the laboratory to reduce the risk of judgment errors and misinterpretations.*
2. *Any positive result should be confirmed by an alternative method capable to detect IgG and IgM antibodies (confirmation test) before a diagnosis of viral hepatitis is formulated.*
3. *As proved in the Performance Evaluation of the product, the assay is able to detect seroconversion to anti HCV core antibodies* ***earlier*** *than some other commercial kits. Therefore a positive result, not confirmed with these commercial kits, does not have to be ruled out as a false positive result ! The sample has to be anyway submitted to a confirmation test (supplied upon request by DiaPro srl, code CCONF).*
4. *As long as the assay is able to detect also IgM antibodies some discrepant results with other commercial products for the detection of anti HCV antibodies - lacking anti hIgM conjugate in the formulation of the enzyme tracer and therefore missing IgM reactivity - may be present. The real positivity of the sample for antibodies to HCV should be then confirmed by examining also IgM reactivity, important for the diagnosis of HCV infection.*
5. *When test results are transmitted from the laboratory to an informatics centre, attention has to be done to avoid erroneous data transfer.*
6. *Diagnosis of viral hepatitis infection has to be done and released to the patient only by a qualified medical doctor.*

An example of calculation is reported below:

The following data must not be used instead or real figures obtained by the user.
Negative Control: 0.019 – 0.020 – 0.021 OD450nm
Mean Value: 0.020 OD450nm
Lower than 0.050 – Accepted
Positive Control: 2.189 OD450nm
Higher than 1.000 – Accepted
Cut-Off = 0.020+0.350 = 0.370
Calibrator: 0.550 - 0.530 OD450nm
Mean value: 0.540 OD450nm S/Co = 1.4
S/Co higher than 1.1 – Accepted
Sample 1: 0.070 OD450nm
Sample 2: 1.690 OD450nm
Sample 1 S/Co < 0.9 = negative
Sample 2 S/Co > 1.1 = positive

R. PERFORMANCES

Evaluation of Performances has been conducted in accordance to what reported in the Common Technical Specifications or CTS (art. 5, Chapter 3 of IVD Directive 98/79/EC).

1. LIMIT OF DETECTION

The limit of detection of the assay has been calculated by means of the British Working Standard for anti-HCV, NIBSC code 99/588-003-WI. The table below reports the mean OD450nm values of this standard when diluted in negative plasma and then examined.

Dilution	**Lot # 1**	**Lot # 2**
Factor	S/Co	S/Co
1 X	**2.0**	**2.0**
2 X	**1.1**	**1.2**
4 X	0.7	0.8
8 X	0.5	0.5
Negative plasma	0.3	0.3

In addition the sample coded Accurun 1 – series 3000 - supplied by Boston Biomedica Inc., USA, has been evaluated "in toto" showing the results below:

CVAB.CE Lot ID	**Accurun 1 Series**	**S/Co**
1201	3000	1.5
0602	3000	1.5
1202	3000	1.9

In addition, n° 7 samples, tested positive for HCV Ab with Ortho HCV 3.0 SAVe, code 930820, lot. # EXE065-1, were diluted in HCV Ab negative plasma in order to generate limiting dilutions and then tested again on CVAB.CE, lot. # 1202, and Ortho.
The following table reports the data obtained.

Sample n°	**Limit Dilution**	**CVAB.CE S/Co**	**Ortho 3.0 S/Co**
1	256 X	**1.9**	**1.3**
2	256 X	**1.9**	0.7
3	256 X	**2.4**	**1.0**
4	128 X	**2.5**	**3.2**
5	85 X	**3.3**	**1.4**
6	128 X	**2.2**	0.8
7	135 X	**3.2**	**2.2**

2. DIAGNOSTIC SPECIFICITY AND SENSITIVITY

The Performance Evaluation of the device was carried out in a trial conducted on more than total 5000 samples.

2.1 Diagnostic specificity:

It is defined as the probability of the assay of scoring negative in the absence of specific analyte. In addition to the first study, where a total of 5043 unselected blood donors,(including 1st time donors), 210 hospitalized patients and 162 potentially interfering specimens (other infectious diseases, E.coli antibody positive, patients affected by non viral hepatic diseases, dialysis patients, pregnant women, hemolized, lipemic, etc.) were examined, the diagnostic specificity was recently assessed by testing a total of 2876 negative blood donors on six different lots. A value of specificity of 100% was found.
No false reactivity due to the method of specimen preparation has been observed. Both plasma, derived with different standard techniques of preparation (citrate, EDTA and heparin), and sera have been used to determine the value of specificity.
Frozen specimens have been tested, as well, to check for interferences due to collection and storage.
No interference was observed.

2.2 Diagnostic Sensitivity

It defined as the probability of the assay of scoring positive in the presence of specific analyte.
The diagnostic sensitivity has been assessed externally on a total number of 359 specimens; a diagnostic sensitivity of 100% was found. Internally more than other 50 positive samples were tested, providing a value of diagnostic sensitivity of again 100%.
Positive samples from infections carried out by different genotypes of HCV were tested as well.
Furthermore, most of seroconversion panels available from Boston Biomedica Inc., USA, (PHV) and Zeptometrix, USA, (HCV) have been studied.
Results are reported below for some of them.

Panel	N° samples	DiaPro*	Ortho* **
PHV 901	11	9	9
PHV 904	7	2	4
PHV 905	9	3	4
PHV 906	7	7	7
PHV 907	7	3	2
PHV 908	13	10	8
PHV 909	3	2	2
PHV 910	5	3	3
PHV 911	5	3	3
PHV 912	3	1	1
PHV 913	4	2	2
PHV 914	9	5	5
PHV 915	4	3	0
PHV 916	8	4	3
PHV 917	10	6	6
PHV 918	8	2	0
PHV 919	7	3	3
PHV 920	10	6	6
HCV 10039	5	2	0
HCV 6212	9	6	7
HCV 10165	9	5	4

*Note: * Positive samples detected ** HCV v.3.0*

Finally the Product has been tested on the panel EFS Ac HCV, lot n° 01/08.03.22C/01/A, supplied by the Etablissement Francais Du Sang (EFS), France, with the following results:

EFS Panel Ac HCV

Sample	Lot # 1 S/Co	Lot # 2 S/Co	Lot # 2 S/Co	Results expected
HCV 1	**2.2**	**2.4**	**2.6**	**positive**
HCV 2	**1.6**	**2.0**	**2.1**	**positive**
HCV 3	**1.5**	**1.7**	**1.6**	**positive**
HCV 4	**5.2**	**6.5**	**5.5**	**positive**
HCV 5	**1.6**	**1.8**	**1.6**	**positive**
HCV 6	0.4	0.4	0.4	negative

3. PRECISION:
It has been calculated on two samples, one negative and one low positive, examined in 16 replicates in three separate runs. Results are reported as follows:

Lot # 1202

Negative Sample (N = 16)

Mean values	1st run	2nd run	3^{rd} run	Average value
OD 450nm	0.094	0.099	0.096	0.096
Std.Deviation	0.008	0.007	0.008	0.007
CV %	8.7	6.6	7.9	7.7

Cal # 2 – 7K (N = 16)

Mean values	1st run	2nd run	3^{rd} run	Average value
OD 450nm	0.396	0.403	0.418	0.406
Std.Deviation	0.023	0.029	0.027	0.026
CV %	5.9	7.1	6.4	6.5
S/Co	1.1	1.1	1.2	1.1

Lot # 0602

Negative Sample (N = 16)

Mean values	1st run	2nd run	3^{rd} run	Average
OD 450nm	0.097	0.096	0.094	0.096
Std.Deviation	0.009	0.010	0.008	0.009
CV %	8.9	10.1	8.4	9.1

Cal # 2 – 7K (N = 16)

Mean values	1st run	2nd run	3^{rd} run	Average value
OD 450nm	0.400	0.395	0.393	0.396
Std.Deviation	0.021	0.025	0.026	0.024
CV %	5.4	6.2	6.6	6.1
S/Co	1.2	1.2	1.1	1.2

Lot # 0602/2

Negative Sample (N = 16)

Mean values	1st run	2nd run	3^{rd} run	Average
OD 450nm	0.087	0.091	0.088	0.089
Std.Deviation	0.009	0.007	0.008	0.008
CV %	10.0	8.2	8.6	8.9

Cal # 2 – 7K (N = 16)

Mean values	1st run	2nd run	3^{rd} run	Average
OD 450nm	0.386	0.390	0.391	0.389
Std.Deviation	0.023	0.021	0.023	0.022
CV %	6.0	5.3	5.8	5.7
S/Co	1.1	1.2	1.2	1.2

The variability shown in the tables above did not result in sample misclassification.

S. LIMITATIONS
Repeatable false positive results, not confirmed by RIBA or similar confirmation techniques, were assessed as less than 0.1% of the normal population.
Frozen samples containing fibrin particles or aggregates after thawing have been observed to generate some false results.

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HCV Ab

Versión 4.0 del Ensayo Inmunoenzimático para la determinación de anticuerpos frente Virus de la Hepatitis C en plasma y suero humanos.

Uso exclusivo para diagnóstico “in vitro”

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REF CVAB.CE
96/192/480/960 pruebas

HCV Ab

A. OBJETIVO DEL EQUIPO.
Versión 4.0 del Ensayo Inmunoenzimático (ELISA) para la determinación de anticuerpos al virus de la Hepatitis C en plasma y suero humanos.
El equipo está diseñado para el cribado en unidades de sangre así como para el seguimiento de pacientes infectados con HCV.
Uso exclusivo para diagnóstico "in vitro".

B. INTRODUCCIÓN.
La Organización Mundial de la Salud (OMS) define la infección por el virus de la Hepatitis C como:

"La Hepatitis C es una infección viral del hígado, definida como hepatitis de transmisión parenteral "no A no B" hasta el descubrimiento del agente causal en 1989. El descubrimiento y la caracterización del virus de la hepatitis C (HCV) ha permitido comprender su papel primario en la hepatitis post-transfusional y su tendencia a inducir la infección persistente. El virus de la hepatitis C es la causa principal de hepatitis aguda y enfermedad hepática crónica, incluyendo cirrosis y cáncer de hígado. A nivel mundial se estima que 170 millones de personas estén infectadas de forma crónica con HCV y que de 3 a 4 millones se infecten cada año.

El virus se transmite por contacto directo con sangre humana. Las causas principales de infección por HCV en el mundo son las transfusiones sanguíneas no controladas y la reutilización de jeringuillas y agujas sin una correcta esterilización previa. En la actualidad aún no existe una vacuna eficaz contra el virus y el tratamiento para la hepatitis C crónica es demasiado costoso para la mayoría de las personas en países en vías de desarrollo. Desde una perspectiva global, el mayor impacto contra la hepatitis C puede lograrse a través de esfuerzos orientados hacia la prevención y el control de la transmisión por exposiciones nosocomiales (como las transfusiones sanguíneas y las prácticas invasoras inseguras) y los comportamientos que conllevan alto riesgo (como el consumo de drogas inyectables).

El virus de la hepatitis C aparece en la mayoría de los casos de hepatitis viral. Es un virus RNA envuelto, perteneciente a la familia Flaviviridae *y que parece tener un estrecho margen de huéspedes. Humanos y chimpancés son las únicas especies susceptibles conocidas y ambas desarrollan una enfermedad similar. Una característica importante del virus es su variabilidad genómica, la cual pudiera estar relacionada a su elevada capacidad (80%) de inducir infección crónica. El HCV ha sido agrupado por genotipos, lo cual puede ser útil para determinar la gravedad de la enfermedad y la respuesta al tratamiento.*

El periodo de incubación varía desde 15 hasta 150 días. En la infección aguda los síntomas más comunes son fatiga e ictericia, sin embargo la mayoría de los casos (entre el 60% y el 70%), incluso aquellos que desarrollan la infección crónica, son asintomáticos. Cerca del 80% de los nuevos pacientes infectados progresan a la infección crónica. Del 10 al 20% de las personas con infección crónica desarrollan cirrosis, mientras que el cáncer de hígado lo presentan entre el 1 y el 5% de las personas con este tipo de infección, en un periodo de 20 a 30 años. Muchos pacientes que padecen cáncer de hígado y no están infectados por el virus de la hepatitis B, presentan evidencias de infección por el virus de la hepatitis C. Los mecanismos que relacionan la infección por HCV y el desarrollo de cáncer hepático no han sido aún esclarecidos. La hepatitis C puede exacerbar la gravedad de una enfermedad subyacente del hígado cuando coexiste con otras disfunciones hepáticas; particularmente la enfermedad progresa más rápidamente en personas alcohólicas e infectadas por HCV. Las formas de transmisión más frecuentes son a través de transfusiones sanguíneas sin controlar y por la reutilización de agujas, jeringuillas y material médico contaminados. La transmisión sexual y perinatal puede suceder aunque es menos frecuente. Determinadas prácticas y comportamientos sociales y culturales (perforaciones en orejas y otras partes del cuerpo (piercing), circuncisiones y tatuajes) pueden constituir modos de transmisión si existe una inadecuada esterilización de los instrumentos usados. El HCV no se transmite por estornudos, tos, abrazos, agua o alimentos, estrechar la mano, compartir cubiertos o en general por contactos casuales. Tanto en países desarrollados como en aquellos en vías de desarrollo, los grupos de alto riesgo incluyen drogadictos, receptores de transfusiones sin analizar, hemofílicos, pacientes sometidos a diálisis y personas con actividad sexual promiscua y sin la debida protección. En los países desarrollados, se ha estimado que el 90% de las personas con infección crónica por HCV son o han sido drogadictos o han recibido donaciones de sangre o hemoderivados contaminados. En muchos países en vías de desarrollo, donde aún se utilizan transfusiones o hemoderivados sin analizar, los principales medios de transmisión son los instrumentos para inyecciones y las transfusiones sin analizar.

La OMS estima que cerca de 170 millones de personas, es decir el 3% de la población mundial, están infectadas por el HCV y bajo riesgo de desarrollar cirrosis y/o cáncer hepático. La prevalencia de la infección por HCV en países de África, el Mediterráneo oriental, Sudeste Asiático y el Pacífico Occidental es alta, comparada con países de Norteamérica y Europa.
Las pruebas de diagnóstico para el HCV contribuyen a prevenir la infección mediante el cribado de la sangre y plasma del donante, son útiles para establecer un diagnóstico clínico y en el seguimiento de los pacientes. Las pruebas de diagnóstico comerciales disponibles en la actualidad, se basan en ensayos enzimáticos de imnunoabsorción (EIA) para la detección de anticuerpos específicos contra HCV. Estos métodos pueden detectar más del 95% de los pacientes con infección crónica, pero solo entre el 50 y el 70% de las infecciones agudas. Para confirmar los resultados positivos por EIA se usa frecuentemente el sistema inmunoblot recombinante (RIBA), el cual identifica anticuerpos contra los antígenos individuales del HCV. Por otra parte, algunas técnicas de biología molecular (amplificación de ácidos nucleicos: Reacción en Cadena de la Polimerasa (PCR) y DNA ramificado) han sido utilizadas para confirmar los resultados serológicos así como para determinar la efectividad de la terapia antiviral. Un resultado positivo indica la presencia de una infección activa, de una fuente potencial de transmisión y/o del desarrollo de una enfermedad hepática crónica.
Para el tratamiento de personas con hepatitis C crónica se emplean fármacos antivirales como el interferón (administrado solo o en combinación con la ribavirina), pero el costo del tratamiento es elevado. Si se emplea solo el tratamiento con interferón, la eficacia en los pacientes es de 10 a 20%, mientras que en combinación con la ribavirina es eficaz en cerca del 30-50% de los casos. El tratamiento solo con ribavirina no parece ser efectivo.
No existe en la actualidad una vacuna contra HCV, debido en parte, a la alta frecuencia de mutaciones del virus. El escaso conocimiento de la respuesta inmune protectora que sigue a la infección por HCV ha dificultado el desarrollo de la vacuna. No se conoce tampoco acerca de los mecanismos del sistema inmune para la eliminación del virus. Algunos estudios, sin embargo, han demostrado la aparición de anticuerpos neutralizantes en pacientes con infección HCV. En ausencia de la vacuna, es conveniente tomar todas las medidas posibles para prevenir la infección (a) cribado y análisis de sangre y órganos de donantes; (b) inactivación del virus en productos derivados del plasma; (c) implementación y mantenimiento de las prácticas para el control de la infección incluyendo la

esterilización del material médico y dental; (d) promover cambios en la conducta entre el público en general y el personal sanitario para evitar las prácticas incorrectas y (e) vigilancia de los grupos de riesgo (personas con promiscuidad sexual y drogadictos)."

El genoma codifica para componentes estructurales: una proteína de la nucleocápside y dos glicoproteínas de la envoltura, así como para proteinas funcionales involucradas en la replicación viral y la síntesis de proteinas. La región que codifica para la nucleocápside parece estar altamente conservada entre los aislamientos obtenidos en todo el mundo.

C. PRINCIPIOS DEL ENSAYO.

Las microplacas están recubiertas con antígenos específicos del HCV correspondientes a las regiones del "*core"* y "*ns"* que codifican para determinantes antigénicos inmunodominantes y conservados (péptido del *core* y péptidos recombinantes NS3, NS4 y NS5).
Se añade la muestra diluida y los anticuerpos contra HCV, presentes en la muestra, son capturados por los antígenos de la fase sólida.
Después del lavado, en la 2ª incubación, los anticuerpos IgG e IgM son detectados mediante anticuerpos policlonales específicos anti-IgG/IgM humanos, conjugados con Peroxidasa (HPR).
La enzima capturada en la fase sólida, combinada con la mezcla substrato/cromógeno, genera una señal óptica proporcional a la cantidad de anticuerpos anti-HCV presentes en la muestra. Posteriormente, mediante un valor de corte calculado, las densidades ópticas pueden interpretarse como resultados negativos o positivos a la presencia de anticuerpos al HCV.

D. COMPONENTES.

Cada equipo (Código CVAB.CE) contiene reactivos suficientes para realizar 192 pruebas.

1. Microplaca: MICROPLATE
n° 2 microplacas
12 tiras de 8 pocillos recubiertos con péptidos recombinantes para el "core" y para NS3, NS4 y NS5. Las placas están empaquetadas en bolsas selladas con desecante.

