

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 (6 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 2026).

Nous, ELITech Clinical Systems SAS, zone industrielle 61500 SEES France, déclarons les électrodes conformes à la Directive 2011/65/UE du parlement européen et du conseil du 8 juin 2011 relative à la limitation de l'utilisation de certaines substances dangereuses dans les équipements électriques et électroniques incluant la DIRECTIVE DÉLÉGUÉE (UE) 2015/863 DE LA COMMISSION du 31 mars 2015 modifiant l'annexe II de la Directive 2011/65/UE du Parlement européen et du Conseil en ce qui concerne la liste des substances soumises à limitations.

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 (6 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, 2026).

We, ELITech Clinical Systems SAS, Zone Industrielle 61500 SEES France, hereby certify electrodes; conform to Directive 2011/65/EU of the European Parliament and of the Council of 8 June 2011 on the restriction of the use of certain hazardous substances in electrical and electronic equipment, including Commission Delegated Directive (EU) 2015/863 of 31 March 2015 amending Annex II to Directive 2011/65/EU of the European Parliament and of the Council as regards the list of restricted substances.

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 (6 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 2026).

Nosotros, ELITech Clinical Systems SAS, Zone Industrielle 61500 SEES France, declaramos los electrodos conformes con la Directiva 2011/65/UE del parlamento europeo y del consejo del 8 de junio de 2011 sobre restricciones a la utilización de algunas sustancias peligrosas en aparatos eléctricos y electrónicos incluyendo la Directiva delegada (UE) 2015/863 de la comisión del 31 de marzo de 2015 por la que se modifica el anexo II de la Directiva 2011/65/UE del Parlamento Europeo y del Consejo en cuanto a la lista de sustancias restringidas.

Sées, le 12 octobre 2023

Valérie LAMBERT,

Responsable des Affaires Réglementaires

Regulatory Affairs Manager

Responsable de los Asuntos Reglamentarios



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



Annex

REF	PRODUCT NAME	GMDN Code
3918-004	Sodium Electrode (Na+)	52896
3918-005	Potassium Electrode (K+)	52892
3918-006	Chloride Electrode (Cl-)	52876
3918-003	Carbon Dioxide Electrode (CO2)	60773
3918-002	Reference Electrode (REF)	59241
ALBU-0250	ALBUMIN	53597
ALBU-5220	ALBUMIN	53597
ALBU-0600	ALBUMIN	53597
ALBU-5600	ALBUMIN	53597
ALBU-0700	ALBUMIN	53597
ALBU-5700	ALBUMIN	53597
ALBU-M830	ALBUMIN	53597
ALBU-5M30	ALBUMIN	53597
ALPI-0230	ALP IFCC	52928
ALPI-5100	ALP IFCC	52928
ALPI-6050	ALP IFCC	52928
ALSL-0250	ALT/GPT 4+1 SL	52923
ALSL-5220	ALT/GPT 4+1 SL	52923
ALSL-6050	ALT/GPT 4+1 SL	52923
ALSL-0410	ALT/GPT 4+1 SL	52923
ALSL-5415	ALT/GPT 4+1 SL	52923
ALSL-6255	ALT/GPT 4+1 SL	52923
ALSL-0430	ALT/GPT 4+1 SL	52923
ALSL-0455	ALT/GPT 4+1 SL	52923
ALSL-0510	ALT/GPT 4+1 SL	52923
ALSL-5515	ALT/GPT 4+1 SL	52923
ALSL-6615	ALT/GPT 4+1 SL	52923
ALSL-M490	ALT/GPT	52923
ALSL-5M90	ALT/GPT	52923
ALSL-6M30	ALT/GPT	52923
AMSL-0230	AMYLASE SL	52940
AMSL-5220	AMYLASE SL	52940
AMSL-0390	AMYLASE SL	52940
AMSL-5405	AMYLASE SL	52940
AMSL-0400	AMYLASE SL	52940
AMSL-M430	AMYLASE	52940
AMSL-5M30	AMYLASE	52940
ASLO-0250	ANTI-STREPTOLYSIN O	59055
ASLO-5025	ANTI-STREPTOLYSIN O	59055
ASLO-6006	ANTI-STREPTOLYSIN O	59055
ASLO-4001	ANTI-STREPTOLYSIN O	51744
ASSL-0250	AST/GOT 4+1 SL	52954
ASSL-5220	AST/GOT 4+1 SL	52954
ASSL-6050	AST/GOT 4+1 SL	52954
ASSL-0410	AST/GOT 4+1 SL	52954
ASSL-5415	AST/GOT 4+1 SL	52954
ASSL-6255	AST/GOT 4+1 SL	52954
ASSL-0430	AST/GOT 4+1 SL	52954
ASSL-0455	AST/GOT 4+1 SL	52954
ASSL-0510	AST/GOT 4+1 SL	52954
ASSL-5515	AST/GOT 4+1 SL	52954
ASSL-6615	AST/GOT 4+1 SL	52954
ASSL-M490	AST/GOT	52954
ASSL-5M90	AST/GOT	52954
ASSL-6M30	AST/GOT	52954
AUML-0250	URIC ACID MONO SL	53583
AUML-5220	URIC ACID MONO SL	53583
AUML-0420	URIC ACID MONO SL	53583
AUML-5405	URIC ACID MONO SL	53583
AUML-0427	URIC ACID MONO SL	53583
AUML-0497	URIC ACID MONO SL	53583
AUML-5505	URIC ACID MONO SL	53583
AUML-0500	URIC ACID MONO SL	53583
AUML-0507	URIC ACID MONO SL	53583
AUML-0707	URIC ACID MONO SL	53583
AUML-5710	URIC ACID MONO SL	53583
AUML-M830	URIC ACID	53583
AUML-5M30	URIC ACID	53583
AUSL-0250	URIC ACID SL	53583
AUSL-5220	URIC ACID SL	53583
AUSL-6050	URIC ACID SL	53583
BIDI-0250	BILIRUBIN DIRECT 4+1	53233
BIDI-5220	BILIRUBIN DIRECT 4+1	53233
BIDI-6050	BILIRUBIN DIRECT 4+1	53233
BIDI-0500	BILIRUBIN DIRECT	53233
BIDI-5600	BILIRUBIN DIRECT	53233
BITD-6250	BILIRUBIN DIRECT	53233