2. Control Negativo: CONTROL -
1x4.0ml/vial
Listo para el uso. Contiene 1% de proteinas del suero de cabra, tampón Citrato sódico 10mM pH 6.0 +/-0.1, 0.5% de Tween 20, además de azida sódica 0.09% y ProClin 300 al 0,045% como conservantes. El control negativo está codificado con el color verde olivo.

3. Control Positivo: CONTROL +
1x4.0ml/vial
Listo para el uso. Contiene 1% de proteinas del suero de cabra, anticuerpos humanos anti-HCV, tampón Citrato sódico10mM pH 6.0 +/-0.1, 0.5% de Tween 20, así como azida sódica 0.09% y ProClin 300 al 0,045% como conservantes. El control positivo está codificado con el color azul.

4. Calibrador CAL ….
n° 2 viales
Liofilizado. Para disolver en agua calidad EIA como se indica en la etiqueta. Contiene suero fetal bovino, anticuerpos humanos al HCV, calibrados según el código Estándar de Trabajo de NIBSC 99/588-003-WI, tampón Citrato sódico10mM pH 6.0 +/- 0.1, además de sulfato de gentamicina 0.3 mg/ml y ProClin 300 al 0,045% como conservantes.

Nota: El volumen necesario para disolver el contenido del frasco varía en cada lote. Se recomienda usar el volumen indicado en la etiqueta.

5. Tampón de Lavado Concentrado: WASHBUF 20X
2x60ml/botella. Solución concentrada 20x.
Una vez diluida, la solución de lavado contiene tampón fosfato 10 mM a pH 7.0 +/- 0.2, Tween 20 al 0.05% y ProClin 300 al 0,045%.

6. Conjugado CONJ
2x16ml/vial. Solución lista para el uso. Contiene 5% de albúmina de suero bovino, tampón Tris 10mM a pH 6.8 +/- 0.1, anticuerpo policlonal de cabra anti-IgM/IgG humanos conjugado con peroxidasa (HPR) en presencia de 0.2 % de sulfato de gentamicina y ProClin 300 al 0,045% como conservantes. El conjugado está codificado con el color rosa/rojo.

7. Cromógeno/Substrato SUBS TMB
2x16ml/vial. Contiene una solución tamponada citrato-fosfato 50mM pH 3.5-3.8, tetra-metil-benzidina (TMB) 0.03% y peróxido de hidrógeno (H_2O_2) 0.02% así como dimetilsulfóxido 4%.
Nota: Evitar la exposición a la luz, la sustancia es fotosensible.

8. Diluente de ensayo: DILAS
1x15ml/vial. Contiene una solución tamponada Tris 10 mM pH 8.0 +/- 0.1 y 0.1% de ProClin 300 al 0,045% para el pre-tratamiento de muestras y controles, bloquea posibles interferencias.
Nota: Usar todo el contenido del vial antes de abrir un segundo. El reactivo es sensible a oxidación.

9. Ácido Sulfúrico: H_2SO_4 O.3 M
1x32ml/vial. Contiene solución de H_2SO_4 0.3M
Atención: Irritante (H315, H319; P280, P302+P352, P332+P313, P305+P351+P338, P337+P313, P362+P363).

10. Diluente de muestras DILSPE
2x50ml. Contiene una solución tamponada citrato sódico 10 mM pH 6.0 +/- 0.1, 1% de proteinas del suero de cabra, 0.5% de Tween 20, azida sódica 0.09% y ProClin 300 al 0,045% como conservantes. Se usa para diluir las muestras.

11. Sellador adhesivo, n° 4

12. Manual de instrucciones, n° 1

Nota importante: A solicitud del cliente, Dia.Pro puede suministrar reactivos para realizar 96, 480 ó 960 pruebas, según se reporta a continuación:

1.Microplaca 2.ControlNegativo 3.ControlPositivo 4.Calibrador 5.Soluc. Lav. conc 6.Conjugado 7.Cromóg/Subs 8.Diluent. ensayo 9.Acido Sulfúrico 10.Diluent.muestr. 11.Sellador adhes. 12.Manual de instrucciones	n°1 1x2.0ml/vial 1x2.0ml/vial n° 1 vial 1x60ml/bot. 1x16ml/vial 1x16ml/vial 1x8ml/vial 1x15ml/vial 1x50ml/vial n° 2 n° 1	n°5 1x10ml/vial 1x10ml/vial n° 5 vials 5x60ml/frasc. 2x40ml/frasc. 2x40ml/frasc. 1x40ml/ frasc. 2x40ml/ frasc. 5x50ml/frasc. n° 10 n° 1	n°10 1x20.ml/vial 1x20.ml/vial n° 10 vials 4x150ml/frasc. 4x40ml/frasc. 4x40ml/frasc. 1x80ml/frasc. 2x80ml/frasc. 4x125ml/frasc. n° 20 n° 1
Número de pruebas	**96**	**480**	**960**
Código	**CVAB.CE.96**	**CVAB.CE.480**	**CVAB.CE.960**

E. MATERIALES NECESARIOS NO SUMINISTRADOS.

1. Micropipetas calibradas (200μl y 10μl) y puntas plásticas desechables.
2. Agua de calidad EIA (bidestilada o desionizada, tratada con carbón para remover químicos oxidantes usados como desinfectantes).
3. *Timer* con un rango de 60 minutos como mínimo.
4. Papel absorbente.
5. Incubador termostático de microplacas ELISA, calibrado (en seco o húmedo) fijo a 37ºC.
6. Lector calibrado de microplacas de ELISA con filtros de 450nm (lectura) y de filtros de 620-630 nm.
7. Lavador calibrado de microplacas ELISA.
8. Vórtex o similar.

F. ADVERTENCIAS Y PRECAUCIONES.

1. El equipo debe ser usado por personal técnico adecuadamente entrenado, bajo la supervisión de un doctor responsable del laboratorio.
2. Cuando el equipo es usado para cribado en unidades de sangre, el laboratorio debe estar certificado y calificado para realizar este tipo de análisis (Ministerio de Salud o entidad similar).
3. Todas las personas encargadas de la realización de las pruebas deben llevar las ropas protectoras adecuadas de laboratorio, guantes y gafas. Evitar el uso de objetos cortantes (cuchillas) o punzantes (agujas). El personal debe ser adiestrado en procedimientos de bioseguridad, según ha sido recomendado por el Centro de Control de Enfermedades de Atlanta, Estados Unidos, y publicado por el Instituto Nacional de Salud: “Biosafety in Microbiological and Biomedical Laboratories”, ed.1984.
4. Todo el personal involucrado en el manejo de muestras debe estar vacunado contra HBV y HAV, para lo cual existen vacunas disponibles, seguras y eficaces.
5. Se debe controlar el ambiente del laboratorio para evitar la contaminación de los componentes con polvo o agentes microbianos cuando se abran los equipos, así como durante la realización del ensayo. Evitar la exposición del substrato a la luz y las vibraciones de la mesa de trabajo durante el ensayo.
6. Conservar el equipo a temperaturas entre 2-8 ºC, en un refrigerador con temperatura regulada o en cámara fría.
7. No intercambiar reactivos de diferentes lotes ni tampoco de diferentes equipos.
8. Comprobar que los reactivos no contienen precipitados ni agregados en el momento del uso. De darse el caso, informar al responsable para realizar el procedimiento pertinente y reemplazar el equipo.
9. Evitar contaminación cruzada entre muestras de suero/ plasma usando puntas desechables y cambiándolas después de cada uso. No reutilizar puntas desechables
10. Evitar contaminación cruzada entre los reactivos del equipo usando puntas desechables y cambiándolas después de cada uso. No reutilizar puntas desechables
11. No usar el producto después de la fecha de caducidad indicada en el equipo e internamente en los reactivos. Según estudios realizados, no se ha detectado pérdida relevante de actividad en equipos abiertos, en uso por un período de hasta 6 meses.
12. Tratar todas las muestras como potencialmente infecciosas. Las muestras de suero humano deben ser manipuladas al nivel 2 de bioseguridad, según ha sido recomendado por el Centro de Control de Enfermedades de Atlanta, Estados Unidos y publicado por el Instituto Nacional de Salud: “Biosafety in Microbiological and Biomedical Laboratories”, ed.1984.
13. Se recomienda el uso de material plástico desechable para la preparación de las soluciones de lavado y para la transferencia de los reactivos a los diferentes equipos automatizados a fin de evitar contaminaciones.
14. Los desechos producidos durante el uso del equipo deben ser eliminados según lo establecido por las directivas nacionales y las leyes relacionadas con el tratamiento de los residuos químicos y biológicos de laboratorio. En particular, los desechos líquidos provenientes del proceso de lavado deben ser tratados como potencialmente infecciosos y deben ser inactivados. Se recomienda la inactivación con lejía al 10% de 16 a 18 horas o el uso de la autoclave a 121°C por 20 minutos.
15. En caso de derrame accidental de algún producto, se debe utilizar papel absorbente embebido en lejía y posteriormente en agua. El papel debe eliminarse en contenedores designados para este fin en hospitales y laboratorios.
16. El ácido sulfúrico es irritante. En caso de derrame, se debe lavar la superficie con abundante agua.
17. Otros materiales de desecho generados durante la utilización del equipo (por ejemplo: puntas usadas en la manipulación de las muestras y controles, microplacas usadas) deben ser manipuladas como fuentes potenciales de infección de acuerdo a las directivas nacionales y leyes para el tratamiento de residuos de laboratorio.

G. MUESTRA: PREPARACIÓN Y RECOMENDACIONES.

1. Extraer la sangre asépticamente por punción venosa y preparar el suero o plasma según las técnicas estándar de los laboratorios de análisis clínico. No se ha detectado que el tratamiento con citrato, EDTA o heparina afecte las muestras.
2. Evitar el uso de conservantes, en particular azida sódica, ya que pudiera afectar la actividad enzimática del conjugado, generando resultados falsos negativos.
3. Las muestras deben estar identificadas claramente mediante código de barras o nombres, a fin de evitar errores en los resultados. Cuando el equipo se emplea para el cribado en unidades de sangre, se recomienda el uso del código de barras.
4. Las muestras hemolizadas (color rojo) o hiperlipémicas (aspecto lechoso) deben ser descartadas para evitar falsos resultados, al igual que aquellas donde se observe la presencia de precipitados, restos de fibrina o filamentos microbianos.
5. El suero y el plasma pueden conservarse a una temperatura entre +2° y +8°C en tubos de recolección principales hasta cinco días después de la extracción. No congelar tubos de recolección principales. Para periodos de almacenamiento más prolongados, las muestras de plasma o suero, retiradas cuidadosamente del tubo de extracción principal, pueden almacenarse congeladas a –20°C durante varios meses, evitando luego descongelar cada muestra más de una vez, ya que se pueden generar partículas que podrían afectar al resultado de la prueba.
6. Si hay presencia de agregados, la muestra se puede aclarar mediante centrifugación a 2000 rpm durante 20 minutos o por filtración con un filtro de 0,2-0,8 micras.

H. PREPARACIÓN DE LOS COMPONENTES Y PRECAUCIONES.

Según estudios realizados, no se ha detectado pérdida relevante de actividad en equipos abiertos, utilizados hasta 6 veces, en un período de hasta 6 meses.

1. Microplacas:

Dejar la microplaca a temperatura ambiente (aprox. 1 hora) antes de abrir el envase. Compruebe que el desecante no esté de un color verde oscuro, lo que indicaría un defecto de fabricación. De ser así, debe solicitar el servicio de Dia.Pro: atención al cliente.

Las tiras de pocillos no utilizadas, deben guardarse herméticamente cerradas en la bolsa de aluminio con el desecante a 2-8ºC. Una vez abierto el envase, las tiras sobrantes, se mantienen estables hasta que el indicador de humedad dentro de la bolsa del desecante cambie de amarillo a verde.

2. Control Negativo:
Listo para el uso. Mezclar bien con la ayuda de un vórtex, antes de usar.

3. Control Positivo:
Listo para el uso. Mezclar bien con la ayuda de un vórtex, antes de usar. Manipule este reactivo como potencialmente infeccioso, aunque las partículas virales presentes en el control han sido inactivadas quimicamente.

4. Calibrador:
Disolver cuidadosamente el contenido del vial en el volumen de agua de calidad EIA indicado en la etiqueta. Mezclar bien con el vórtex antes de usar.
Manipule este reactivo como potencialmente infeccioso, aunque las partículas virales presentes en el control han sido inactivadas quimicamente.
Nota: *Una vez reconstituida, la solución no es estable. Se recomienda mantenerla congelada en alícuotas a –20ºC.*

5. Solución de Lavado Concentrada:
Todo el contenido de la solución concentrada 20x debe diluirse con agua bidestilada fino a 1200 ml y mezclarse suavemente antes de usarse.
Por que en los frascos pueden estar presente los cristales, cuando se prepara la solucion prestar mucha atencion en diluir todo el contenido. Durante la preparación evitar la formación de espuma y burbujas, lo que podría influir en la eficiencia de los ciclos de lavado.
Nota: *Una vez diluida, la solución es estable por una semana a temperaturas entre +2 y 8ºC.*

6. Conjugado:
Listo para el uso. Mezclar bien con un vórtex antes de usar. Evitar posible contaminación del líquido con oxidantes químicos, polvo o microbios. En caso de que deba transferirse el reactivo, usar contenedores de plástico, estériles y desechables, siempre que sea posible.

7. Cromógeno/ Substrato:
Listo para el uso. Mezclar bien con un vórtex antes de usar. Evitar posible contaminación del líquido con oxidantes químicos, polvo o microbios. Evitar la exposición a la luz, agentes oxidantes y superficies metálicas. En caso de que deba transferirse el reactivo, usar contenedores de plástico, estériles y desechables, siempre que sea posible.

8. Diluente de ensayo:
Listo para el uso. Mezclar bien con un vórtex antes de usar.

9. Ácido Sulfúrico:
Listo para el uso. Mezclar bien con un vórtex antes de usar.
Atención: Irritante (H315, H319; P280, P302+P352, P332+P313, P305+P351+P338, P337+P313, P362+P363).

Leyenda:

Indicación de peligro, **Frases H**
H315 – Provoca irritación cutánea.
H319 – Provoca irritación ocular grave.

Consejo de prudencia, **Frases P**
P280 – Llevar guantes/prendas/gafas/máscara de protección.
P302 + P352 – EN CASO DE CONTACTO CON LA PIEL: Lavar con agua y jabón abundantes.
P332 + P313 – En caso de irritación cutánea: Consultar a un médico.
P305 + P351 + P338 – EN CASO DE CONTACTO CON LOS OJOS: Aclarar cuidadosamente con agua durante varios minutos. Quitar las lentes de contacto, si lleva y resulta fácil. Seguir aclarando.
P337 + P313 – Si persiste la irritación ocular: Consultar a un médico.
P362 + P363 – Quitarse las prendas contaminadas y lavarlas antes de volver a usarlas.

10. Diluente de muestras :
Listo para el uso. Mezclar bien con un vórtex antes de usar.

I. INSTRUMENTOS Y EQUIPAMIENTO UTILIZADOS EN COMBINACIÓN CON EL EQUIPO.

1. Las micropipetas deben ser calibradas para dispensar correctamente el volumen requerido en el ensayo y sometidas a una descontaminación periódica de las partes que pudieran entrar accidentalmente en contacto con la muestra o los reactivos (lejía 10%, de calidad de los desinfectantes hospitalarios). Deben además, ser regularmente revisadas para mantener una precisión del 1% y una confiabilidad de +/- 2%. Deben descontaminarse periodicamente los residuos de los componentes del equipo.
2. La incubadora de ELISA debe ser ajustada a 37ºC (+/- 0.5ºC) y controlada periódicamente para mantener la temperatura correcta. Pueden emplearse incubadoras secas o baños de agua siempre que estén validados para la incubación de pruebas de ELISA.
3. El **lavador ELISA** es extremadamente importante para el rendimiento global del ensayo.El lavador debe ser validado de forma minuciosa previamente, revisado para comprobar que suministra el volumen de dispensación correcto y enviado regularmente a mantenimiento de acuerdo con las instrucciones de uso del fabricante. En particular, deben lavarse minuciosamente las sales con agua desionizada del lavador al final de la carga de trabajo diaria. Antes del uso, debe suministrarse extensivamente solución de lavado diluida al lavador. Debe enviarse el instrumento semanalmente a descontaminación según se indica en su manual (se recomienda descontaminación con NaOH 0.1 M). Para asegurar que el ensayo se realiza conforme a los rendimientos declarados, basta con 5 ciclos de lavado (aspiración + dispensado de 350 µl/pocillo de solución de lavado + 20 segundos de remojo = 1 ciclo). Si no es posible remojar, añadir un ciclo de lavado adicional. Un ciclo de lavado incorrecto o agujas obstruidas con sal son las principales causas de falsas reacciones positivas.
4. Los tiempos de incubación deben tener un margen de $\pm$5%.
5. El lector de microplacas ELISA debe estar provisto de un filtro de lectura de 450 nm y de un segundo filtro de 620-630 nm, obligatorio para el blanco. El procedimiento estándar debe contemplar: a) Ancho de banda $\leq$ 10 nm; b) Rango de absorbancia de 0 a $\geq$ 2,0; c) Linealidad $\geq$ 2,0; d) Reproducibilidad $\geq$ 1%. El blanco se prueba en el pocillo indicado en la sección “Procedimiento del ensayo”. El sistema óptico del lector debe calibrarse periódicamente para garantizar que se mide la densidad óptica correcta. Periódicamente se debe proceder al mantenimiento según las instrucciones del fabricante.
6. En caso de usar un sistema automatizado de ELISA, los pasos críticos (dispensado, incubación, lavado, lectura, agitación y procesamiento de datos) deben ser cuidadosamente fijados, calibrados, controlados y periódicamente ajustados, para garantizar los valores indicados en la seccione “Control interno de calidad”. El protocolo del ensayo debe ser instalado en el sistema operativo de la unidad y validado tanto para el lavador como para el lector. Por otro lado, la parte del sistema que maneja los líquidos (dispensado y lavado) debe ser validada y fijada correctamente. Debe prestarse particular

atención a evitar el arrastre por las agujas de dispensación y de lavado, a fin de minimizar la posibilidad de ocurrencia de falsos positivos por contaminación de los pocillos adyacentes por muestras fuertemente reactivas. Se recomienda el uso de sistemas automatizados para el cribado en unidades de sangre y cuando la cantidad de muestras supera las 20-30 unidades por ensayo.