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REF	PRODUCT NAME	GMDN Code
BIDI-M430	DIRECT BILIRUBIN	53233
BIDI-5M30	DIRECT BILIRUBIN	53233
BIDI-6M10	DIRECT BILIRUBIN	53233
BIDV-0850	DIRECT BILIRUBIN ENVOY	53233
BITO-0250	BILIRUBIN TOTAL 4+1	53229
BITO-5220	BILIRUBIN TOTAL 4+1	53229
BITO-6050	BILIRUBIN TOTAL 4+1	53229
BITO-0600	BILIRUBIN TOTAL 4+1	53229
BITO-5600	BILIRUBIN TOTAL 4+1	53229
BITD-6400	BILIRUBIN TOTAL 4+1	53229
BITO-M430	TOTAL BILIRUBIN	53229
BITO-5M30	TOTAL BILIRUBIN	53229
BITO-6M10	TOTAL BILIRUBIN	53229
BITV-0850	TOTAL BILIRUBIN ENVOY	53229
CALA-0250	CALCIUM ARSENAZO	45789
CALA-5220	CALCIUM ARSENAZO	45789
CALA-0600	CALCIUM ARSENAZO	45789
CALA-5600	CALCIUM ARSENAZO	45789
CALA-M430	CALCIUM ARSENAZO	45789
CALA-5M30	CALCIUM ARSENAZO	45789
CALI-0550	ELICAL 2	47868
CALI-1550	ELICAL 2	47868
CHDL-0250	HDL CHOLESTEROL	53391
CHDL-5021	HDL CHOLESTEROL	53391
CHDL-6014	HDL CHOLESTEROL	53391
CHDL-0600	HDL CHOLESTEROL	53391
CHDL-5090	HDL CHOLESTEROL	53391
CHDL-6060	HDL CHOLESTEROL	53391
CHDL-M330	HDL CHOLESTEROL	53391
CHDL-5M30	HDL CHOLESTEROL	53391
CHDL-6M30	HDL CHOLESTEROL	53391
CHEB-0250	CHOLINESTERASE	52971
CHEB-5008	CHOLINESTERASE	52971
CHEB-6005	CHOLINESTERASE	52971
CHSL-0250	CHOLESTEROL SL	53359
CHSL-5220	CHOLESTEROL SL	53359
CHSL-0455	CHOLESTEROL SL	53359
CHSL-0497	CHOLESTEROL SL	53359
CHSL-5505	CHOLESTEROL SL	53359
CHSL-0500	CHOLESTEROL SL	53359
CHSL-0507	CHOLESTEROL SL	53359
CHSL-0700	CHOLESTEROL SL	53359
CHSL-5710	CHOLESTEROL SL	53359
CHSL-0707	CHOLESTEROL SL	53359
CHSL-M690	CHOLESTEROL	53359
CHSL-5M90	CHOLESTEROL	53359
CKMB-0900	CK-MB CONTROL	44693
CKMB-1030	CK-MB CONTROL	44693
CKSL-0230	CK NAC SL	53003
CKSL-5220	CK NAC SL	53003
CKSL-6050	CK NAC SL	53003
CKSL-0410	CK NAC SL	53003
CKSL-5405	CK NAC SL	53003
CKSL-6255	CK NAC SL	53003
CKSL-0430	CK NAC SL	53003
CKSL-M230	CK NAC	53003
CKSL-5M30	CK NAC	53003
CKSL-6M10	CK NAC	53003
CLDL-0250	LDL CHOLESTEROL	53395
CLDL-5021	LDL CHOLESTEROL	53395
CLDL-6014	LDL CHOLESTEROL	53395
CLDL-M330	LDL CHOLESTEROL	53395
CLDL-5M30	LDL CHOLESTEROL	53395
CLDL-6M30	LDL CHOLESTEROL	53395
CMSL-0230	CK-MB	52994
CMSL-5220	CK-MB	52994
CMSL-6220	CK-MB	52994
CMSL-WR	CK-MB	52994
CMSL-0410	CK-MB SL	52994
CMSL-5405	CK-MB SL	52994
CMSL-6255	CK-MB SL	52994
CONT-0060	ELITROL I	47869
CONT-1060	ELITROL I	47869
CONT-0160	ELITROL II	47869
CONT-1160	ELITROL II	47869
CRCO-0600	CREATININE JAFFE	53251
CRCO-5600	CREATININE JAFFE	53251
CRCO-6600	CREATININE JAFFE	53251
CRCO-0700	CREATININE JAFFE	53251