7. Cuando se utilizan instrumentos automaticos, en el caso en que los contenedores para los frascos del in strumento no sean adecuados a los frascos del kit, transferir la solucion en ellos contenida en frascos idoneos al instrumento y etiquetarlos con la misma etiqueta utilizada en el frasco original. Esta operacion es importante para evitar el cambio del contenido de los frascos durante el transferimiento. Cuando el test a terminado colocar los contenedores secundarios etiquetados y tapados a 2..8°C.
8. El servicio de atención al cliente en Dia.Pro, ofrece apoyo al usuario para calibrar, ajustar e instalar los equipos a usar en combinación con el equipo, con el propósito de asegurar el cumplimiento de los requerimientos descritos.

L. OPERACIONES Y CONTROLES PREVIOS AL ENSAYO.

1. Compruebe la fecha de caducidad indicada en la parte externa del equipo (envase primario). No usar si ha caducado.
2. Compruebe que los componentes líquidos no están contaminados con partículas o agregados visibles. Asegúrese de que el cromógeno (TMB) es incoloro o azul pálido, aspirando un pequeño volumen de este con una pipeta estéril de plástico. Compruebe que no han ocurrido rupturas ni derrames de líquido dentro de la caja (envase primario) durante el transporte. Asegurarse de que la bolsa de aluminio que contiene la microplaca no esté rota o dañada.
3. Diluir totalmente la solución de lavado concentrada 20X, como se ha descrito anteriormente.
4. Disolver el Calibrador como se ha descrito anteriormente y mezclar suavemente.
5. Dejar los componentes restantes alcanzar la temperatura ambiente (aprox. 1 hora), mezclar luego suavemente en el vórtex todos los reactivos líquidos.
6. Ajustar la incubadora de ELISA a 37ºC y cebar el lavador de ELISA utilizando la solución de lavado, según las instrucciones del fabricante. Fijar el número de ciclos de lavado según se indica en la sección específica.
7. Comprobar que el lector de ELISA esté conectado al menos 20 minutos antes de realizar la lectura.
8. En caso de trabajar automáticamente, conectar el equipo y comprobar que los protocolos estén correctamente programados.
9. Comprobar que las micropipetas estén fijadas en el volumen requerido.
10. Asegurarse de que el equipamiento a usar esté en perfecto estado, disponible y listo para el uso.
11. En caso de surgir algún problema, se debe detener el ensayo y avisar al responsable.

M. PROCEDIMIENTO DEL ENSAYO.

El ensayo debe realizarse según las instrucciones que siguen a continuación, es importante mantener en todas las muestras el mismo tiempo de incubación.

Ensayos Automatizados.

En el caso de que el ensayo se realice de manera automatizada con un sistema ELISA, se recomienda programar al equipo para aspirar 200µl de Diluente de Muestras, y posteriormente 10µl de muestra.

La mezcla debe ser dispensada cuidadosamente en los pocillos correspondientes a cada muestra. Antes de aspirar la muestra siguiente, las agujas deben lavarse debidamente para evitar cualquier contaminación cruzada entre las muestras.

No diluir el Calibrador ni los controles ya que están listos para el uso.

Dispensar 200µl de controles/Calibrador en los pocillos correspondientes.

Nota importante: *Controle a simple vista que las muestras han sido diluidas y dispensadas en los pocillos adecuados, para lo cual el color de las muestras dispensadas debe ser verde azul oscuro, mientras que el del control negativo debe permanecer verde olivo.*

Para las operaciones siguientes, consulte las instrucciones que aparecen debajo para el Ensayo Manual.

Es muy importante comprobar que el tiempo entre el dispensado de la primera y la última muestra sea calculado por el instrumento y considerado para los lavados.

Ensayo Manual.

1. Poner el número de tiras necesarias en el soporte de plástico. Dejar el primer pocillo vacío para el blanco.
2. Dispensar 200µl del Control Negativo, por triplicado, 200µl de Calibrador por duplicado y 200µl del Control Positivo. No diluir el Calibrador ni los controles ya que están listos para el uso!
3. Dispensar 200µl del Diluente de muestras (DILSPE) a todos los pocillos de muestras, después dispensar 10 µl de cada muestra en su pocillo correspondiente. Resuspender suavemente evitando la formación de espuma y la contaminación de los pocillos adyacentes.

Nota importante*: Comprobar que el color del Diluente de muestras, después de adicionada la misma, cambia de verde a verde azul oscuro.*

4. Dispensar 50 ul de Diluente de ensayo (DILAS) en los pocillos de los controles/Calibrador y muestras. Compruebe que el color de las muestras sea azul oscuro.
5. Incubar la microplaca **45 min a +37°C**.

Nota importante*: Las tiras se deben sellar con el adhesivo suministrado solo cuando se hace el test manualmente. No sellar cuando se emplean equipos automatizados de ELISA.*

6. Lavar la microplaca con el lavador automático dispensando y aspirando 350 µl/pocillo de solución de lavado diluída, segun según se indica (section I.3).
7. Dispensar 100µl del Conjugado en todos los pocillos, excepto en el A1 y cubrir con el sellador. Compruebe que este reactivo de color rosa/rojo ha sido añadido en todos los pocillos excepto el A1.

Nota importante*: Tener cuidado de no tocar la pared interna del pocillo con la punta de la pipeta al dispensar el conjugado. Podría producirse contaminación.*

8. Incubar la microplaca **45 min a +37°C**.
9. Lavar la microplaca, de igual forma que en el paso 6.
10. Dispensar 100µl del Cromógeno/Substrato en todos los pocillos, incluido el A1. Incubar la microplaca a **temperatura ambiente (18-24°C) durante 15 minutos**.

Nota importante*: No exponer directamente a fuerte iluminación, de lo contrario se generan interferencias.*

11. Dispensar 100µl de ácido sulfúrico en todos los pocillos para detener la reacción enzimática, usar la misma secuencia que en el paso 10. La adición de la solución de parada cambia el color del Control Positivo y las muestras positivas de azul a amarillo/marrón.

12. Medir la intensidad del color de la solución en cada pocillo, según se indica en la sección I.5, con un filtro de 450 nm (lectura) y, otro de 620-630 nm (substracción del fondo), calibrando el instrumento con el pocillo A1 (blanco, obligatorio).

Notas importantes:

1. *Asegurarse de que no hay impresiones digitales ni polvo en el fondo de los pocillos antes de leer. Podrían generarse falsos positivos en la lectura.*
2. *La lectura debe hacerse inmediatamente después de añadir la solución de parada y, en cualquier caso, nunca transcurridos 20 minutos después de su adición. Se podría producir auto oxidación del cromógeno causando un elevado fondo.*
3. *Se ha probado que la agitación a 350 +/- 150 rpm, durante la incubación, aumenta en un 20% la sensibilidad del ensayo.*
4. *El calibrador (CAL) no afecta al cálculo del valor de corte y, por lo tanto, no afecta al cálculo de los resultados de la prueba. El calibrador (CAL) se usa solo si la gestión requiere un control interno de calidad del laboratorio.*

N. ESQUEMA DEL ENSAYO.

Método	Operaciones
Controles & Calibrador Muestras Diluente de ensayo (DILAS)	200 µl 200µl dil.+10µl 50 µl
1ra incubación	**45 min**
Temperatura	+37°C
Lavado	5 ciclos con 20''de remojo o 6 ciclos sin remojo
Conjugado	100 µl
2da incubación	**45 min**
Temperatura	+37°C
Lavado	5 ciclos con 20''de remojo o 6 ciclos sin remojo
TMB/H2O2	100 µl
3ra incubación	**15 min**
Temperatura	18-24°C
Acido Sulfúrico	100 µl
Lectura D.O.	450nm / 620-630nm

A continuación se describe un ejemplo del esquema de dispensado.

Microplaca

	1	2	3	4	5	6	7	8	9	10	11	12
A	BL	M2										
B	CN	M3										
C	CN	M4										
D	CN	M5										
E	CAL	M6										
F	CAL	M7										
G	CP	M8										
H	M 1	M9										

Leyenda: BL = Blanco CN = Control Negativo CAL = Calibrador CP = Control Positivo M = Muestra

O. CONTROL DE CALIDAD INTERNO.

Se realiza un grupo de pruebas con los controles/calibrador cada vez que se usa el equipo para verificar si los valores DO450nm son los esperados.

Asegurar el cumplimiento de los siguientes parámetros:

Parámetro	Exigencia
Pocillo Blanco	Valor < 0.100 DO450nm
Control Negativo (CN)	Valor medio < 0.050 DO450nm después de leer el blanco
Calibrador	M/Co > 1.1
Control Positivo	Valor > 1.000 DO450nm

Si los resultados del ensayo coinciden con lo establecido anteriormente, pase a la siguiente sección.

En caso contrario, detenga el ensayo y compruebe:

Problema	Compruebe que
Pocillo blanco > 0.100DO450nm	la solución cromógeno/substrato no se ha contaminado durante el ensayo.
Control Negativo (CN) > 0.050 DO450nm después de leer el blanco	1. el proceso de lavado y los parámetros del lavador estén validados según los estudios previos de calificación. 2. se ha usado la solución de lavado apropiada y que el lavador ha sido cebado con la misma antes del uso. 3. no se han cometido errores en el procedimiento (dispensar el control positivo en lugar del negativo). 4. no ha existido contaminación del control negativo o de sus pocillos debido a muestras positivas derramadas, o al conjugado. 5. las micropipetas no se han contaminado con muestras positivas o con el conjugado. 6. las agujas del lavador no estén parcial o totalmente obstruidas.
Calibrador M/Co < 1.1	1. el procedimiento ha sido realizado correctamente. 2. no ha habido errores durante su distribución (dispensar el control negativo en lugar del calibrador). 3. el proceso de lavado y los parámetros del lavador estén validados según los estudios previos de calificación. 4. no ha ocurrido contaminación externa del calibrador.
Control Positivo < 1.000 DO450nm	1. el procedimiento ha sido realizado correctamente. 2. no se han cometido errores en el procedimiento (dispensar el control negativo en lugar del positivo). En este caso el control negativo debe tener un valor de DO450nm > 0.150. 3. el proceso de lavado y los parámetros del lavador estén validados según los estudios previos de calificación. 4. no ha ocurrido contaminación externa del control positivo.

Si ocurre alguno de los problemas anteriores, después de comprobar, informe al responsable para tomar las medidas pertinentes.

P. CÁLCULO DEL VALOR DE CORTE.

Los resultados se calculan por medio de un valor de corte (cut-off) hallado con la siguiente fórmula:

Valor de corte = CN medio DO450nm + 0.350

El valor encontrado para el ensayo se usa para la interpretación de los resultados, según se describe a continuación:

***Nota Importante**: Cuando el cálculo de los resultados se halla mediante el sistema operativo de un equipo de ELISA automático, asegurarse de que la formulación usada para el cálculo del valor de corte, y para la interpretación de los resultados sea correcta.*

Q. INTERPRETACIÓN DE LOS RESULTADOS.

La interpretación de los resultados se realiza mediante la razón entre las DO a 450nm de las muestras y el Valor de corte (M/Co).

Los resultados se interpretan según la siguiente tabla:

(M/Co)	Interpretación
< 0.9	Negativo
0.9 – 1.1	Equívoco
> 1.1	**Positivo**

Un resultado negativo indica que el paciente no está infectado por HCV y la unidad de sangre se puede transfundir.

Cualquier paciente, cuya muestra resulte equívoca debe someterse a una nueva prueba con una segunda muestra de sangre colectada 1 ó 2 semanas después de la inicial. En este caso la unidad de sangre no debe ser transfundida.

Un resultado positivo es indicativo de infección por HCV y por consiguiente el paciente debe ser tratado adecuadamente. La unidad de sangre debe ser descartada.

Notas importantes:

1. *La interpretación de los resultados debe hacerse bajo la vigilancia del responsable del laboratorio para reducir el riesgo de errores de juicio y de interpretación.*
2. *Antes de formular un diagnóstico de hepatitis viral, los resultados positivos deben comprobarse a través de un método alternativo, capaz de detectar anticuerpos IgG e IgM (prueba confirmatoria).*
3. *Según se demuestra en la Evaluación del Performance del producto, el ensayo es capaz de detectar los anticuerpos anti HCV core, en etapas más tempranas en comparación con otros equipos comerciales. Sin embargo, un resultado positivo, no confirmado con estos equipos comerciales, no debe necesariamente considerarse como falso positivo! Es necesario realizar una prueba de confirmación (suministrada, bajo solicitud del cliente, por Dia.pro srl. Codificada CCONF).*
4. *Como el ensayo es capaz de detectar además anticuerpos IgM, pueden presentarse resultados discrepantes (pérdida de reactividad IgM) con respecto a otros productos comerciales para la detección de anticuerpos anti-HCV. La positividad real de una muestra debe confirmarse probando la reactividad IgM, lo cual resulta muy importante para el diagnóstico de infección por HCV.*
5. *Cuando se transmiten los resultados de la prueba, del laboratorio a otras instalaciones, debe ponerse mucha atención para evitar el traslado de datos erróneos.*
6. *El diagnóstico de infección con un virus de la hepatitis debe ser evaluado y comunicado al paciente por un médico calificado.*

A continuación, un ejemplo de los cálculos a realizar:

Los siguientes datos no deben usarse en lugar de los valores reales obtenidos en el laboratorio.

Control Negativo: 0.019 – 0.020 – 0.021 DO450nm
Valor medio: 0.020 DO450nm
Menor de 0.050 – Válido

Control Positivo: 2.189 DO450nm
Mayor de 1.000 – Válido
Valor de corte = 0.020+0.350 = 0.370

Calibrador: 0.550 - 0.530 DO450nm
Valor medio: 0.540 DO450nm M/Co = 1.4
M/Co Mayor de 1.1 – Válido

Muestra 1: 0.070 DO450nm
Muestra 2: 1.690 DO450nm
Muestra 1 M/Co < 0.9 = negativa
Muestra 2 M/Co > 1.1 = positiva

R. FUNCIONAMIENTO.

La evaluación del funcionamiento ha sido realizada según lo reportado en las Especificaciones Técnicas Comunes (ETC) (art. 5, Capítulo 3 de las Directivas IVD 98/79/EC).

1. LÍMITE DE DETECCIÓN.

El límite de detección ha sido calculado por medio del estándar de trabajo británico anti-HCV NIBSC, código 99/558-003-WI).

La siguiente tabla muestra los valores medios de DO450nm de este estándar diluído en plasma negativo y examinado:

Dilución	Lote # 1	Lote # 2
Factor	M/Co	M/Co
1 X	**2.0**	**2.0**
2 X	**1.1**	**1.2**
4 X	0.7	0.8
8 X	0.5	0.5
Plasma Negativo	0.3	0.3

Se evaluó además la muestra Accurun 1 –serie 3000- suministrado por Boston Biomedica Inc., Estados Unidos.

Los resultados son los siguientes:

CVAB.CE Lote ID	Accurun 1 Serie	M/Co
1201	3000	1.5
0602	3000	1.5
1202	3000	1.9

Por otra parte, un total de 7 muestras, positivas para HCVAb según Ortho HCV 3.0 SAVe, código 930820, lote # EXE065-1, fueron diluídas en plasma negativo a HCVAb con el fin de obtener diluciones limitantes y luego fueron probadas nuevamente en CVAB.CE, lote # 1202, y Ortho.

Las tablas siguientes reflejan los resultados obtenidos:

Muestra n°	Dilución Límite	CVAB.CE M/Co	Ortho 3.0 M/Co
1	256 X	**1.9**	**1.3**
2	256 X	**1.9**	0.7
3	256 X	**2.4**	**1.0**
4	128 X	**2.5**	**3.2**
5	85 X	**3.3**	**1.4**
6	128 X	**2.2**	0.8
7	135 X	**3.2**	**2.2**

2. ESPECIFICIDAD Y SENSIBILIDAD DIAGNÓSTICAS.

La evaluación del procedimiento diagnóstico se realizó mediante un ensayo con más de 5000 muestras.

2.1 Especificidad Diagnóstica:

Se define como la probabilidad del ensayo de detectar negativos en ausencia del analito específico.

Además del primer estudio, donde se examinaron en total 5043 muestras de donantes de sangre no seleccionados, (incluyendo donantes por 1ª vez), 210 muestras de pacientes hospitalizados y 162 muestras que pudieran provocar interferencia (otras enfermedades infecciosas, positivas para anticuerpos de E. coli, pacientes con enfermedades hepáticas no virales, pacientes en diálisis, mujeres embarazadas, hemolizadas, lipémicas, etc.), la especificidad diagnóstica se evaluó recientemente examinando un total de 2876 muestras de donantes de sangre negativas en seis lotes distintos. Se observó un valor de especificidad de 100%.
Se emplearon además, plasma sometido a métodos de tratamiento estándar (citrato, EDTA y heparina) y suero humanos. No se ha observado falsa reactividad debida a los métodos de tratamiento de muestras.
Por último se analizaron muestras congeladas, para determinar posibles interferencias debidas a la toma de muestra y al almacenamiento. No se observaron interferencias.