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REF	PRODUCT NAME	GMDN Code
CRSL-0250	CREATININE PAP SL	53250
CRSL-5221	CREATININE PAP SL	53250
CRSL-6070	CREATININE PAP SL	53250
CRSL-0630	CREATININE PAP SL	53250
CRSL-5505	CREATININE PAP SL	53250
CRSL-6470	CREATININE PAP SL	53250
CRSL-M490	CREATININE PAP	53250
CRSL-5M90	CREATININE PAP	53250
CRSL-6M30	CREATININE PAP	53250
FEFE-0230	IRON FERENE	54758
FEFE-5140	IRON FERENE	54758
FEFE-6040	IRON FERENE	54758
FEFE-0600	IRON FERENE	54758
FEFE-5600	IRON FERENE	54758
FEFE-6400	IRON FERENE	54758
FEFE-0850	IRON ENVOY	54758
FEFE-M230	IRON FERENE	54758
FEFE-5M30	IRON FERENE	54758
FEFE-6M10	IRON FERENE	54758
GHSL-0250	GLUCOSE HK SL	53301
GHSL-5220	GLUCOSE HK SL	53301
GHSL-6050	GLUCOSE HK SL	53301
GHSL-0600	GLUCOSE HK SL	53301
GHSL-5505	GLUCOSE HK SL	53301
GHSL-6605	GLUCOSE HK SL	53301
GHSL-M490	GLUCOSE HK	53301
GHSL-5M90	GLUCOSE HK	53301
GHSL-6M30	GLUCOSE HK	53301
GISL-0250	GAMMA-GT PLUS SL	53027
GISL-5220	GAMMA-GT PLUS SL	53027
GISL-6050	GAMMA-GT PLUS SL	53027
GISL-0400	GAMMA-GT PLUS SL	53027
GISL-0420	GAMMA-GT PLUS SL	53027
GISL-5405	GAMMA-GT PLUS SL	53027
GISL-6255	GAMMA-GT PLUS SL	53027
GISL-M230	GAMMA-GT	53027
GISL-5M30	GAMMA-GT	53027
GISL-6M10	GAMMA-GT	53027
GPSL-0250	GLUCOSE PAP SL	53301
GPSL-5220	GLUCOSE PAP SL	53301
GPSL-0455	GLUCOSE PAP SL	53301
GPSL-0497	GLUCOSE PAP SL	53301
GPSL-5505	GLUCOSE PAP SL	53301
GPSL-0500	GLUCOSE PAP SL	53301
GPSL-0507	GLUCOSE PAP SL	53301
GPSL-0700	GLUCOSE PAP SL	53301
GPSL-5710	GLUCOSE PAP SL	53301
GPSL-0707	GLUCOSE PAP SL	53301
GPSL-M690	GLUCOSE PAP	53301
GPSL-5M90	GLUCOSE PAP	53301
HBAC-0043	HbA1c CALIBRATOR SET	53315
HBAC-4301	HbA1c CALIBRATOR SET	53315
HBAC-4302	HbA1c CALIBRATOR SET	53315
HBAC-4303	HbA1c CALIBRATOR SET	53315
HBAC-4304	HbA1c CALIBRATOR SET	53315
HBAC-0049	HbA1c CONTROL L + H	44435
HBAC-4605	HbA1c CONTROL L + H	44435
HBAC-4705	HbA1c CONTROL L + H	44435
HBAC-0240	HbA1c	59090
HBAC-5224	HbA1c	59090
HBAC-6076	HbA1c	59090
HBAC-6004	HbA1c	59090
HBAC-7225	HbA1c	59090
HBAE-0043	HbA1c Enzymatic Calibrator Set	53315
HBAE-4301	HbA1c Enzymatic Calibrator Set	53315
HBAE-4303	HbA1c Enzymatic Calibrator Set	53315
HBAE-M130	HbA1c Enzymatic	63151
HBAE-5M30	HbA1c Enzymatic	63151
HBAE-6M30	HbA1c Enzymatic	63151
HBAE-7050	HbA1c Enzymatic	63151
HDLL-0011	CHOLESTEROL HDL 2G CALIBRATOR	44696
HDLL-0041	CHOLESTEROL HDL 2G CALIBRATOR	44696
HDLL-0230	CHOLESTEROL HDL SL 2G	53391
HDLL-0380	CHOLESTEROL HDL SL 2G	53391
HDLL-0390	CHOLESTEROL HDL SL 2G	53391
HLCA-0041	HDL LDL CALIBRATOR	47868
HLCA-4001	HDL LDL CALIBRATOR	47868
ICRP-0043	CRP IP CALIBRATOR SET	41838