2.2 Sensibilidad Diagnóstica.

Se define como la probabilidad del ensayo de detectar positivos en presencia del analito específico.
La sensibilidad diagnóstica ha sido estimada de forma externa en un total de 359 muestras, el valor obtenido fue de 100%. Más de 50 muestras positivas fueron probadas de forma interna, en este caso el resultado fue también de 100%.
Se evaluaron además, muestras positivas producto de infecciones por diferentes genotipos de HCV, así como también se estudió gran parte de los paneles de seroconversión de Boston Biomedica Inc (PHV) y Zeptometrix, USA (HCV). disponibles.
Los resultados para algunos de ellos se describen a continuación:

Panel	N° samples	DiaPro*	Ortho* **
PHV 901	11	9	9
PHV 904	7	2	4
PHV 905	9	3	4
PHV 906	7	7	7
PHV 907	7	3	2
PHV 908	13	10	8
PHV 909	3	2	2
PHV 910	5	3	3
PHV 911	5	3	3
PHV 912	3	1	1
PHV 913	4	2	2
PHV 914	9	5	5
PHV 915	4	3	0
PHV 916	8	4	3
PHV 917	10	6	6
PHV 918	8	2	0
PHV 919	7	3	3
PHV 920	10	6	6
HCV 10039	5	2	0
HCV 6212	9	6	7
HCV 10165	9	5	4

Note: * Positive samples detected ** HCV v.3.0

Por último, el producto ha sido probado contra el panel EFS Ac HCV, lote n° 01/08.03.22C/01/A, suministrado por Etablissement Francais Du Sang (EFS), Francia, obteniéndose los siguientes resultados:

EFS Panel Ac HCV

Muestra	Lote # 1 M/Co	Lote # 2 M/Co	Lote# 3 M/Co	Resultados esperados
HCV 1	**2.2**	**2.4**	**2.6**	**positivo**
HCV 2	**1.6**	**2.0**	**2.1**	**positivo**
HCV 3	**1.5**	**1.7**	**1.6**	**positivo**
HCV 4	**5.2**	**6.5**	**5.5**	**positivo**
HCV 5	**1.6**	**1.8**	**1.6**	**positivo**
HCV 6	0.4	0.4	0.4	negativo

3. PRECISIÓN.

Ha sido calculada utilizando dos muestras, una negativa y una débil positiva, examinadas en 16 réplicas en tres corridas separadas.
Los resultados se muestran a continuación:

Lote # 1202

Muestra Negativa (N = 16)

Valores medios	1ra corrida	2da corrida	3ra corrida	Valor Promedio
DO 450nm	0.094	0.099	0.096	0.096
Desviación estándar	0.008	0.007	0.008	0.007
CV %	8.7	6.6	7.9	7.7

Cal # 2 – 7K (N = 16)

Valores medios	1ra corrida	2da corrida	3ra corrida	Valor Promedio
DO 450nm	0.396	0.403	0.418	0.406
Desviación estándar	0.023	0.029	0.027	0.026
CV %	5.9	7.1	6.4	6.5
M/Co	1.1	1.1	1.2	1.1

Lote # 0602

Muestra Negativa (N = 16)

Valores medios	1ra corrida	2da corrida	3ra corrida	Valor Promedio
DO 450nm	0.097	0.096	0.094	0.096
Desviación estándar	0.009	0.010	0.008	0.009
CV %	8.9	10.1	8.4	9.1

Cal # 2 – 7K (N = 16)

Valores medios	1ra corrida	2da corrida	3ra corrida	Valor Promedio
DO 450nm	0.400	0.395	0.393	0.396
Desviación estándar	0.021	0.025	0.026	0.024
CV %	5.4	6.2	6.6	6.1
M/Co	1.2	1.2	1.1	1.2

Lote # 0602/2

Muestra Negativa (N = 16)

Valores medios	1ra corrida	2da corrida	3ra corrida	Valor Promedio
DO 450nm	0.087	0.091	0.088	0.089
Desviación estándar	0.009	0.007	0.008	0.008
CV %	10.0	8.2	8.6	8.9

Cal # 2 – 7K (N = 16)

Valores medios	1ra corrida	2da corrida	3ra corrida	Valor Promedio
DO 450nm	0.386	0.390	0.391	0.389
Desviación estándar	0.023	0.021	0.023	0.022
CV %	6.0	5.3	5.8	5.7
M/Co	1.1	1.2	1.2	1.2

La variabilidad mostrada en las tablas no dió como resultado una clasificación errónea de las muestras.

S. LIMITACIONES.

Los falsos positivos repetibles, no confirmados por RIBA o similares técnicas de confirmación, fueron estimados como menos del 0.1% de la población normal.

Las muestras que después de ser descongeladas presentan partículas de fibrina o partículas agregadas, generan algunos resultados falsos positivos.

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Todos los productos de diagnóstico in vitro fabricados por la empresa son controlados por un sistema certificado de control de calidad aprobado por un organismo notificado para el marcado CE. Cada lote se somete a un control de calidad y se libera al mercado únicamente si se ajusta a las especificaciones técnicas y criterios de aceptación de la CE.

Fabricante:
Dia.Pro Diagnostic Bioprobes S.r.l.
Via G. Carducci n° 27 – Sesto San Giovanni
(Milán) – Italia

CE
0318

DIA. PRO

Dia.Pro
Diagnostic
BioProbes

Letter of Authorization

We, **"Dia.Pro Diagnostic Bioprobes S.r.l."** located at Via G. Carducci, Nr. 27 – **Sesto San Giovanni (Milan) 20099, Italy**, authorize

GLOBAL BIOMARKETING GROUP – MOLDOVA SRL
Str. Tighina 65, Oficiu 607
MD-2001 CHISINAU
REP. MOLDOVA

as our exclusive distributor for the territory of the Republic of Moldova, to participate in various tenders with **Dia.Pro** ELISA products.

We, Dia.Pro Diagnostic Bioprobes S.r.l shall supply our distributor GLOBAL BIOMARKETING GROUP – MOLDOVA SRL with all products in strict compliance with the existing "Distribution Agreement" rev.0121 valid until 31-Dec-2023, with possibility of renewal upon agreement between both parties for an additional period.

Dia.Pro Diagnostic Bioprobes S.r.l will grant the supply of all awarded tenders until their natural expiry, of which a documental proof has to be provided to Dia.Pro by the distributor GLOBAL BIOMARKETING GROUP – MOLDOVA SRL.

Sincerely yours,

Date: **Milan, 04-February-2021**

Dia.Pro Diagnostic Bioprobes S.r.l.

DIA. PRO.
DIAGNOSTIC BIOPROBES S.r.l.

Dr.ssa Fiorenza Scozzesi
Legal Representative

DECLARATION OF CONFORMITY

1) Manufacturer *(Name, department)*: **Monobind Inc.**

Address: **100 North Pointe, LAKE FOREST, CA 92630. UNITED STATES**

and

2) European authorized representative: **CEpartner4U BV,**

Address: **ESDOORNLAAN 13, 3951DB MAARN, THE NETHERLANDS**;
(on product labels printed as:
CEpartner4U , ESDOORNLAAN 13, 3951DB MAARN, THE NETHERLANDS Tel.: +31 (0)6 516 536 26;
or as: CEpartner4U, 3951DB; 13. NL tel: +31 (0)6 – 516.536.26)

3) Product(s) *(name, type or model/batch number, etc.)*:

Immunoassay products;
ELISA,
CLIA,
Control,
Instruments (see appendix)

4) The product(s) described above is in conformity with:

Document No.	Title	Edition / Date of issue
L 331; 98/79/EC	In-Vitro-Diagnostic Directive	1998-10-27

5) Additional information *(conformity procedure, Notified Body, CE certificate, etc.)*:

Conformity assessment procedure for CE marking: IVD Directive, Annex III

Lake Forest, USA;2011-09-27 --
A Shatola

Tony Shatola; QA Director, Monobind Inc.

(Place & date of issue (yyyy-mm-dd)) *(name, function and signature of manufacturer)*

Maarn, NL; 2011-09-27 --

Olga Teirlinck; Consultant, CEpartner4U BV

(Place & date of issue (yyyy-mm-dd)) *(name; function and signature of authorized representative)*

Appendix

Date: 2011-09-26

Device types	Item# ELISA	Item# CLIA	Item# Control	Item# Instrument	EDMS code	Risk Class	Certificate #	First date of CE-marking
Thyroid								
T3 – Triidothyronine	125-300	175-300			12.04.01.05.00	Low		2005-11-11
fT3 – Free Triidothyronine	1325-300	1375-300			12.04.01.01.00	Low		2005-11-11
T4 – Thyroxine	225-300	275-300			12.04.01.07.00	Low		2005-11-11
fT4 – Free Thyroxine	1225-300	1275-300			12.04.01.02.00	Low		2005-11-11
TSH – Thyrotropin	325-300	375-300			12.04.01.11.00	Low		2005-11-11
Rapid TSH – Rapid Thyrotropin	6025-300	6075-300			12.04.01.11.00	Low		2010-06-29
T3U – Triidothyronine Uptake	525-300	575-300			12.04.01.06.00	Low		2005-11-11
TBG – Thyroxine-Binding Globulin	3525-300	3575-300			12.04.01.09.00	Low		2005-11-11
Tg – Thyroglobulin	2225-300	2275-300			12.04.01.08.00	Low		2005-11-11
T3, T4 & TSH – Triidothyronine, Thyroxine & Thyrotropin Combo (VAST)	8025-300	8075-300			12.04.01.01.00	Low		2005-11-11
T3 – Triidothyronine (SBS)	8125-300	8175-300			12.04.01.01.00	Low		2010-06-29
T4- Thyroxine (SBS)	8225-300	8275-300			12.04.01.01.00	Low		2010-06-29
fT3, fT4 & TSH – Free Triidothyronine, Free Thyroxine & Thyrotropin Combo (VAST)	7025-300	7075-300			12.04.01.01.00	Low		2010-06-29
Neonatal Thyroid & Genetics								
NTSH – Neonatal Thyrotropin	3425-300	3475-300			12.04.01.90.00	Low		2005-11-11
NT4 – Neonatal Thyroxine	2625-300	2675-300			12.04.01.12.00	Low		2005-11-11
N 17OHP – Neonatal 17 OH Progesterone	5525-300				12.05.01.07	Low		2008-02-01
Biotinidase	8825-300				12 07 02 90 00	Low		2011-09-26
AutoImmune Thyroid								
Anti-Tg – Anti-Thyroglobulin Antigen	1025-300	1075-300			12.10.03.04.00	Low		2005-11-11
Anti-TPO – Anti-Thyroperoxidase Antigen	1125-300	1175-300			12.10.03.01.00	Low		2005-11-11
Fertility & Prenatal								
LH – Lutropin	625-300	675-300			12.05.01.05.00	Low		2005-11-11
FSH – Follitropin	425-300	475-300			12.05.01.04.00	Low		2005-11-11
PRL – Prolactin	725-300	775-300			12.05.01.08.00	Low		2005-11-11
PRL – Prolactin Sequential	6025-300	6075-300			12.05.01.08.00	Low		2005-11-11
hCG – Human Chorionic Gonadotropin	825-300	875-300			12.05.02.05.00	Low		2005-11-11
Rapid hCG – Rapid Human Chorionic Gonadotropin	3325-300				12.05.02.05.00	Low		2005-11-11
FSH, LH, hCG, sPRL Combo (VAST)	8325-300	8375-300			12.05.01.90.00	Low		2006-08-24
AFP, hCG, uE3 Combo (VAST)	8525-300	8575-300			12.05.01.90.00	Low		2010-06-29
Steroid								
Cortisol	3625-300	3675-300			12.06.02.04.00	Low		2005-11-11
DHEA-S – Dehydroepiandrosterone sulfate	5125-300	5175-300			12.05.01.02.00	Low		2010-06-29
DHEA - Dehydroepiandrosterone	7425-300	7475-300			12.05.01.02.00	Low		2011-09-26

Device types	Item# ELISA	Item# CLIA	Item# Control	Item# Instrument	EDMS code	Risk Class	Certificate #	First date of CE-marking
E2 – Estradiol	4925-300	4975-300			12.05.01.03.00	Low		2010-06-29
uE3 – Estriol, Unconjugated	5025-300	5075-300			12.05.02.02.00	Low		2010-06-29
Progesterone	4825-300	4875-300			12.05.01.06.00	Low		2010-06-29
Testosterone	3725-300	3775-300			12.05.01.10.00	Low		2007-11-01
Free Testosterone	5325-300	5375-300			12.05.01.10.00	Low		2010-06-29
17OHP - 17-Hydroxyprogesterone	5225-300	5275-300			12.05.01.07.00	Low		2010-06-29
17OHP - 17-Hydroxyprogesterone Ext. Range	9925-300	9975-300			12.05.01.07.00	Low		2010-10-18
Vitamin D3 – 25-Hydroxyvitamin D3	7725-300	7775-300			12.06.03.10.00	Low		2011-09-26
Growth & Bone Metabolism								
hGH - Human Growth Hormone	1725-300	1775-300			12.06.04.02.00	Low		2005-11-11
PTH - Parathyroid Hormone	7825-300	7875-300			12.06.03.13.00	Low		2011-09-26
Diabetes								
Insulin	2425-300	2475-300			12.06.01.03.00	Low		2005-11-11
Insulin Rapid	5825-300				12.06.01.03.00	Low		2010-06-29
C-peptide	2725-300	2775-300			12.06.01.01.00	Low		2005-11-11
Insulin & C-peptide Combo (VAST)	7325-300	7375-300			12.06.01.03.00	Low		2005-11-11
Cardiac Markers								
CKMB – Circulating Creatine Kinase (MB)	2925-300	2975-300			12.13.01.02.00	Low		2005-11-11
CTnI – Troponin I	3825-300	3875-300			12.13.01.07.00	Low		2005-11-11
DIG – Digoxin	925-300	975-300			12.08.01.01.00	Low		2005-11-11
HS-CRP – High Sensitivity C-Reactive Protein	3125-300	3175-300			12.13.01.90.00	Low		2005-11-11
Myoglobin	3225-300	3275-300			12.13.01.05.00	Low		2005-11-11
Infectious Diseases								
IgG – Anti/H. Pylori	1425-300	1475-300			15.01.04.03.00	Low		2005-11-11
IgM – Anti/H. Pylori	1525-300	1575-300			15.01.04.03.00	Low		2005-11-11
IgA – Anti/H. Pylori	1625-300	1675-300			15.01.04.03.00	Low		2005-11-11
Cancer Markers								
AFP – Alpha-Fetoprotein	1925-300	1975-300			12.03.90.01.00	Low		2005-11-11
CA 125 Ovarian Cancer Antigen	3025-300	3075-300			12.03.01.06.00	Low		2005-11-11
CA 15-3 Breast Cancer Antigen	5625-300	5675-300			12.03.01.02.00	Low		2010-06-29
CA 19-9 - Pancreatic Cancer Antigen	3925-300	3975-300			12.03.01.03.00	Low		2005-11-11
CEA – Carcinoembryonic Antigen	1825-300	1875-300			12.03.01.31.00	Low		2005-11-11
CEA - Carcinoembryonic Antigen Next Generation	4625-300	4675-300			12.03.01.31.00	Low		2010-06-29
fβhCG – Free Beta Human Chorionic Gonadotropin	2025-300	2075-300			12.03.01.90.00	Low		2005-11-11
Allergy & Anemia								
Ferritin	2825-300	2875-300			12.07.01.02.00	Low		2005-11-11
Folate	7525-300	7575-300			12.07.01.03.00	Low		2010-06-29
IgE – Immunoglobulin E	2525-300	2575-300			12.02.01.02.00	Low		2005-11-11
sTfR - Transferrin Soluble Receptor	8625-300	8675-300			12.07.01.06.00	Low		2010-06-29
Vitamin B12	7625-300	7675-300			12.07.02.04.00	Low		2011-09-26

Miscellaneous Controls								
Anti-Tg & Anti-TPO – Positive & Negative - Anti-Thyroglobulin, Anti-Thyroperoxidase			AIT-101		12.50.01.16.00	Low		2010-06-29
High Level Fertility Control – Single Level – Progesterone, Estradiol, Human Chorionic Gonadotropin			FC-300		12.50.01.16.00	Low		2010-06-29
Maternal Control – Tri Level - Human Chorionic Gonadotropin, Free Beta Human Chorionic Gonadotropin Subunit, Alpha Feta Protein, Estriol			MC-300		12.50.01.16.00	Low		2010-06-29
Thyroglobulin Control – Tri Level			TG-300		12.50.01.16.00	Low		2010-06-29
H. Pylori IgG Control – Positive & Negative			HPy-IgG-300		12.50.01.16.00	Low		2010-06-29
Miscellaneous Instruments								
IC hardware + dedicated accessories + software – Autoplex ELISA Analyzer & CLIA Processor				IN006	21.02.10.01	Low		2010-06-29
IC hardware + dedicated accessories + software – Lumax Chemiluminescence Strip Reader				IN001	21.02.10.01	Low		2006-08-24
IC hardware + dedicated accessories + software – Neo-Lumax Chemiluminescence Strip Reader				IN010	21.02.10.01	Low		2011-09-26
IC hardware + dedicated accessories + software – Impulse 2 Chemiluminescence Strip Reader				IN005	21.02.10.01	Low		2006-08-24
IC hardware + dedicated accessories + software – Impulse 3 Chemiluminescence Strip Reader				IN007	21.02.10.01	Low		2010-06-29
IC hardware + dedicated accessories + software – Lumax96 Chemiluminescence Plate Reader				IN004	21.02.10.01	Low		2007-03-01
IC hardware + dedicated accessories + software – LuMatic Chemiluminescence Plate Reader				IN008	21.02.10.01	Low		2011-09-26
IC hardware + dedicated accessories + software – Eldex 3.8 ELISA Strip Reader				IN003	21.02.10.01	Low		2007-09-10
IC hardware + dedicated accessories + software – Neo-Eldex ELISA Strip Reader				IN009	21.02.10.01	Low		2011-09-26
IC hardware + dedicated accessories + software – Mircoplate Washer				IN002	21.02.10.01	Low		2010-06-29

Monobind Inc.
Lake Forest, CA 92630, USA

AccuBind
ELISA Microwells

Total Prostate Specific Antigen (tPSA) Test System

Product Code: 2125-300

1.0 INTRODUCTION

Intended Use: The Quantitative Determination of Total Prostrate Specific Antigen (tPSA) Concentration in Human Serum by a Microplate Immunoenzymometric assay

2.0 SUMMARY AND EXPLANATION OF THE TEST

Prostate Specific antigen (PSA) is a serine protease with chymotrypsin-like activity (1,2). The protein is a single chain glycoprotein with a molecular weight of 28.4 kDA (3). PSA derives its name from the observation that it is a normal antigen of the prostrate but is not found in any other normal or malignant tissue.

PSA is found in benign, malignant and metastatic prostrate cancer. Since prostate cancer is the second most prevalent form of male malignancy, the detection of elevated PSA levels plays an important role in the early diagnosis. Serum PSA levels have been found too more useful than prostatic acid phosphatase (PAP) in the diagnosis and management of patients due to increased sensitivity (4).

In this method, PSA calibrator, patient specimen or control is first added to a streptavidin coated well. Biotinylated monoclonal and enzyme labeled antibodies (directed against distinct and different epitopes of PSA) are added and the reactants mixed. Reaction between the various PSA antibodies and native PSA forms a sandwich complex that binds with the streptavidin coated to the well.