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REF	PRODUCT NAME	GMDN Code
ICRP-4311	CRP IP CALIBRATOR SET	41838
ICRP-4312	CRP IP CALIBRATOR SET	41838
ICRP-4313	CRP IP CALIBRATOR SET	41838
ICRP-4314	CRP IP CALIBRATOR SET	41838
ICRP-4315	CRP IP CALIBRATOR SET	41838
ICRP-0046	CRP IP CONTROL I	41839
ICRP-4610	CRP IP CONTROL I	41839
ICRP-0047	CRP IP CONTROL II	41839
ICRP-4710	CRP IP CONTROL II	41839
ICRP-0400	CRP IP	53705
ICRP-6125	CRP IP	53705
ICRP-5025	CRP IP	53705
ICRP-M230	CRP IP	53705
ICRP-6M30	CRP IP	53705
ICRP-5M30	CRP IP	53705
IFRT-0042	FERRITIN CALIBRATOR	41927
IFRT-4230	FERRITIN CALIBRATOR	41927
IFRT-0230	FERRITIN	53718
IFRT-5020	FERRITIN	53718
IFRT-6005	FERRITIN	53718
IHAP-0400	HAPTOGLOBIN IP	53737
IHAP-6125	HAPTOGLOBIN IP	53737
IHAP-5025	HAPTOGLOBIN IP	53737
IIGA-0400	IgA IP	53760
IIGA-6125	IgA IP	53760
IIGA-5025	IgA IP	53760
IIGG-0400	IgG IP	53787
IIGG-6125	IgG IP	53787
IIGG-5025	IgG IP	53787
IIGM-0400	IgM IP	53795
IIGM-6125	IgM IP	53795
IIGM-5025	IgM IP	53795
IMAL-0043	µALBUMIN IP CALIBRATOR SET	53477
IMAL-4311	µALBUMIN IP CALIBRATOR SET	53477
IMAL-4312	µALBUMIN IP CALIBRATOR SET	53477
IMAL-4313	µALBUMIN IP CALIBRATOR SET	53477
IMAL-4314	µALBUMIN IP CALIBRATOR SET	53477
IMAL-4315	µALBUMIN IP CALIBRATOR SET	53477
IMAL-0046	µALBUMIN IP CONTROL I	53478
IMAL-4610	µALBUMIN IP CONTROL I	53478
IMAL-0047	µALBUMIN IP CONTROL II	53478
IMAL-4710	µALBUMIN IP CONTROL II	53478
IMAL-0400	µALBUMIN IP	53475
IMAL-6125	µALBUMIN IP	53475
IMAL-5025	µALBUMIN IP	53475
IMAL-M230	MICROALBUMIN IP	53475
IMAL-6M30	MICROALBUMIN IP	53475
IMAL-5M30	MICROALBUMIN IP	53475
IORO-0400	OROSOMUCOID IP	53606
IORO-6125	OROSOMUCOID IP	53606
IORO-5025	OROSOMUCOID IP	53606
IPAL-0400	PREALBUMIN IP	53957
IPAL-6125	PREALBUMIN IP	53957
IPAL-5025	PREALBUMIN IP	53957
IPRO-0043	PROTEIN IP CALIBRATOR SET	53593
IPRO-4311	PROTEIN IP CALIBRATOR SET	53593
IPRO-4312	PROTEIN IP CALIBRATOR SET	53593
IPRO-4313	PROTEIN IP CALIBRATOR SET	53593
IPRO-4314	PROTEIN IP CALIBRATOR SET	53593
IPRO-4315	PROTEIN IP CALIBRATOR SET	53593
IRCT-0046	RHEUMATOLOGY CONTROL I	47869
IRCT-4610	RHEUMATOLOGY CONTROL I	47869
IRCT-0047	RHEUMATOLOGY CONTROL II	47869
IRCT-4710	RHEUMATOLOGY CONTROL II	47869
IRFA-0042	RF CALIBRATOR	42230
IRFA-4220	RF CALIBRATOR	42230
IRFA-0230	RHEUMATOID FACTOR	55111
IRFA-5020	RHEUMATOID FACTOR	55111
IRFA-6005	RHEUMATOID FACTOR	55111
ISCA-0250	ISE CALIBRATORS	52867
ISCA-4221	ISE CALIBRATORS	52867
ISCA-4222	ISE CALIBRATORS	52867
ITRF-0400	TRANSFERRIN IP	59041
LACI-0250	LACTATE	53342
LACI-5008	LACTATE	53342
LACI-6005	LACTATE	53342
LDLL-0011	CHOLESTEROL LDL 2G CALIBRATOR	41728
LDLL-0041	CHOLESTEROL LDL 2G CALIBRATOR	41728