After the completion of the required incubation period, the enzyme-PSA antibody bound conjugate is separated from the unbound enzyme-PSA conjugate by aspiration or decantation. The activity of the enzyme present on the surface of the well is quantitated by reaction with a suitable substrate to produce color.

The employment of several serum references of known prostate specific antigen (PSA) levels permits the construction of a dose response curve of activity and concentration. From comparison to the dose response curve, an unknown specimen's activity can be correlated with PSA concentration.

3.0 PRINCIPLE

Immunoenzymometric assay (TYPE 3):

The essential reagents required for an immunoenzymometric assay include high affinity and specificity antibodies (enzyme and immobilized), with different and distinct epitope recognition, **in excess,** and native antigen. In this procedure, the immobilization takes place during the assay at the surface of a microplate well through the interaction of streptavidin coated on the well and exogenously added biotinylated monoclonal anti-PSA antibody.

Upon mixing monoclonal biotinylated antibody, the enzyme-labeled antibody and a serum containing the native antigen, reaction results between the native antigen and the antibodies, without competition or steric hindrance, to form a soluble sandwich complex. The interaction is illustrated by the following equation:

$$^{Enz}Ab_{(p)} + Ag_{PSA} + {}^{Btn}Ab_{(m)} \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} {}^{Enz}Ab_{(p)}\text{-}Ag_{PSA}\text{-}{}^{Btn}Ab_{(m)}$$

$^{Btn}Ab_{(m)}$ =Biotinylated Antibody (Excess Quantity)

Ag_{PSA} = Native Antigen (Variable Quantity)

$^{Enz}Ab_{(p)}$ = Enzyme labeled Antibody (Excess Quantity)

$^{Enz}Ab_{(p)}\text{-}Ag_{PSA}\text{-}{}^{Btn}Ab_{(m)}$ =Antigen-Antibodies Complex

k_a = Rate Constant of Association

k_{-a} = Rate Constant of Dissociation

Simultaneously, the complex is deposited to the well through the high affinity reaction of streptavidin and biotinylated antibody. This interaction is illustrated below:

$^{Enz}Ab_{(p)}\text{-}Ag_{PSA}\text{-}{}^{Btn}Ab_{(m)} + Streptavidin_{C.W.} \Rightarrow$ Immobilized complex

$Streptavidin_{C.W.}$ = Streptavidin immobilized on well

Immobilized complex = complex bound to the solid surface

After equilibrium is attained, the antibody-bound fraction is separated from unbound antigen by decantation or aspiration. The enzyme activity in the antibody-bound fraction is directly proportional to the native antigen concentration. By utilizing several different serum references of known antigen values, a dose response curve can be generated from which the antigen concentration of an unknown can be ascertained.

4.0 REAGENTS

Materials Provided:

A. Prostrate Specific antigen (PSA) 1ml/vial – Icons A-F
Six (6) vials of references PSA Antigen at levels of 0(**A**), 5(**B**), 10(**C**), 25(**D**), 50(**E**) and 100(**F**) ng/ml. Store at 2-8°C. A preservative has been added.

Note: The calibrators, human serum based, were calibrated using a reference preparation, which was assayed against the 1st IS 96/670.

B. PSA Enzyme Reagent – 13ml/vial - Icon E
One (1) vial containing enzyme labeled antibody, biotinylated monoclonal mouse IgG in buffer, dye, and preservative. Store at 2-8°C.

C. Streptavidin Coated Plate – 96 wells - Icon ⇓
One 96-well microplate coated with streptavidin and packaged in an aluminum bag with a drying agent. Store at 2-8°C.

D. Wash Solution Concentrate – 20 ml - Icon
One (1) vial containing a surfactant in buffered saline. A preservative has been added. Store at 2-30°C.

E. Substrate A – 7ml/vial - Icon S^A
One (1) bottle containing tetramethylbenzidine (TMB) in buffer. Store at 2-8°C.

F. Substrate B – 7ml/vial - Icon S^B
One (1) bottle containing hydrogen peroxide (H_2O_2) in buffer. Store at 2-8°C.

G. Stop Solution – 8ml/vial - Icon STOP
One (1) bottle containing a strong acid (1N HCl). Store at 2-30°C.

H. Product Instructions.

Note 1: Do not use reagents beyond the kit expiration date.

Note 2: Avoid extended exposure to heat and light. **Opened reagents are stable for sixty (60) days when stored at 2-8°C. Kit and component stability are identified on the label.**

Note 3: Above reagents are for a single 96-well microplate

4.1 Required But Not Provided:

1. Pipette(s) capable of delivering 25 & 50µl volumes with a precision of better than 1.5%.
2. Dispenser(s) for repetitive deliveries of 0.100ml and 0.350ml volumes with a precision of better than 1.5%.
3. Microplate washers or a squeeze bottle (optional).
4. Microplate Reader with 450nm and 620nm wavelength absorbance capability.
5. Absorbent Paper for blotting the microplate wells.
6. Plastic wrap or microplate cover for incubation steps.
7. Vacuum aspirator (optional) for wash steps.
8. Timer.
9. Quality control materials

5.0 PRECAUTIONS

For In Vitro Diagnostic Use
Not for Internal or External Use in Humans or Animals

All products that contain human serum have been found to be non-reactive for Hepatitis B Surface Antigen, HIV 1&2 and HCV Antibodies by FDA licensed reagents. Since no known test can offer complete assurance that infectious agents are absent, all human serum products should be handled as potentially hazardous and capable of transmitting disease. Good laboratory procedures for handling blood products can be found in the Center for Disease Control / National Institute of Health, "Biosafety in Microbiological and Biomedical Laboratories," 2nd Edition, 1988, HHS Publication No. (CDC) 88-8395.

Safe Disposal of kit components must be according to local regulatory and statutory requirement.

6.0 SPECIMEN COLLECTION AND PREPARATION

The specimens shall be blood, serum in type and the usual precautions in the collection of venipuncture samples should be observed. For accurate comparison to established normal values, a fasting morning serum sample should be obtained. The blood should be collected in a plain redtop venipuncture tube without additives or anti-coagulants. Allow the blood to clot. Centrifuge the specimen to separate the serum from the cells. Samples may be refrigerated at 2-8°C for a maximum period of five (5) days. If the specimen(s) cannot be assayed within this time, the sample(s) may be stored at temperatures of -20°C for up to 30 days. Avoid use of contaminated devices. Avoid repetitive freezing and thawing. When assayed in duplicate, 0.050ml of the specimen is required.

7.0 QUALITY CONTROL

Each laboratory should assay controls at levels in the low, normal and elevated range for monitoring assay performance. These controls should be treated as unknowns and values determined in every test procedure performed. Quality control charts should be maintained to follow the performance of the supplied reagents. Pertinent statistical methods should be employed to ascertain trends. Significant deviation from established performance can indicate unnoticed change in experimental conditions or degradation of kit reagents. Fresh reagents should be used to determine the reason for the variations.

8.0 REAGENT PREPARATION:

1. **Wash Buffer**
   Dilute contents of wash concentrate to 1000ml with distilled or deionized water in a suitable storage container. Store at room temperature 20-27°C for up to 60 days.
2. **Working Substrate Solution**
   Pour the contents of the amber vial labeled Solution 'A' into the clear vial labeled Solution 'B'. Place the yellow cap on the clear vial for easy identification. Mix and label accordingly. Store at 2 - 8°C.
   Note1 : Do not use the working substrate if it looks blue.

Note 2: Do not use reagents that are contaminated or have bacteria growth.

9.0 TEST PROCEDURE

Before proceeding with the assay, bring all reagents, serum references and controls to room temperature (20 - 27°C).

*****Test Procedure should be performed by a skilled individual or trained professional*****

1. Format the microplates' wells for each serum reference, control and patient specimen to be assayed in duplicate. **Replace any unused microwell strips back into the aluminum bag, seal and store at 2-8°C.**
2. Pipette 0.025 ml (25µl) of the appropriate serum reference, control or specimen into the assigned well.
3. Add 0.100 ml (100µl) of the PSA Enzyme Reagent to each well. **It is very important to dispense all reagents close to the bottom of the coated well.**
4. Swirl the microplate gently for 20-30 seconds to mix and cover.
5. Incubate 30 minutes at room temperature.
6. Discard the contents of the microplate by decantation or aspiration. If decanting, tap and blot the plate dry with absorbent paper.
7. Add 350µl of wash buffer (see Reagent Preparation Section), decant (tap and blot) or aspirate. Repeat two (2) additional times for a total of three (3) washes. **An automatic or manual plate washer can be used. Follow the manufacturer's instruction for proper usage. If a squeeze bottle is employed, fill each well by depressing the container (avoiding air bubbles) to dispense the wash. Decant the wash and repeat two (2) additional times.**
8. Add 0.100 ml (100µl) of working substrate solution to all wells (see Reagent Preparation Section). **Always add reagents in the same order to minimize reaction time differences between wells.**

   DO NOT SHAKE THE PLATE AFTER SUBSTRATE ADDITION
9. Incubate at room temperature for fifteen (15) minutes.
10. Add 0.050ml (50µl) of stop solution to each well and mix gently for 15-20 seconds. **Always add reagents in the same order to minimize reaction time differences between wells.**
11. Read the absorbance in each well at 450nm (using a reference wavelength of 620-630nm to minimize well imperfections) in a microplate reader. **The results should be read within thirty (30) minutes of adding the stop solution.**

10.0 CALCULATION OF RESULTS

A dose response curve is used to ascertain the concentration of PSA in unknown specimens.

1. Record the absorbance obtained from the printout of the microplate reader as outlined in Example 1.
2. Plot the absorbance for each duplicate serum reference versus the corresponding PSA concentration in ng/ml on linear graph paper (do not average the duplicates of the serum references before plotting).
3. Draw the best-fit curve through the plotted points.
4. To determine the concentration of PSA for an unknown, locate the average absorbance of the duplicates for each unknown on the vertical axis of the graph, find the intersecting point on the curve, and read the concentration (in ng/ml) from the horizontal axis of the graph (the duplicates of the unknown may be averaged as indicated). In the following example, the average absorbance (1.142) intersects the dose response curve at (23.6 ng/ml) PSA concentration (See Figure 1).

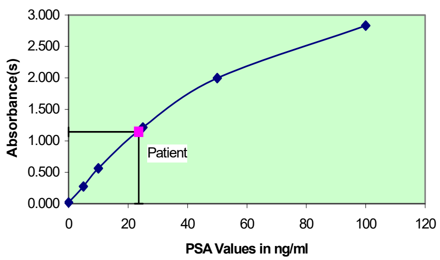
Note: Computer data reduction software designed for ELISA assays may also be used for the data reduction. If such software is utilized, the validation of the software should be ascertained.

EXAMPLE 1

Sample I.D.	Well Number	Abs (A)	Mean Abs (B)	Value (ng/ml)
Cal A	A1	0.019	0.019	0
	B1	0.019		
Cal B	C1	0.279	0.276	5
	D1	0.273		
Cal C	E1	0.567	0.563	10
	F1	0.559		
Cal D	G1	1.248	1.213	25
	H1	1.179		
Cal E	A2	2.051	1.999	50
	B2	1.947		
Cal F	C2	2.892	2.833	100
	D2	2.775		
Patient	E3	1.186	1.142	**23.6**
	F3	1.099		

*The data presented in Example 1 and Figure 1 is for illustration only and **should not** be used in lieu of a dose response curve prepared with each assay.

Figure 1



11.0 Q.C. PARAMETERS

In order for the assay results to be considered valid the following criteria should be met:

1. The absorbance (OD) of calibrator F should be $\geq$ 1.3.
2. Four out of six quality control pools should be within the established ranges.

12.0 RISK ANALYSIS

The MSDS and Risk Analysis Form for this product is available on request from Monobind Inc.

12.1 Assay Performance

1. It is important that the time of reaction in each well is held constant to achieve reproducible results.
2. Pipetting of samples should not extend beyond ten (10) minutes to avoid assay drift.
3. Highly lipemic, hemolyzed or grossly contaminated specimen(s) should not be used.
4. If more than one (1) plate is used, it is recommended to repeat the dose response curve.
5. The addition of substrate solution initiates a kinetic reaction, which is terminated by the addition of the stop solution. Therefore, the substrate and stop solution should be added in the same sequence to eliminate any time-deviation during reaction.
6. Plate readers measure vertically. Do not touch the bottom of the wells.
7. Failure to remove adhering solution adequately in the aspiration or decantation wash step(s) may result in poor replication and spurious results.
8. Use components from the same lot. No intermixing of reagents from different batches.
9. Patient specimens with PSA concentrations above 100 ng/ml may be diluted (for example 1/10 or higher) with normal female serum (PSA = 0 ng/ml) and re-assayed. The sample's concentration is obtained by multiplying the result by the dilution factor (10).
10. Accurate and precise pipetting, as well as following the exact time and temperature requirements prescribed are essential. Any deviation from Monobind's IFU may yield inaccurate results.
11. All applicable national standards, regulations and laws, including, but not limited to, good laboratory procedures, must be strictly followed to ensure compliance and proper device usage.
12. It is important to calibrate all the equipment e.g. Pipettes, Readers, Washers and/or the automated instruments used with this device, and to perform routine preventative maintenance.
13. Risk Analysis- as required by CE Mark IVD Directive ISO 14971:2009 - for this and other devices, made by Monobind, can be requested via email from Monobind@monobind.com.

12.2 Interpretation

1. ***Measurements and interpretation of results must be performed by a skilled individual or trained professional.***
2. Laboratory results alone are only one aspect for determining patient care and should not be the sole basis for therapy, particularly if the results conflict with other determinants.
3. For valid test results, adequate controls and other parameters must be within the listed ranges and assay requirements.
4. If test kits are altered, such as by mixing parts of different kits, which could produce false test results, or if results are incorrectly interpreted, Monobind shall have no liability.
5. If computer controlled data reduction is used to interpret the results of the test, it is imperative that the predicted values for the calibrators fall within 10% of the assigned concentrations.
6. PSA is elevated in benign prostrate hypertrophy (BPH). Clinically an elevated **PSA value alone is not of diagnostic value as a specific test for cance**r and should only be used in conjunction with other clinical manifestations (observations) and diagnostic procedures (prostate biopsy). Free PSA determinations may be helpful in regard to the discrimination of BPH and prostrate cancer conditions (5).

13.0 EXPECTED RANGES OF VALUES

Healthy males are expected to have values below 4 ng/ml (4).

TABLE I
Expected Values for the PSA Elisa Test System

Healthy Males	<4 ng/ml

It is important to keep in mind that establishment of a range of values which can be expected to be found by a given method for a population of "normal"-persons is dependent upon a multiplicity of factors: the specificity of the method, the population tested and the precision of the method in the hands of the analyst. For these reasons each laboratory should depend upon the range of expected values established by the Manufacturer only until an in-house range can be determined by the analysts using the method with a population indigenous to the area in which the laboratory is located.

14.0 PERFORMANCE CHARACTERISTICS

14.1 Precision

The within and between assay precisions of the tPSA AccuBind™ ELISA test system were determined by analyses on three different levels of control sera. The number, mean value, standard deviation and coefficient of variation for each of these control sera are presented in Table 2 and Table 3.

TABLE 2
Within Assay Precision (Values in ng/ml)

Sample	N	X	S.D.	C.V.
Level 1	20	0.7	0.05	7.1%
Level 2	20	4.5	0.20	4.4%
Level 3	20	28.3	1.07	3.7%

TABLE 3
Between Assay Precision* (Values in ng/ml)

Sample	N	X	S.D.	C.V.
Level 1	10	0.8	0.09	11.3%
Level 2	10	4.3	0.25	5.8%
Level 3	10	27.5	1.42	5.2%

*As measured in ten experiments in duplicate.

14.2 Sensitivity

The tPSA AccuBind™ ELISA test system has a sensitivity of 0.012 ng. This is equivalent to a sample containing 0.5 ng/ml tPSA concentration.

14.3 Accuracy

The tPSA AccuBind™ ELISA method was compared with a reference Elisa method. Biological specimens from low, normal, and elevated concentrations were assayed. The total number of such specimens was 241. The least square regression equation and the correlation coefficient were computed for the tPSA AccuBind™ ELISA test method in comparison with the reference method. The data obtained is displayed in Table 4.

TABLE 4

Method	Mean	Least Square Regression Analysis	Correlation Coefficient
This Method (X)	5.62	y = -0.0598+0.98(X)	0.987
Reference (Y)	5.57		

Only slight amounts of bias between the tPSA AccuBind™ ELISA method and the reference method are indicated by the closeness of the mean values. The least square regression equation and correlation coefficient indicates excellent method agreement.

14.4 Specificity:

No interference was detected with the performance of tPSA AccuBind™ ELISA test system upon addition of massive amounts of the following substances to a human serum pool.

Acetylsalicylic Acid	100 µg/ml
Ascorbic Acid	100 µg/ml
Caffeine	100 µg/ml
CEA	10 µg/ml
AFP	10 µg/ml
CA-125	10,000 U/ml
hCG	1000 IU/ml
hLH	10 IU/ml
hTSH	100 mIU/ml
hPRL	100 µg/ml

15.0 REFERENCES

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2. Watt KW, et al., *Proc Nat Acad Sci USA*, **83,** 3166-70 (1986).
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9. Horton GL, Bahnson RR, Datt M, Cfhan KM, Catalona WJ and Landenson JH, "Differences in values obtained with two assays of Prostate Specific Antigen", *J Urol*, **139,** 762-72 (1988).
10. Stenman UH, Leinonen J, Alfthan H, Rannikko S, Tuhkanen K and Alfthan O,"*A* complex between prostate specific antigen and α1-anticymotrypsin is the major form of prostate specific antigen in serum of patients with prostate cancer:assay of complex improves clinical sensitivity for cancer", *Cancer Res*, **51,** 222-26 (1991).

Revision: 3 Date: 081511 DCO: 0524

Cat #: *2125-300*

	Size	96(A)	192(B)
Reagent (fill)	A)	1ml set	1ml set
	B)	1 (13ml)	2 (13ml)
	C)	1 plate	2 plates
	D)	1 (20ml)	1 (20ml)
	E)	1 (7ml)	2 (7ml)
	F)	1 (7ml)	2 (7ml)
	G)	1 (8ml)	2 (8ml)

For Orders and Inquiries, please contact

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Please visit our website to learn more about our other interesting products and services.