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REF	PRODUCT NAME	GMDN Code
LDLL-0230	CHOLESTEROL LDL SL 2G	53395
LDLL-0380	CHOLESTEROL LDL SL 2G	53395
LDLL-0390	CHOLESTEROL LDL SL 2G	53395
LLSL-0230	LDH-L SL	53072
LLSL-5220	LDH-L SL	53072
LLSL-6050	LDH-L SL	53072
LLSL-0400	LDH-L SL	53072
LLSL-5400	LDH-L SL	53072
LLSL-6250	LDH-L SL	53072
LLSL-0420	LDH-L SL	53072
LLSL-M230	LDH IFCC	53072
LLSL-5M30	LDH IFCC	53072
LLSL-6M10	LDH IFCC	53072
LPSL-0230	LIPASE SL	53108
LPSL-0250	LIPASE	53108
LPSL-5088	LIPASE	53108
LPSL-6061	LIPASE	53108
LPSL-0850	LIPASE ENVOY	53108
LXCR-0112	CRP LATEX	53707
MAGX-0230	MAGNESIUM XYLIDYL	46795
MAGX-0600	MAGNESIUM XYLIDYL	46795
MAGX-0850	MAGNESIUM ENVOY	46795
MGXB-0250	MAGNESIUM XB	46795
MGXB-5220	MAGNESIUM XB	46795
MGXB-0600	MAGNESIUM XB	46795
MGXB-5600	MAGNESIUM XB	46795
MGXB-M430	MAGNESIUM XB	46795
MGXB-5M30	MAGNESIUM XB	46795
PASL-0230	ALP (DEA) SL	52928
PASL-5220	ALP (DEA) SL	52928
PASL-6050	ALP (DEA) SL	52928
PASL-0400	ALP (DEA) SL	52928
PASL-5405	ALP (DEA) SL	52928
PASL-6255	ALP (DEA) SL	52928
PASL-0420	ALP (DEA) SL	52928
PHOS-0230	PHOSPHORUS	59123
PHOS-5220	PHOSPHORUS	59123
PHOS-0600	PHOSPHORUS	59123
PHOS-5600	PHOSPHORUS	59123
PHOS-M430	PHOSPHORUS	59123
PHOS-5M30	PHOSPHORUS	59123
PIVD-0850	ALP ENVOY	52928
PROB-0250	TOTAL PROTEIN PLUS	53985
PROB-5220	TOTAL PROTEIN PLUS	53985
PROB-0600	TOTAL PROTEIN PLUS	53985
PROB-5600	TOTAL PROTEIN PLUS	53985
PROB-0700	TOTAL PROTEIN PLUS	53985
PROB-5700	TOTAL PROTEIN PLUS	53985
PROB-M830	TOTAL PROTEIN	53985
PROB-5M30	TOTAL PROTEIN	53985
PRTU-0022	MICROPROTEIN PLUS Standard 100 mg/dL	53482
PRTU-0250	MICROPROTEIN PLUS	53481
PRTU-0600	MICROPROTEIN PLUS	53481
PRTU-5600	MICROPROTEIN PLUS	53481
PRTU-M230	URINE PROTEIN	53481
PRTU-5M30	URINE PROTEIN	53481
RHFA-M130	RHEUMATOID FACTOR	55111
RHFA-5M30	RHEUMATOID FACTOR	55111
RHFA-6M30	RHEUMATOID FACTOR	55111
RHFA-4220	RHEUMATOID FACTOR	42230
TGML-0250	TRIGLYCERIDES SL	53460
TGML-5220	TRIGLYCERIDES SL	53460
TGML-0425	TRIGLYCERIDES MONO SL NEW	53460
TGML-5415	TRIGLYCERIDES MONO SL NEW	53460
TGML-0427	TRIGLYCERIDES MONO SL NEW	53460
TGML-0455	TRIGLYCERIDES SL	53460
TGML-0497	TRIGLYCERIDES MONO SL NEW	53460
TGML-5515	TRIGLYCERIDES MONO SL NEW	53460
TGML-0515	TRIGLYCERIDES MONO SL NEW	53460
TGML-0517	TRIGLYCERIDES MONO SL NEW	53460
TGML-0700	TRIGLYCERIDES MONO SL NEW	53460
TGML-5710	TRIGLYCERIDES MONO SL NEW	53460
TGML-0707	TRIGLYCERIDES MONO SL NEW	53460
TGML-M690	TRIGLYCERIDES	53460
TGML-5M90	TRIGLYCERIDES	53460
TIBC-0250	Direct TIBC	53904
TIBC-5025	Direct TIBC	53904
TIBC-6007	Direct TIBC	53904
TIBC-M130	Direct TIBC	53904

Annex

REF	PRODUCT NAME	GMDN Code
TIBC-5M30	Direct TIBC	53904
TIBC-6M30	Direct TIBC	53904
TRF2-M230	TRANSFERRIN	59041
TRF2-5M30	TRANSFERRIN	59041
TRF2-6M10	TRANSFERRIN	59041
URSL-0250	UREA UV SL	53587
URSL-5220	UREA UV SL	53587
URSL-6050	UREA UV SL	53587
URSL-0420	UREA UV SL	53587
URSL-5405	UREA UV SL	53587
URSL-6255	UREA UV SL	53587
URSL-0427	UREA UV SL	53587
URSL-0455	UREA UV SL	53587
URSL-0500	UREA UV SL	53587
URSL-5505	UREA UV SL	53587
URSL-6605	UREA UV SL	53587
URSL-0507	UREA UV SL	53587
URSL-M830	UREA	53587
URSL-5M30	UREA	53587
URSL-6M10	UREA	53587
VITD-0043	VITAMIN D CALIBRATOR SET	54474
VITD-4311	VITAMIN D CALIBRATOR SET	54474
VITD-4312	VITAMIN D CALIBRATOR SET	54474
VITD-4313	VITAMIN D CALIBRATOR SET	54474
VITD-4314	VITAMIN D CALIBRATOR SET	54474
VITD-4315	VITAMIN D CALIBRATOR SET	54474
VITD-0049	VITAMIN D CONTROL SET	54475
VITD-4630	VITAMIN D CONTROL SET	54475
VITD-4730	VITAMIN D CONTROL SET	54475
VITD-0250	VITAMIN D	54476
VITD-5021	VITAMIN D	54476
VITD-6005	VITAMIN D	54476

vlo
Ce

Certificate of Registration

QUALITY MANAGEMENT SYSTEM - ISO 13485:2016

This is to certify that:

ELITechGroup Inc.
370 West 1700 South
Logan
Utah
84321
USA

Facility ID Number: F000174

Holds Certificate No:

MDSAP 689350

Statement of Conformity: The company listed on this certificate has been audited to and found to conform with the following criteria: ISO 13485:2016 and Australia - Therapeutic Goods (Medical Devices) Regulations, 2002, Schedule 3 Part 1 (excluding Part 1.6) - Full Quality Assurance Procedure; Brasil - RDC ANVISA n. 16/2013, RDC ANVISA n. 23/2012, RDC ANVISA n. 67/2009; Canada - Medical Devices Regulations - Part 1 - SOR 98/282; Japan - MHLW Ministerial Ordinance 169, Article 4 to Article 68, PMD Act; USA - 21 CFR 820, 21 CFR 803, 21 CFR 806, 21 CFR 807 - Subparts A to D

The design, manufacture, distribution and servicing of automated slide stainers, cyto centrifuges, cystic fibrosis sweat testing systems, and osmometers, and proprietary standards, controls disposables and reagents for use with these types of equipment. Manufacture and distribution of controls, standards, consumables, accessories and supplies for in vitro diagnostic systems, laboratory equipment, and erythrocyte sedimentation rate test systems.

For and on behalf of BSI:

Gary E Slack, Senior Vice President - Medical Devices

Original Registration Date: 2019-03-28

Effective Date: 2022-01-11

Expiry Date: 2025-01-10



BSI Group America Inc. is an MDSAP authorized auditing organization

GMED certifie que le système de management de la qualité développé par
GMED certifies that the quality management system developed by

ELITECH CLINICAL SYSTEMS SAS
Zone Industrielle
61500 SEES FRANCE

pour les activités
for the activities

Conception, production, contrôle et commercialisation de produits de chimie cliniques pour le diagnostic in vitro. Validation de la combinaison réactifs et automates. Distribution d'automates et de produits de chimie cliniques pour le diagnostic in vitro.