IVD CE 0050 2° 8°

EC REP **CEpartner4U**, 3951 DB; 13.NL
Tel: +31 (0) 6-516.536.26

Quality System Approval Certificate
In Vitro Diagnostic Medical Devices Directive 98/79/EC

*The National Standards Authority of Ireland as a duly designated Notified Body, (identification number **0050**), for the purposes of the European Communities (In Vitro Diagnostics Medical Devices) Regulations (S.I. No. 304 of 2001)*

APPROVES THE QUALITY SYSTEM APPLIED BY

Monobind Inc.

100 North Pointe Drive
Lake Forest
CA 92630
USA

For the Product Family

Total and Free Prostate Specific Antigen (PSA and Free PSA) IVD, kit, chemiluminescent immunoassay (CLIA) and enzyme immunoassay (ELISA) and control

GMDN Code: 54664, 54669

On the basis of examination under the requirements of Annex IV, Section 3 of Directive 98/79/EC,
The use of the NSAI Notified Body identification number **0050** in conjunction with CE Marking of Conformance for this product is hereby authorized.

Registration Number:	**304.1006**
Original Registration:	**28 October 2011**
Last Amended on:	**10 July 2018**
Remains valid until:	**27 October 2022**

Signed:

Approved by:
Geraldine Larkin
Chief Executive Officer, NSAI

Approved by:
Susan Murphy
European Medical Device Operations Manager

This certificate remains valid on condition that the Approved Quality System is maintained in an adequate and efficacious manner.
Details of the current product range and operational locations included within the scope of this approval can be obtained from NSAI

National Standards Authority of Ireland, 1 Swift Square, Northwood, Santry, Dublin 9, Ireland.

CERTIFICATE

EC No 1434-IVDD-134/2019

Full Quality Assurance System

Directive 98/79/EC on in vitro diagnostic medical devices

Polish Centre for Testing and Certification certifies
that the quality assurance system in the organization:

Lorne Laboratories Ltd

Unit 1 Cutbush Park Industrial Estate, Danehill, Lower Earley, Berkshire RG6 4UT, United Kingdom

for the design, manufacture and final inspection of in vitro diagnostic medical devices
List A

Products list in attachments: 1

complies with requirements of Annex IV excluding section 4 and 6 to Directive 98/79/EC (as amended)
implemented into Polish law, as evidenced by the audit conducted by the PCBC.

Validity of Certificate: from 10.04.2019 to 23.05.2023

The date of issue of the Certificate: 10.04.2019

The date of the first issue of the Certificate: 10.04.2019

CE 1434

Application No: 649/2019
Module: H7

mgr Anna Wyroba
Vice-President

Certificate No **1434-IVDD-134/2019**
Issued under the Contract No MD-59/2019
Bears the PCBC hologram.
Warsaw, 10.04.2019

ANNEX 1 TO CERTIFICATE
VALID ONLY WITH CERTIFICATE
No 1434-IVDD-134/2019

The products detailed below are covered under the scope of this certificate:

Name:	GMDN code:
Anti-A Monoclonal, 600010	52532
Anti-B Monoclonal, 610010	52538
Anti-A,B Monoclonal, 620010	46442
Anti-D Clone 1 Monoclonal, 730010	52647
Anti-D Clone 2 Monoclonal, 710010	52647
Anti-D Duoclone Monoclonal, 740010	52647
Anti-C Monoclonal, 690005	52546
Anti-E Monoclonal, 691005	52562
Anti-c Monoclonal, 692005	52547
Anti-e Monoclonal, 693005	52563
Anti-C+D+E Monoclonal, 700010	52550
Anti-K Monoclonal, 760010	52593

CE 1434

mgr Anna Wyroba
Vice-President

Annex 1 to certificate No. **1434-IVDD-134/2019**
Issued under the Contract No. MD-59/2019
Bears the PCBC hologram.
Warsaw, 10.04.2019

LORNE LABORATORIES

EC DECLARATION OF CONFORMITY

Lorne Laboratories Ltd declares that the following in vitro diagnostic reagent:

Product name	Catalogue number
ASO Latex kit	031100A

has been classified as non List A, non List B (Directive 98/79/EC, Annex II) and complies with the essential requirements and provisions of Directive 98/79/EC of the European Parliament and of the Council (also SI 2002 No.618 which transposes the requirements of Directive 98/79/EC).

and is in conformity with the national standards transposing harmonised standards:

- BS EN 980:2008
- BS EN ISO 13485:2012
- BS EN 13612:2002
- BS EN 13640:2002
- BS EN 13641:2002
- BS EN ISO 14971:2012
- BS EN ISO 18113, parts 1&2

The conformity assessment procedure performed was in accordance with Annex III of Directive 98/79/EC.

This declaration of conformity is issued under the sole responsibility of Lorne Laboratories Ltd and is valid from 13 April 2016.

Eddy Velthuis
Technical Director

LORNE
LABORATORIES

EC DECLARATION OF CONFORMITY

Lorne Laboratories Ltd declares that the following in vitro diagnostic reagent:

Product name	Catalogue number
RF Latex kit	830100A

has been classified as non List A, non List B (Directive 98/79/EC, Annex II) and complies with the essential requirements and provisions of Directive 98/79/EC of the European Parliament and of the Council (also SI 2002 No.618 which transposes the requirements of Directive 98/79/EC).

and is in conformity with the national standards transposing harmonised standards:

- BS EN 980:2008
- BS EN ISO 13485:2012
- BS EN 13612:2002
- BS EN 13640:2002
- BS EN 13641:2002
- BS EN ISO 14971:2012
- BS EN ISO 18113, parts 1&2

The conformity assessment procedure performed was in accordance with Annex III of Directive 98/79/EC.

This declaration of conformity is issued under the sole responsibility of Lorne Laboratories Ltd and is valid from 13 April 2016.

Eddy Velthuis
Technical Director

EC DECLARATION OF CONFORMITY

Lorne Laboratories Ltd declares that the following in vitro diagnostic reagent:

Product name	Catalogue number
CRP Latex kit	850100A

has been classified as non List A, non List B (Directive 98/79/EC, Annex II) and complies with the essential requirements and provisions of Directive 98/79/EC of the European Parliament and of the Council (also SI 2002 No.618 which transposes the requirements of Directive 98/79/EC).

and is in conformity with the national standards transposing harmonised standards:

- BS EN 980:2008
- BS EN ISO 13485:2012
- BS EN 13612:2002
- BS EN 13640:2002
- BS EN 13641:2002
- BS EN ISO 14971:2012
- BS EN ISO 18113, parts 1&2

The conformity assessment procedure performed was in accordance with Annex III of Directive 98/79/EC.

This declaration of conformity is issued under the sole responsibility of Lorne Laboratories Ltd and is valid from 13 April 2016.

Eddy Velthuis
Technical Director

LORNE LABORATORIES LTD.
GREAT BRITAIN

RAPID LATEX KIT
DIRECTIONS FOR USE

ASO Latex Kit: For Detection Of Anti-Streptolysin O (ASO) In Serum

SUMMARY

In acute streptococcal infections, the toxic immunogenic exoenzyme streptolysin O (ASO) is produced in response to streptolysin O antigens liberated by haemolytic streptococci of groups A, C and G. Information on extent and degree of infection can be obtained by measuring serum ASO levels. Elevated ASO levels have also been found in patients suffering from scarlet fever, acute rheumatoid arthritis, tonsillitis, and other streptococcal infections as well as in healthy carriers.

INTENDED PURPOSE

The reagent is a latex test reagent intended to be used to qualitatively and semi-quantitatively determine the presence or absence of Anti-Streptolysin O antibodies in the serum or plasma of patients when tested in accordance with the recommended techniques stated in this IFU.

PRINCIPLE

When used by the recommended techniques, latex particles in the reagent will agglutinate (clump) in the presence of anti-streptolysin O antibodies. No agglutination generally indicates the absence of anti-streptolysin O antibodies (see **Limitations**).

KIT DESCRIPTION

Lorne ASO Latex Kit is a serologic test for the detection of ASO antibodies. The reagents do not contain or consist of CMR substances, or endocrine disrupting substances or that could result in sensitisation or an allergic reaction by the user. All the reagents are supplied at optimal dilution for use with all recommended techniques without the need for further dilution or addition. For lot reference number and expiry date see **Vial Labels**.

STORAGE

Do not freeze. Reagent vials should be stored at 2 - 8ºC on receipt. Prolonged storage at temperatures outside this range may result in accelerated loss of reagent reactivity.

SPECIMEN COLLECTION

Specimens should be drawn with or without anticoagulant using an aseptic phlebotomy technique. If testing is delayed specimens can be stored at 2-8ºC for 7 days or for up to 3 months at or below –20ºC. Specimens must be free from bacterial contamination, fibrin, gross lipemia and gross haemolysis.

PRECAUTIONS

1. The kit is for *in vitro* diagnostic use only.
2. Do not use kit past expiration date (see **Vial and Box Labels**).
3. Protective clothing should be worn when handling the reagents, such as disposable gloves and a laboratory coat.
4. The reagents in this kit have been processed to reduce the bio-burden, but are not supplied sterile. Once a vial has been opened the contents should remain viable up until the expiry date.
5. Materials used to produce the kit were tested at source and found to be negative for HIV 1+2 and HBsAg using approved microbiological tests. However no known tests can guarantee that products derived from human or animal sources are free from infectious agents. Care must be taken in the use and disposal of each vial and its contents.

DISPOSAL OF KIT REAGENT AND DEALING WITH SPILLAGES

For information on disposal of kit reagent and decontamination of a spillage site see **Material Safety Data Sheets**, available on request.

CONTROLS AND ADVICE

1. ASO Positive and Negative Controls must be tested in parallel with each batch of tests. Tests must be considered invalid if controls do not show expected results.
2. All the reagents must be allowed to reach 18-25ºC before use.
3. Shake the reagents well before use to ensure homogeneity.
4. Do not interchange components between different kits.
5. Use of kit and interpretation of results must be carried out by properly trained and qualified personnel in accordance with the requirements of the country where the kit is in use.
6. The user must determine the suitability of the kit for use in other techniques.

KIT COMPONENTS SUPPLIED

1) ASO Latex Reagent (White cap, 5.0 mL): Latex particles coated with streptolysin O, pH, 8.2 containing a preservative.
2) ASO Positive Control (Red cap, 1.0 mL Red cap): Human serum with an ASO concentration > 200 IU/mL containing a preservative.
3) ASO Negative Control (Blue cap, 1.0 mL): Animal serum containing a preservative.
4) Pipette-Stirrers.
5) Disposable agglutination Slides.

REAGENTS AND MATERIALS REQUIRED BUT NOT SUPPLIED

a) Small glass / plastic test tubes.
b) Serological pipettes.
c) Graduated container.
d) 9 g/L saline solution.

RECOMMENDED QUALITATIVE TECHNIQUE

1. Allow the reagents and samples to reach room temperature. The sensitivity of the test may be reduced at low temperatures.
2. Place 50 µL of the sample and one drop of each Positive and Negative controls into separate circles on the slide test.
3. Swirl the ASO-latex reagent gently before using and add one drop (50 µL) next to the sample to be tested.
4. Mix the drops with a stirrer, spreading them over the entire surface of the circle. Use different stirrers for each sample.
5. Swirl the slide gently and after 2 minutes read the results macroscopically. False positive results could appear if the test is read after more than two minutes.

INTERPRETATION OF QUALITATIVE RESULTS

1. **Positive:** Agglutination of latex particles constitutes a positive result and within the accepted limitations of the test procedure, indicates a level of ASO in the specimen > 200 I.U/ml.
2. **Negative:** No visible agglutination of latex particles constitutes a negative result and within the accepted limitations of the test procedure, indicates a level of ASO in specimen < 200 I.U/ml.

RECOMMEDED SEMI-QUANTITATIVE TECHNIQUE

1. The semi-quantitative test can be performed in the same way as the quantitative technique using dilutions of the serum in 9 g/L saline solution.
2. Make doubling dilutions of specimen as follows:

Dilution	Serum	Saline
1/2	100 µl undiluted serum	100 µl
1/4	100 µl 1/2 diluted serum	100 µl
1/8	100 µl 1/4 diluted serum	100 µl

3. Test the specimen dilutions in the same way as for the quantitative technique above.
4. Agglutination of the sera indicates:

Dilution	ASO Levels (I.U. / ml)
1/2	400 (200 x 2)
1/4	800 (200 x 4)
1/8	1600 (200 x 8)

5. Normal levels of ASO in adults is < 200 I.U/ml.

RESULTS

The titre is expressed as the reciprocal of the highest dilution showing macroscopic agglutination, e.g. if this occurs in the 1/8 dilution, the titre is 1600.

INTERPRETATION OF SEMI-QUANITATIVE RESULTS

Positive results may indicate an acute streptococcal infection. In which case the test should be repeated at weekly intervals to determine the progression of infection.

STABILITY OF THE REACTIONS

Slide tests should be interpreted immediately after the 2-minute period to avoid the possibility that a negative result may be incorrectly interpreted as positive due to drying of the reagent.

LIMITATIONS

1. False positive results may be obtained in conditions such as scarlet fever, acute rheumatoid arthritis, tonsillitis and other streptococcal infections as well as in healthy carriers.
2. Hemoglobin (≤ 10 g/L), bilirubin (≤ 20 mg/dL), lipemia (≤ 10 g/L), rheumatoid factors (≤ 300 IU/mL) do not interfere. Other substances may interfere[7].
3. Early infections in children from 6 months to 5 years may cause false negative results.
4. A single ASO determination does not produce much information about the actual state of the disease. Titrations at biweekly intervals during 4 or 6 weeks are advisable to follow the disease evolution.
5. Clinical diagnosis should not be made on findings of a single test result, but should integrate both clinical and laboratory data.
6. False positive or false negative results may also occur due to:
   a) Contamination of test materials
   b) Improper storage of test materials or omission of reagents
   c) Deviation from the recommended techniques

SPECIFIC PERFORMANCE CHARACTERISTICS

1. The kit has been characterised by all the procedures mentioned in the **Recommended Techniques**.
2. Prior to release, each lot of Lorne ASO Latex Kit is tested by **Recommended Techniques** to ensure suitable reactivity.
3. The ASO-latex sensitivity is calibrated against the WHO 1st International Standard for ASO available from NIBSC.
4. Analytical sensitivity: 200 (± 50) IU/mL, under the described assay conditions.
5. Prozone effect: No prozone effect was detected up to 1500 IU/mL.
6. Diagnostic sensitivity: 98 %.
7. Diagnostic specificity: 97 %.

DISCLAIMER

1. The user is responsible for the performance of the kit by any method other than those mentioned in the **Recommended Techniques**.
2. Any deviations should be validated prior to use using established laboratory procedures.

BIBLIOGRAPHY

1. David S.Jacobs et al. Laboratory Test Handbook, 3rd edition, Lexi-Comp Inc, 1994.

AVAILABLE KIT SIZES

Kit Size	Catalogue Number
100 Tests Per Kit	031100A

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LORNE LABORATORIES LTD.
GREAT BRITAIN

RAPID LATEX KIT
DIRECTIONS FOR USE

RF Latex kit: For Detection Of Rheumatoid Factor (RF).

SUMMARY

Rheumatoid factors are a group of antibodies directed to determinants in the Fc portion of the IgG molecule. Although rheumatoid factors are found in a number of rheumatoid disorders, such as systemic lupus erythematosis (sLE) and Sjögren's syndrome, as well as in non-rheumatoid conditions, it's central role lies in aiding in the diagnosis of rheumatoid arthritis.

INTENDED PURPOSE

The reagent is a latex test reagent intended to be used to qualitatively and semi-quantitatively determine the presence or absence of Rheumatoid Factors in the serum or plasma of patients when tested in accordance with the recommended techniques stated in this IFU.

PRINCIPLE

When used by recommended techniques, latex particles in the reagent will agglutinate (clump) in presence of rheumatoid factor (RF). No agglutination (no clumping) generally indicates absence of RF (see **Limitations**).

KIT DESCRIPTION

Lorne RF Latex Kit is for the detection of rheumatoid factor. The latex reagent is a suspension of polystyrene latex particles coated with human gamma globulins, which agglutinate in the presence of Rheumatoid Factor (RF). The reagents do not contain or consist of CMR substances, or endocrine disrupting substances or that could result in sensitisation or an allergic reaction by the user. All latex reagents are supplied at optimal dilution for use with all recommended techniques without the need for further dilution or addition. For lot reference number and expiry date see **Vial Labels**.

STORAGE

Do not freeze. Reagent vials should be stored at 2 - 8ºC on receipt. Prolonged storage at temperatures outside this range may result in accelerated loss of reagent reactivity.

SPECIMEN COLLECTION

Specimens should be drawn without anticoagulant using an aseptic phlebotomy technique. If testing is delayed, fresh serum can be stored at 2-8ºC for 7 days or for up to 3 months at or below
–20ºC. Specimens must be free from bacterial contamination, fibrin, gross lipeamia and gross haemolysis.

PRECAUTIONS

1. The kit is for *in vitro* diagnostic use only.
2. Do not use kit past expiration date (see **Vial and Box Labels**).
3. Protective clothing should be worn when handling the reagents, such as disposable gloves and a laboratory coat.
4. All the reagents must be allowed to reach 18-25ºC before use.
5. The reagents in this kit have been processed to reduce the bio-burden, but are not supplied sterile. Once a vial has been opened the contents should remain viable up until the expiry date.
6. Materials used to produce the kit were tested at source and found to be negative for HIV 1+2 and HBsAg using approved microbiological tests. However, no known tests can guarantee that products derived from human or animal sources are free from infectious agents. Care must be taken in the use and disposal of each vial and its contents.

DISPOSAL OF KIT REAGENT AND DEALING WITH SPILLAGES

For information on disposal of kit reagent and decontamination of a spillage site see **Material Safety Data Sheets**, available on request.

CONTROLS AND ADVICE

1. It is recommended that the RF Positive and Negative Controls are tested in parallel with each batch of tests. Tests must be considered invalid if controls do not show expected results.
2. All the reagents must be allowed to reach 18-25ºC before use.
3. Shake the reagents well before use to ensure homogeneity.
4. Do not interchange components between different kits.
5. Use of kit and interpretation of results must be carried out by properly trained and qualified personnel in accordance with the requirements of country where kit is in use. The user must determine the suitability of the kit for use in other techniques.
6. Results obtained with a latex method do not compare with those obtained with the Rose Waaler test. Differences in the results between methods do not reflect differences in the ability to detect rheumatoid factors.