Design, production, control and sales of clinical chemistry products intended to be used for in vitro diagnostics. Validation of the combination reagents and analyzers. Distribution of clinical chemistry analyzers and products for in vitro diagnostics.

réalisées sur le(s) site(s) de
performed on the location(s) of

ELITech Clinical Systems SAS
Zone industrielle - 61500 SEES - FRA

est conforme aux exigences des normes internationales
complies with the requirements of the international standards

NF EN ISO 13485 : 2016

Début de validité / Effective date : July 25th, 2023 (included)

Valable jusqu'au / Expiry date : July 27th, 2026 (included)

Etabli le / Issued on : July 25th, 2023



Accréditation n°4-0608
Liste des sites accrédités
et portée disponible sur
www.cofrac.fr

GMED N° 10462-8

Ce certificat est délivré selon les règles de certification GMED / This certificate is issued according to the rules of GMED certification

Renouvelle le certificat 10462-7



On behalf of the President
Marjorie PERRIMON
Certification Director

ELITechGroup B.V.
P.O.Box 100
6950 AC Dieren
Van Rensselaerweg 4
6956 AV Spankeren
The Netherlands
T: +31 313 430 500
F: +31 313 427 807
info.ecsnl@elitechgroup.com
www.elitechgroup.com
Chamber of Commerce 09175642

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				✓	

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

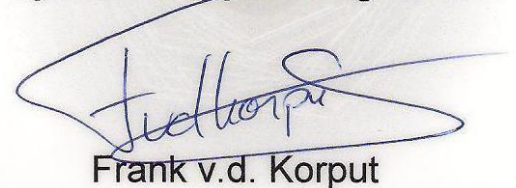
Date of training: April 20th – April 23rd, 2010

System Support Manager:



Jan Oostendorp

System Support Engineer:



Frank v.d. Korput

LLSL

LLSL-0230

R1 4 x 20 mL + **R2** 4 x 5 mL

LLSL-0400

R1 2 x 50 mL + **R2** 1 x 26 mL

LLSL-0420

R1 4 x 50 mL + **R2** 2 x 26 mL

FTRO-LLSL-v14 (03/2022) (PIT-LLSL-4-v14)

SCOPUL UTILIZĂRII

ELITech Clinical Systems LDH-L este un reactiv de diagnostic in vitro destinat pentru determinarea cantitativă a lactat dehidrogenazei (LDH) în probele de ser și plasmă umană pe analizoare automate sau semi-automate.

Acest dispozitiv de diagnostic in vitro este doar pentru uz profesional.

SEMNIFICAȚIE CLINICĂ (1-3)

Lactat dehidrogenaza (LDH) poate fi găsită în aproape toate celulele organismului cu cele mai mari activități în miocard, ficat, rinichi, mușchii scheletici și eritrocite. Acesta este un tetrametru prezent în ser în formă de cinci izoenzime principale.

LDH-ul crește în cazul infarctului miocardic acut, afecțiunile hepatice (hepatita virală, ciroză), anemie (hemolitică, megaloblastică), unele cancere și în toate bolile care implică deteriorarea celulară. Astfel, creșterile LDH-ului în ser sunt nespecifice.

Măsurarea LDH-ului este indicată pentru a ajuta la diagnosticarea deteriorării țesuturilor din corp și uneori pentru a ajuta la monitorizarea progresului anumitor patologii.

LIMITAREA UTILIZĂRII

Analiza cantitativă doar a lactat dehidrogenazei (LDH) nu poate fi utilizată pentru diagnosticarea unei boli sau a unei patologii specifice.

Rezultatele trebuie interpretate în conjuncție cu alte rezultate ale testelor de diagnosticare, constatările clinice și istoricul medical al pacientului.

METODĂ ȘI PRINCIPIU (4)

Metoda IFCC - Cinetică.

$$LDH$$
$$L\text{-Lactat} + NAD^+ \longrightarrow \text{Piruvat} + NADH + H^+$$
COMPOZIȚIE**Reactivul 1: R1**

N-Metil-D-Glucamină pH 9.4 (37 °C)

Litiu L-Lactat 68 mmol/L

Azidă de sodiu < 0.1 % (m/m)

Reactivul 2: R2

NAD 50 mmol/L

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Soluție salină obișnuită (NaCl 9g/L)

- Aalizoare automate sau semi-automate.
- Echipamente generale de laborator (de ex. pipetă).
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Consultați Fișa cu date de Securitate (FDS) pentru o manipulare adecvată.

- Reactivul R1 conține azidă de sodiu care poate reacționa cu plumbul sau cuprul pentru a forma azide metalice cu potențial exploziv. În momentul eliminării acestor reactivi, spălați întotdeauna cu apă din abundență pentru a preveni acumularea de azide.

- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.

- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.

- Nu interschimbați fiolele de reactiv din truse diferite.

STABILITATE

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

A nu se utiliza după data de expirare indicată pe etichetele fiolelor.

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivul este gata de utilizare.

DETERIORAREA PRODUSULUI

- Produsul trebuie să fie limpede. Aspectul tulbure indică deteriorarea produsului.

- Nu utilizați produsul dacă există semne vizibile de contaminare sau deteriorare (de ex. materia cu particule).

- Deteriorarea containerului de reactiv poate afecta negativ performanța produsului. Nu utilizați reactivul dacă există dovezi fizice de deteriorare (de ex. scurgeri sau container perforat).