KIT COMPONENTS SUPPLIED

1) RF Latex Reagent (5 mL): Latex particles coated with human γ-globulin, pH, 8.2, and a preservative.
2) RF Positive Control (Red cap, 1 mL): Human serum with a RF concentration > 30 IU/mL and a preservative.
3) RF Negative Control (Blue cap, 1 mL): Animal serum and a preservative.
4) Pipette-Stirrers.
5) Reusable Agglutination Slide (18 each).

MATERIALS AND EQUIPMENT REQUIRED BUT NOT SUPPLIED

1) Glass Test Tubes (10 x 75 mm or 12 x 75 mm).
2) Pasteur and Graduated Pipettes.
3) Vortex mixer.
4) Mechanical rotator with adjustable speed of 80-100 rpm.

RECOMMENDED QUALITATIVE TECHNIQUE

1. Allow the reagents and samples to reach room temperature. The sensitivity of the test may be reduced at low temperatures.
2. Place 50 µL of the sample and one drop of each Positive and Negative controls into separate circles on the slide test.
3. Shake the RF-latex reagent vigorously or use a vortex mixer before use and add one drop (50 µL) next to the sample to be tested.
4. Mix the drops with a stirrer, spreading them over the entire surface of the circle. Use different stirrers for each sample.
5. Place the slide on a rotary shaker at 80-100 r.p.m. for 2 minutes. False positive results could appear if the test is read after more than two minutes.

INTERPRETATION OF QUALITATIVE RESULTS

1. **Positive:** Visible agglutination of latex particles constitutes a positive result and within the accepted limitations of the test procedure, indicates a level of RF in the specimen > 8 IU/ml.
2. **Negative:** No visible agglutination of latex particles in a milky liquid constitutes negative result and within accepted limitations of test procedure, indicates level of < 8 IU/ml RF in specimen.

RECOMMENDED SEMI-QUANTITATIVE TECHNIQUE

1. The semi-quantitative test can be performed in the same way as the qualitative test using dilutions of the serum.
2. Make doubling dilutions of serum specimen in 9 g/L saline as follows:

Dilution	Serum	Saline
1/2	100 µl undiluted serum	100 µl
1/4	100 µl 1/2 diluted serum	100 µl
1/8	100 µl 1/4 diluted serum	100 µl
1/16	100 µl 1/8 diluted serum	100 µl

3. Test the specimen dilutions in the same way as for the quantitative technique above.
4. Agglutination of the sera indicates:

Dilution	RF Levels (I.U/mL)
1/2	16 (8 x 2)
1/4	32 (8 x 4)
1/8	64 (8 x 8)
1/16	128 (8 x 16)

5. Normal levels of RF in adults is < 8 IU/mlL

RESULTS

The titre is expressed as the reciprocal of the highest dilution showing macroscopic agglutination: e.g. if this occurs in dilution 1/8, the titre is (8 x 8 IU/mL) = 64 IU/mL.

STABILITY OF THE REACTIONS

Slide tests should be interpreted straight after the 2-minute rotation period to avoid the possibility that a negative result may be incorrectly interpreted as positive due to drying of the reagent.

LIMITATIONS

1. Using a latex test system, positive results are not always found with every case of clinically defined rheumatoid arthritis, the number of positives reported using various types of latex reagent range from 70% to over 90%.
2. The incidence of false positive results is about 3-5 %. Individuals suffering from infectious mononucleosis, hepatitis, syphilis as well as elderly people may give positive results.
3. Diagnosis should not be solely based on the results of latex method but also should be complemented with a Rose Waaler test along with the clinical examination.
4. Haemoglobin (≤ 10 g/L), bilirubin (≤ 20 mg/dL) and lipaemia (≤ 10 g/L) do not interfere. Other substances may interfere[6].
5. False positive or false negative results may also occur due to:
   a) Contamination of test materials
   b) Improper storage of test materials or omission of reagents
   c) Deviation from the recommended techniques

SPECIFIC PERFORMANCE CHARACTERISTICS

1. The kit has been characterised by all the procedures mentioned in the **Recommended Techniques**.
2. The RF latex sensitivity is calibrated against the RF International Calibrator from the WHO (WHO 64/2 Rheumatoid Arthritis Serum).
3. Analytical sensitivity: 8 (6-16) IU/mL, under the described assay conditions.
4. Prozone effect: No prozone effect was detected up to 1500 IU/mL.
5. Diagnostic sensitivity: 100 %.
6. Diagnostic specificity: 100 %.
   The diagnostic sensitivity and specificity have been obtained using 139 samples compared with the same method of a competitor.

DISCLAIMER

1. The user is responsible for the performance of the kit by any method other than those mentioned in the **Recommended Techniques**.
2. Any deviations should be validated prior to use using established laboratory procedures.

BIBLIOGRAPHY

1. David S.Jacobs et al. Laboratory Test Handbook, 3rd edition, Lexi-Comp Inc, 1994.

AVAILABLE KIT SIZES

Kit Size	Catalogue Number
100 Tests Per Kit	830100A

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LORNE LABORATORIES LTD.
GREAT BRITAIN

RAPID LATEX KIT
DIRECTIONS FOR USE

CRP Latex Kit: For Detection Of C-Reactive Protein (CRP) In Serum.

SUMMARY

C-Reactive Protein (CRP) usually appears in serum of individuals in response to inflammatory conditions and tissue necrosis and disappears when causative conditions subside. It is routinely found in cases of bacterial infection, active rheumatic fever and many malignant diseases and is often seen in association with rheumatoid arthritis, viral infections and tuberculosis. CRP has also been detected in patients following blood transfusions and surgical operations as well as in patients with burns, pemphigus vulgaris and other bullous lesions.

INTENDED PURPOSE

The reagent is a latex test reagent intended to be used to qualitatively and semi-quantitatively determine the presence or absence of CRP in the serum or plasma of patients when tested in accordance with the recommended techniques stated in this IFU.

PRINCIPLE

When used by the recommended techniques, latex particles in the reagent will agglutinate (clump) in the presence of CRP. No agglutination (no clumping) generally indicates absence of CRP (see **Limitations**).

KIT DESCRIPTION

Lorne CRP Latex Test Kit is for the detection of CRP. Test reagent consists of latex particles coated with rabbit Anti-CRP (IgG). The reagents do not contain or consist of CMR substances, or endocrine disrupting substances or that could result in sensitisation or an allergic reaction by the user. All the latex reagents are supplied at optimal dilution for use with all recommended techniques without need for further dilution or addition. For lot reference number and expiry date see **Vial Labels**.

STORAGE

Do not freeze. Reagent vials should be stored at 2 - 8ºC on receipt. Prolonged storage at temperatures outside this range may result in accelerated loss of reagent reactivity.

SPECIMEN COLLECTION

Specimens should be drawn with or without anticoagulant using an aseptic phlebotomy technique. If testing is delayed specimens can be stored at 2-8ºC for 7 days or for up to 3 months at or below –20ºC. Specimens must be free from bacterial contamination, fibrin, gross lipaemia and gross haemolysis.

PRECAUTIONS

1. The kit is for *in vitro* diagnostic use only.
2. Do not use kit past expiration date (see **Vial and Box Label**).
3. Protective clothing should be worn when handling the reagents, such as disposable gloves and a laboratory coat.
4. The reagents in this kit have been processed to reduce the bio-burden, but are not supplied sterile. Once a vial has been opened the contents should remain viable up until the expiry date.
5. Materials used to produce the kit were tested at source and found to be negative for HIV 1+2 and HBsAg using approved microbiological tests. However, no known tests can guarantee that products derived from human or animal sources are free from infectious agents. Care must be taken in the use and disposal of each vial and its contents.

DISPOSAL OF KIT REAGENT AND DEALING WITH SPILLAGES

For information on disposal of kit reagent and decontamination of a spillage site see **Material Safety Data Sheets**, available on request.

CONTROLS AND ADVICE

1. It is recommended that the CRP Positive and Negative Controls are tested in parallel with each batch of tests. Tests must be considered invalid if controls do not show expected results.
2. All the reagents must be allowed to reach 18-25ºC before use.
3. Shake the reagents well before use to ensure homogeneity.
4. Do not interchange components between different kits.
5. Use of kit and interpretation of results must be carried out by properly trained and qualified personnel in accordance with the requirements of country where kit is in use. The user must determine the suitability of the kit for use in other techniques.

KIT COMPONENTS SUPPLIED

1. CRP Latex Reagent (White cap, 5 mL): Latex particles coated with goat IgG anti-human CRP, pH, 8.2, containing a preservative.
2. CRP Positive Control (Red cap, 1 mL): Human serum with a CRP concentration > 20 mg/L containing a preservative.
3. CRP Negative Control (Blue cap, 1 mL): Animal serum containing a preservative.
4. Pipette stirrers.
5. Disposable agglutination slide.

MATERIALS AND EQUIPMENT REQUIRED BUT NOT SUPPLIED

1. Serological Pipettes.
2. Mechanical rotator capable with adjustable speed of 80-100 rpm.
3. Vortex mixer.
4. Small Glass or Plastic Test Tubes.
5. Distilled or Deionised Water.
6. 9 g/L saline solution.

RECOMMENDED QUALITATIVE TECHNIQUE

1. Allow the reagents and samples to reach room temperature. The sensitivity of the test may be reduced at low temperatures.
2. Place 50 µL of the sample (Note 1) and one drop of each Positive and Negative controls into separate circles on the slide test.
3. Swirl the CRP Latex Reagent thoroughly but gently before use and add one drop (50 µL) next to the samples to be tested.
4. Mix the drops with a stirrer, spreading them over the entire surface of the circle. Use different stirrers for each sample.
5. Place the slide on a rotary shaker at 80-100 r.p.m. for 2 minutes. False positive results could appear if the test is read after more than two minutes.

INTERPRETATION OF QUALITATIVE RESULTS

1. **Positive:** Visible agglutination of latex particles constitutes a positive result and within the accepted limitations of the test procedure, indicates a level of CRP in the specimen > 6 mg/l.
2. **Negative:** No visible agglutination of latex particles constitutes a negative result and within the accepted limitations of the test procedure, indicates a level of CRP in the specimen < 6 mg/l.

RECOMMENDED SEMI-QUANTITATIVE TECHNIQUE

1. The semi-quantitative test can be performed in the same way as the qualitative test using dilutions of the serum.
2. Make doubling dilutions of the specimen using 9 g/L saline solution as follows:

Dilution	Serum	Saline
1/2	100 µl undiluted serum	100 µl
1/4	100 µl 1/2 diluted serum	100 µl
1/8	100 µl 1/4 diluted serum	100 µl
1/16	100 µl 1/8 diluted serum	100 µl

3. Test the specimen dilutions in the same way as for the quantitative technique above.
4. Agglutination of the sera indicates:

Dilution	CRP Levels (mg / l)
1/2	12 (6 x 2)
1/4	24 (6 x 4)
1/8	48 (6 x 8)
1/16	96 (6 x 16)

5. Normal levels of CRP in adults are < 6 mg/l.

NOTES

1. High CRP concentration samples may give false negative results (pro-zone effect). Re-test the sample again using a drop of 20 µl.

RESULTS

The titre is expressed as the reciprocal of the highest dilution showing macroscopic agglutination: e.g. if this occurs in dilution 1/8, the titre is 48.

INTERPRETATION OF SEMI-QUANTITATIVE RESULTS

The elevation of CRP levels above normal indicates tissue damage, inflammation, or both with greater reliability. Regular monitoring of CRP levels is often used as a means of assessing disease activity and of guiding therapy. CRP determination is considered of greater practical significance than other indicators of inflammatory disease. Erythrocyte sedimentation rate (ESR) may become elevated as a result of non-inflammatory conditions. In these circumstances inflammatory disease may be excluded if CRP is absent.

STABILITY OF THE REACTIONS

Slide tests should be interpreted immediately after the 2-minute rotation period to avoid the possibility that a negative result may be incorrectly interpreted as positive due to drying of the reagent.

LIMITATIONS

1. Reactions read beyond the two-minute interval may be invalid.
2. The results obtained from this assay must be considered a part of the differential diagnosis and medical history of the patient.
3. There is no relationship between the strength of reactivity and C-reactive protein levels.
4. Hemoglobin (≤ 10 g/L), bilirubin (≤ 20 mg/dL) and lipemia (≤ 10 g/L), do not interfere. Rheumatoid factors (≥ 100 IU/mL), interfere. Other substances may interfere[7].
5. False positive or false negative results may also occur due to:
   a) Contamination of test materials
   b) Improper storage of test materials or omission of reagents
   c) Deviation from the recommended techniques

SPECIFIC PERFORMANCE CHARACTERISTICS

1. The kit has been characterised by all the procedures mentioned in the **Recommended Techniques**.
2. Prior to release, each lot of Lorne CRP Latex Test Kit is tested by **Recommended Techniques** to ensure suitable reactivity.
3. The CRP-latex sensitivity is calibrated to the Reference Material ERM-DA 474/IFCC.
4. **Analytical sensitivity:** 6 (5-10) mg/L, under the described assay conditions.
5. **Prozone effect:** No prozone effect was detected up to 1600 mg/L (Note 1).
6. **Diagnostic sensitivity:** 95.6 %.
7. **Diagnostic specificity:** 96.2 %.

DISCLAIMER

1. The user is responsible for the performance of the kit by any method other than those mentioned in the **Recommended Techniques**.
2. Any deviations should be validated prior to use using established laboratory procedures.

BIBLIOGRAPHY

1. David S.Jacobs et al. Laboratory Test Handbook, 3rd edition, Lexi-Comp Inc, 1994.

AVAILABLE KIT SIZES

Kit Size	Catalogue Number
100 Tests Per Kit	850100A

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EC REP Advena Ltd. Tower Business Centre, 2nd Flr., Tower Street, Swatar, BKR 4013, Malta

CERTIFICATO N° 505DM07

CERTIFICATE N° 505DM07

Si certifica che il

this is to certify that

Sistema di Gestione per la Qualità

Quality Management System

messo in atto da

implemented by

APTACA S.p.A.

Via Monte Bianco, 4 – IT 20900 MONZA (MB)

nella Sede Operativa di

Operative Unit

Regione Monforte, 30 – IT 14053 CANELLI (AT)

è conforme alla norma

is in compliance with the standard

UNI CEI EN ISO 13485-2016 (ISO 13485-2016)

per i seguenti Processi

concerning the following kinds of Processes

Gestione della fabbricazione e immissione in commercio di tamponi sterili per il prelievo di campioni biologici in orifizi naturali e in ambito chirurgico. Progettazione e fabbricazione di dispositivi medico diagnostici per laboratori di analisi. Gestione della fabbricazione ed immissione in commercio di dispositivi medici invasivi in relazione agli orifizi del corpo in Classe I Sterile. Fabbricazione di dispositivi medici invasivi in relazione agli orifizi del corpo in Classe I Sterile. Commercializzazione di dispositivi medici e diagnostici in vitro.

Management of the manufacturing and placing on the market of sterile tampons for sampling of biological specimens in natural orifice and in surgical field. Design and manufacturing of diagnostic medical devices for laboratories of analysis. Management of the manufacturing and placing on the market of invasive medical devices with respect to body orifices (class I sterile). Manufacturing of invasive medical devices with respect to body orifices (class I sterile). Marketing of medical and diagnostic devices in vitro.

Il presente Certificato è soggetto al rispetto delle condizioni stabilite dai Regolamenti per la certificazione in vigore applicabili.

This Certificate shall satisfy the requirements established in the Rules for the certification in force applicable.

In caso di discordanza tra le lingue utilizzate nella traduzione del contenuto del presente certificato, fare riferimento alla lingua italiana

In cases of discrepancy between the languages used in the translation of the content of this certificate, please refer to the Italian language

L'AMMINISTRATORE DELEGATO

MANAGING DIRECTOR

Dr. Ing. Roberto Cusolito

Data di Prima Emissione *First Issue Date*	Data di Prima Emissione ITALCERT *First Issue Date ITALCERT*	Data di Rinnovo *Renewal Date*	Data di Scadenza *Expiration Date*
2007-10-30	2011-10-30	2020-10-30	2023-10-29

ACCREDIA
L'ENTE ITALIANO DI ACCREDITAMENTO

SGQ N° 023A

Membro degli Accordi di Mutuo Riconoscimento EA, IAF e ILAC

Signatory of EA, IAF and ILAC Mutual Recognition Agreements

CERTIFICATO N° 505SGQ05

CERTIFICATE N° 505SGQ05

Si certifica che il

this is to certify that

Sistema di Gestione per la Qualità

Quality Management System

messo in atto da

implemented by

APTACA S.p.A.

Via Monte Bianco, 4 – IT 20900 MONZA (MB)

nella Sede Operativa di

Operative Unit

Regione Monforte, 30 – IT 14053 CANELLI (AT)

è conforme alla norma

is in compliance with the standard

UNI EN ISO 9001-2015 (ISO 9001-2015)

per i seguenti Processi

concerning the following kinds of Processes

Gestione della fabbricazione ed immissione in commercio di tamponi sterili per il prelievo di campioni biologici in orifizi naturali e in ambito chirurgico. Progettazione e fabbricazione di dispositivi medico diagnostici per laboratori di analisi. Gestione della fabbricazione ed immissione in commercio di dispositivi medici invasivi in relazione agli orifizi del corpo in Classe I Sterile. Fabbricazione di dispositivi medici invasivi in relazione agli orifizi del corpo in Classe I Sterile. Commercializzazione di dispositivi medici e diagnostici in vitro. Commercializzazione di articoli da laboratorio

Management of the manufacturing and placing on the market of sterile tampons for sampling of biological specimens in natural orifice and in surgical field. Design and manufacturing of diagnostic medical devices for laboratories of analysis. Management of the manufacturing and placing on the market of invasive medical devices with respect to body orifices (class I sterile). Manufacturing of invasive medical devices with respect to body orifices (class I sterile). Marketing of medical and diagnostic devices in vitro. Marketing of laboratory articles.

Il presente Certificato è soggetto al rispetto delle condizioni stabilite dai Regolamenti per la certificazione in vigore applicabili.

This Certificate shall satisfy the requirements established in the Rules for the certification in force applicable.

In caso di discordanza tra le lingue utilizzate nella traduzione del contenuto del presente certificato, fare riferimento alla lingua italiana

In cases of discrepancy between the languages used in the translation of the content of this certificate, please refer to the Italian language

L'AMMINISTRATORE DELEGATO

MANAGING DIRECTOR

Dr. Ing. Roberto Cusolito

Data di Prima Emissione *First Issue Date*	Data di Prima Emissione ITALCERT *First Issue Date ITALCERT*	Data di Rinnovo *Renewal Date*	Data di Scadenza *Expiration Date*
1998-07-23	2011-10-30	2020-10-30	2023-10-29

Settore IAF 14 - 29

ACCREDIA
L'ENTE ITALIANO DI ACCREDITAMENTO

SGQ N° 023A

Membro degli Accordi di Mutuo Riconoscimento EA, IAF e ILAC

Signatory of EA, IAF and ILAC Mutual Recognition Agreements

ICIM

CISQ is a member of

IQNet

THE INTERNATIONAL CERTIFICATION NETWORK
www.iqnet-certification.com

IQNet, the association of the world's first class certification bodies, is the largest provider of management System Certification in the world. IQNet is composed of more than 30 bodies and counts over 150 subsidiaries all over the globe.

CERTIFICATO n.
CERTIFICATE No. **4264/4**

SI CERTIFICA CHE IL SISTEMA DI GESTIONE PER LA QUALITÀ DI
WE HEREBY CERTIFY THAT THE QUALITY MANAGEMENT SYSTEM OPERATED BY

GRUPPO VACUTEST KIMA

Sede / *Head Office*
Via dell'Industria,12 – 35020 Arzergrande (PD) - Italia
Unità Operative / *Operative Units*
MEUS S.r.l. - Via Leonardo da Vinci, 24B – 26 – 28 – Zona Industriale Tognana – 35028 Piove di Sacco (PD) - Italia
MEUS S.r.l. - Via dell'Industria, 2 - 16 – 35020 Arzergrande (PD) - Italia
ROLL S.R.L. - Via Leonardo Da Vinci, 24A – Zona Industriale Tognana – 35028 Piove di Sacco (PD) - Italia
KIMA S.R.L. - Via Leonardo da Vinci, 22 – Zona Industriale Tognana – 35028 Piove di Sacco (PD) - Italia
VACUTEST KIMA S.r.l. - Via dell'Industria,12 – 35020 Arzergrande (PD) – Italia
VACUTEST KIMA S.r.l. via L. Da vInci, 22 Zona Industriale Tognana – 35028 Piove di Sacco (PD) - Italia

È CONFORME ALLA NORMA / *IS IN COMPLIANCE WITH THE STANDARD*

UNI EN ISO 9001:2015

Sistema di Gestione per la Qualità / *Quality Management System*

PER LE SEGUENTI ATTIVITÀ / *FOR THE FOLLOWING ACTIVITIES*

EA: 14 - 29

Progettazione e produzione di provette con vuoto predeterminato ad uso prelievo ematico, liquidi biologici e urine. Produzione di provette per microprelievi di sangue. Progettazione e produzione di Holders (camicie) per prelievo sottovuoto. Progettazione e produzione di kit diagnostici per l'analisi del sangue e dei liquidi biologici. Progettazione e produzione di terreni di coltura per microbiologia. Progettazione e produzione di aghi e dispositivi sterili per il prelievo ematico. Commercializzazione di prodotti del Gruppo: kit diagnostici, terreni di coltura per microbiologia, articoli in plastica per laboratorio analisi, provette con vuoto predeterminato e aghi sterili. Progettazione e produzione di stampi per articoli in plastica per laboratorio analisi. Stampaggio di materie termoplastiche ad iniezione per articoli medicali.

Design and production of test tubes with predetermined vacuum for collection of haematological samples, biological liquids and urine samples. Production of test tubes for micro-collection of haematological samples. Design and production of Holders for vacuum sampling. Design and production of diagnostic kits for blood and biological liquids analysis. Design and production of culture media for microbiology. Design and production of sterile needles and devices for collection of haematological samples. Trading of the products of the Group: diagnostic kits, culture media for microbiology, plastic disposable labware, test tubes with predetermined vacuum and sterile needles. Design and production of moulds for plastic labware. Injection moulding of thermoplastic materials for medical devices.

Riferirsi alla documentazione del Sistema di Gestione per la Qualità aziendale per l'applicabilità dei requisiti della norma di riferimento.
Refer to the documentation of the Quality Management System for details of application to reference standard requirements.

Il presente certificato è soggetto al rispetto del documento ICIM "Regolamento per la certificazione dei sistemi di gestione" e al relativo Schema specifico.
The use and the validity of this certificate shall satisfy the requirements of the ICIM document "Rules for the certification of company management systems" and specific Scheme.

Per informazioni puntuali e aggiornate circa eventuali variazioni intervenute nello stato della certificazione di cui al presente certificato, si prega di contattare il n° telefonico +39 02 725341 o indirizzo e-mail info@icim.it.
For timely and updated information about any changes in the certification status referred to in this certificate, please contact the number +39 02 725341 or email address info@icim.it.

Data emissione *First issue*	Emissione corrente *Current issue*	Data di scadenza *Expiring date*
18/01/2007	18/01/2019	17/01/2022

ICIM S.p.A.
Piazza Don Enrico Mapelli, 75 – 20099 Sesto San Giovanni (MI)
www.icim.it

ACCREDIA
L'ENTE ITALIANO DI ACCREDITAMENTO

SGQ N° 004 A

Membro degli Accordi di Mutuo Riconoscimento EA, IAF e ILAC
Signatory of EA, IAF and ILAC Mutual Recognition Agreements

FEDERAZIONE CISQ

www.cisq.com

CISQ è la Federazione Italiana di Organismi di Certificazione dei sistemi di gestione aziendale.
CISQ is the Italian Federation of management system Certification Bodies.

0449CM_03_IT

ФЕДЕРАЛЬНОЕ АГЕНТСТВО
ПО ТЕХНИЧЕСКОМУ РЕГУЛИРОВАНИЮ И МЕТРОЛОГИИ
СИСТЕМА ДОБРОВОЛЬНОЙ СЕРТИФИКАЦИИ ГОСТ Р
«EAC AUDIT»
РЕГИСТРАЦИОННЫЙ НОМЕР РОСС RU.32028.04ЕАС1
ОРГАН ПО СЕРТИФИКАЦИИ ООО «ГОРТЕСТ»
РЕГИСТРАЦИОННЫЙ НОМЕР РОСС RU.32028
ИНН 7717616798 ОГРН 1087746489060
Юридический адрес: 109028, Россия, г. Москва, Серебряническая набережная, д. 27, этаж 4, пом. 1, ком. 17
Телефон: 8 (800) 1000-730, e-mail: info@eacaudit.ru

№003749

СЕРТИФИКАТ СООТВЕТСТВИЯ

Регистрационный номер № 04ЕАС1.СМ.00813

Общество с ограниченной ответственностью «МиниМед»

(наименование лица)

241520, Россия, Брянская область, Брянский район, с. Супонево, ул. Шоссейная, д.17А

(юридический адрес лица)

241520, Россия, Брянская область, Брянский район, с. Супонево, ул. Шоссейная, д.17А

(фактический адрес лица)

ИНН: 3234007127 **ОГРН: 1023202138332**

НАСТОЯЩИЙ СЕРТИФИКАТ УДОСТОВЕРЯЕТ СООТВЕТСТВИЕ

системы менеджмента качества изделий медицинских Общества с ограниченной ответственностью «МиниМед» требованиям ГОСТ ISO 13485-2017 (ISO 13485:2016) «Изделия медицинские. Системы менеджмента качества. Системные требования для целей регулирования» применительно к Производство лабораторной посуды, медицинских изделий, приборов и принадлежностей, красителей, реагентов и наборов реагентов для in-vitro диагностики

Дата регистрации: 19-03-2019

Срок действия до: 18-03-2022

Руководитель органа по сертификации: (подпись) **В. И. Погодин**

Председатель экспертной комиссии: (подпись) **Е. Д. Курбатова**

М.П.

НАСТОЯЩИЙ СЕРТИФИКАТ ОБЯЗЫВАЕТ ОРГАНИЗАЦИЮ ПОДДЕРЖИВАТЬ СОСТОЯНИЕ ВЫПОЛНЯЕМЫХ РАБОТ В СООТВЕТСТВИИ С ВЫШЕУКАЗАННЫМИ СТАНДАРТАМИ, ЧТО БУДЕТ НАХОДИТЬСЯ ПОД КОНТРОЛЕМ ОРГАНА ПО СЕРТИФИКАЦИИ СИСТЕМЫ ДОБРОВОЛЬНОЙ СЕРТИФИКАЦИИ "EAC AUDIT" И ПОДТВЕРЖДАТЬСЯ ПРИ ПРОХОЖДЕНИИ ЕЖЕГОДНОГО ИНСПЕКЦИОННОГО КОНТРОЛЯ www.vacutestkima.it

DICHIARAZIONE DI CONFORMITÁ CE
EC DECLARATION OF CONFORMITY

conforme all'Allegato III della Direttiva 98/79/CE *"Dispositivi Medico-Diagnostici In Vitro" e s.m.i.*
according to Annex III of the Directive 98/79/EC on "In Vitro Diagnostic Medical Devices" as amended

fabbricante / *manufacturer*: ***VACUTEST KIMA S.r.l. - articoli per laboratori analisi***
disposable labware

indirizzo / *address*: ***Via dell'Industria, 12***
35020 Arzergrande (PD) - Italia

telefono / *phone* **+39-049-9720624** fax / *fax* **+39-049-9720182** posta elettronica / *e-mail* **info@vacutestkima.it**

identificazione dei prodotti / *product identification*

Sistema di prelievo di sangue e altri liquidi biologici mediante provette con vuoto predeterminato in plastica "VACUTEST KIMA".

"VACUTEST KIMA" vacuum blood and biological liquids collection tubes in plastic.

nome commerciale / *brand name*: **"VACUTEST KIMA"**

classificazione dei prodotti / *product classification*

dispositivi diversi da quelli elencati nell'Allegato II della Direttiva 98/79/CE e s.m.i.
devices other then those mentioned in Annex II of the Directive 98/79/EC as amended

Si dichiara

sotto la propria responsabilità che tutti i dispositivi sopraelencati rispettano le disposizioni applicabili della Direttiva 98/79/CE e s.m.i.*"Dispositivi Medico–Diagnostici In Vitro"*.
Tutta la documentazione tecnica richiesta dall'Allegato III della succitata Direttiva e comprovante il rispetto dei Requisiti Essenziali di cui all'Allegato I della Direttiva, è conservata a cura del Fabbricante

Hereby we declare

under our sole responsibility that the above mentioned devices meet the applicable provisions of the Directive 98/79/EC as amended on "In Vitro Diagnostic Medical Devices".

All the supporting documents, as required by Annex III, in order to prove conformity to the Essential Requirements as listed in Annex I, are retained under the premises of the Manufacturer

luogo e data / *place and date*: **Arzergrande, 01/01/2015**

firma / *signature*

Assicuratore Qualità / Quality Manager
Giovanni Chiarin

Giovanni Chiarin

***HOLTSCH* Medizinprodukte GmbH**
In den Faltern 13 • D – 65232 Taunusstein
Germany

Declaration of conformity

This is to confirm that

the swab dispenser **Quickpad®**
containing fleece swabs, saturated with 70% isopropyl alcohol (V/V)

is

manufactured, packaged and sterilized in accordance with the rules of GMP and the paragraph 13 of the GERMAN MEDICAL LAW.

These swabs are equal to a
Medical Device Class I (UMNDS Code15-252)
and are checked and released

conform to

the German Medical Product Law according to

the
Medical Device Directive 93/42/EEC
of the European Counsel.

Taunusstein, November 17th , 2021

HOLTSCH Medizinprodukte GmbH
HOLTSCH
Medizinprodukte GmbH
In den Faltern 13 · 65232 Taunusstein
Malte Hertzberg
(Certified Biologist)

Zertifikat-Nr./Certificate no:
DE_SN_01_GMP_2016_0003

Aktenzeichen/Reference Number:
L24-5117/90

BESTÄTIGUNG DER ÜBEREINSTIMMUNG EINES HERSTELLERS MIT GMP

Teil 1

Ausgestellt nach einer Inspektion gemäß

- **Art. 111 (5) der Richtlinie 2001/83/EG**

Die zuständige deutsche Überwachungsbehörde bestätigt:

Der Hersteller
HOLTSCH Medizinprodukte GmbH

Anschrift der Betriebsstätte
HOLTSCH Medizinprodukte GmbH
Leipziger Straße 300
01139 Dresden
Deutschland

- Sonstiges:

Der Hersteller wurde im Rahmen der nationalen Arzneimittelüberwachung inspiziert in Verbindung mit der Herstellungserlaubnis Nr. DE_SN_01_MIA_2012_0045 gemäß Art. 40 der Richtlinie 2001/83/EG umgesetzt in deutsches Recht durch § 13 Abs. 1 Arzneimittelgesetz.

Aufgrund der aus der letzten Inspektion vom 27. November 2015 gewonnenen Erkenntnisse wird für die oben genannte Betriebsstätte des Herstellers die Übereinstimmung mit den Anforderungen der Guten Herstellungspraxis festgestellt, die sich aus

- den Grundsätzen und Leitlinien der Guten Herstellungspraxis gemäß
  - Richtlinie 2003/94/EG

ergeben.

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Part 1

Issued following an inspection in accordance with

- **Art. 111 (5) of Directive 2001/83/EC**

The competent authority of GERMANY confirms the following:

The manufacturer
HOLTSCH Medizinprodukte GmbH

Site address
HOLTSCH Medizinprodukte GmbH
Leipziger Straße 300
01139 Dresden
Germany

- Other:

The manufacturer has been inspected under the national inspection programme in connection with manufacturing authorisation no. DE_SN_01_MIA_2012_0045 in accordance with Art. 40 of Directive 2001/83/EC transposed in the following national legislation: Sec 13 para 1 Arzneimittelgesetz (German Drug Law).

From the knowledge gained during the inspection of this manufacturer, the latest of which was conducted on 27 November 2015, it is considered that it complies with the Good Manufacturing Practice requirements referred to in

- the principles and guidelines of Good Manufacturing Practice laid down in
  - Directive 2003/94/EC

FREISTAAT SACHSEN LANDESDIREKTION SACHSEN

Dieses Zertifikat bestätigt den Status der Betriebsstätte zum Zeitpunkt der oben genannten Inspektion. Es sollte nicht zur Bestätigung der Übereinstimmung herangezogen werden, wenn seit der genannten Inspektion mehr als drei Jahre vergangen sind. Nach Ablauf dieser Zeit sollte mit der zuständigen Behörde Kontakt aufgenommen werden. Das Zertifikat ist nur bei Vorlage sämtlicher Seiten inklusive der Teile 1 und 2 gültig. Die Echtheit dieses Zertifikates kann ggf. durch die ausstellende Behörde bestätigt werden.

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection, after which time the issuing authority should be consulted. This certificate is valid only when presented with all pages and both parts 1 and 2. The authenticity of this certificate may be verified with the issuing authority.

FREISTAAT SACHSEN

LANDESDIREKTION SACHSEN

Teil 2

• Humanarzneimittel

1 HERSTELLUNGSTÄTIGKEITEN

- Die erlaubten Herstellungstätigkeiten umfassen vollständige und teilweise Herstellung (einschließlich verschiedener Prozesse wie Umfüllen, Abpacken oder Kennzeichnen), Chargenfreigabe und -zertifizierung, Lagerung und Vertrieb der genannten Darreichungsformen sofern nicht anders angegeben;

- Die Qualitätskontrolle und/oder Freigabe und/oder Chargenzertifizierung ohne Herstellungsschritte sollten unter den entsprechenden Punkten spezifiziert werden;

- Unter der relevanten Produktart und Darreichungsform sollte auch angegeben werden, wenn der Hersteller Produkte mit speziellen Anforderungen herstellt, z.B. radioaktive Arzneimittel oder Arzneimittel, die Penicilline, Sulfonamide, Zytostatika, Cephalosporine, Stoffe mit hormoneller Wirkung oder andere potenziell gefährliche Wirkstoffe enthalten (anwendbar für alle Bereiche des Teils 1 mit Ausnahme 1.5.2 und 1.6).

1.1 Sterile Produkte

1.1.3 Ausschließlich Chargenfreigabe

1.2 Nichtsterile Produkte

1.2.1 Nichtsterile Produkte

1.2.1.17 Andere nichtsterile Produkte
Alkoholtupfer

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13. Januar 2016

Name und Unterschrift des Bearbeiters der zuständigen Behörde

Klaus Hartmann

Landesdirektion Sachsen
Referat 24, Pharmazie, GMP-Inspektorat
Braustraße 2
04107 Leipzig
Deutschland

Tel.: +49(0)351 825-2411
Fax: +49(0)351 825-9201

Part 2

• Human Medicinal Products

1 MANUFACTURING OPERATIONS

- authorised manufacturing operations include total and partial manufacturing (including various processes of dividing up, packaging or presentation), batch release and certification, storage and distribution of specified dosage forms unless informed to the contrary;

- quality control testing and/or release and batch certification activities without manufacturing operations should be specified under the relevant items;

- if the company is engaged in manufacture of products with special requirements e.g. radiopharmaceuticals or products containing penicillin, sulphonamides, cytotoxics, cephalosporins, substances with hormonal activity or other or potentially hazardous active ingredients this should be stated under the relevant product type and dosage form (applicable to all sections of Part 1 apart from sections 1.5.2 and 1.6)

1.1 Sterile Products

1.1.3 Batch certification only

1.2 Non-sterile products

1.2.1 Non-sterile products

1.2.1.17 Other non-sterile medicinal product
alcoholic pads

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13 January 2016

Name and signature of the authorised person of the Competent Authority

Klaus Hartmann

Landesdirektion Sachsen
Referat 24, Pharmazie, GMP-Inspektorat
Braustraße 2
04107 Leipzig
Deutschland

Tel.: +49(0)351 825-2411
Fax: +49(0)351 825-9201