EȘANTIOANE**Specimene necesare** (1,5)

- Ser
- Plasmă (heparină de litiu).
- Utilizarea oricărui alt tip de specimen trebuie validată de laborator.

Avertismente și precauții

- Eșantioanele trebuie să fie fără hemoliză. ⁽¹⁻³⁾
- Eșantioanele trebuie să fie separate de celule și coagulate cu promptitudine (prezența celulelor poate crește în mod fals rezultatul) ⁽¹⁻³⁾

Eșantioanele trebuie colectate în conformitate cu Buna Practică de Laborator și liniile directe corespunzătoare care pot fi în vigoare.

Depozitare și stabilitate ⁽⁵⁾

- 7 zile la temperatura camerei
- 4 zile la 2-8°C
- 6 săptămâni la -20°C

În anumite patologii care implică creșterea izoenzimei LDH-4 sau LDH-5, este de preferat stocarea probelor la temperatura camerei, aceste izoenzime fiind sensibile la frig. ⁽²⁾

VALORI DE REFERINȚĂ ^(2,3)

Ser, plasmă	U/L	μkat/L
Adulți	125 - 220	2.08 – 3.67

Concentrații mai mari sunt observate la copii și nou-născuți.

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

PROCEDURĂ

Procedura manuală

lungime de undă : 340 nm
Drum optic: 1 cm
Raport probă/reactiv : 1:36
Temperatura: 37 °C
Citiți față de un blank de reactiv.

	BLANKR	PROBA
Reactiv R1	1000 μL	1000 μL
Apă distilată	35 μL	-
Eșantion	-	35 μL

Amestecați, așteptați 3 minute și adăugați:

Reactiv R2	250 μL	250 μL
------------	--------	--------

Se amestecă și după o incubare de 100 de secunde, se citește absorbanta la intervale de 1 minut timp de 3 minute. Calculați modificarea absorbantei pe minut ($\Delta A/\text{min}$).

Procedura automată

Acești reactivi pot fi utilizați pe mai multe analizoare automate. Pentru analizoarele ELITech tip Selectra, aplicațiile validate sunt disponibile la cerere. Pentru software-ul Selectra TouchPro, utilizați aplicația inclusă în codul de bare disponibil la sfârșitul acestui insert.

CALCUL

Activitate (U/L) = $\Delta A / \text{min} \times 5\ 828$

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

CALIBRARE

ELICAL 2 este trasabil pentru metoda de referință IFCC.

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Se recomandă ca serurile pentru controlul calității precum ELITROL I și ELITROL II să fie utilizate pentru a monitoriza performanța analizei.

Controalele trebuie efectuate:

- Înainte de a analiza eșantioanele pacientului,
- Cel puțin o dată pe zi,
- după fiecare calibrare
- și/sau în conformitate cu cerințele laboratorului și de reglementare.

Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsurile corective necesare.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale. (vă rugăm să consultați Fișa cu date de securitate (FDS)).

PERFORMANȚE

Au fost obținute performanțe pe Selectra ProM, urmând recomandările tehnice CLSI, în condiții de mediu controlate.

Interval de măsurare

50 - 800 U/L (0.83 - 13.33 μkat/L)

Eșantioanele care au concentrații mai mari vor fi automat diluate 1:10 cu soluție de NaCl 9 g/L și re-analizate. Această procedură extinde intervalul de măsurare până la 8000 U/L (133.33 μkat/L) Nu raportați rezultatele în afara acestui interval extins.

Pentru utilizatorii cu software Selectra TouchPro, funcția „dilute” efectuează automat diluarea probei. Rezultatele iau în considerare diluția.

Limita de detecție (LoD) și Limita de cuantificare (LoQ)

LoD = 4 U/L (0.07 μkat/L)

LoQ = 10 U/L (0.17 μkat/L)

Precizie

Datele privind imprecizia au fost obținute pe 2 analizoare Selectra ProM timp de 20 de zile (2 cicluri pe zi, teste efectuate de două ori).

Rezultatele reprezentative sunt prezentate mai jos :

	n	Medie		În interiorul ciclului	Total
		U/L	μkat/L		
		CV (%)			
Nivelul 1	80	168	2.80	0.7	4.1
Nivelul 2	80	309	5.15	0.7	2.8
Nivelul 3	80	712	11.87	0.5	3.0

Corelație

A fost efectuat un studiu comparativ între reactivul LDH-L SL pe un analizor Selectra ProM și un sistem similar disponibil în comerț pe eșantioane de ser uman 99.

Concentrațiile eșantioanelor au fost între 45 și 780 U/L (0.75 - 13.00 μkat/L)

Rezultatele sunt după cum urmează:

Coefficient de corelație: (r)=0.997

Regresie liniară: $y = 1.010 x + 3$ U/L (0.05 μkat/L)



☞ - Limitări/ Interferențe analitice

- Eșantioanele hemolizate nu trebuie utilizate deoarece hemoliza semnificativă poate duce la rezultate fals crescute din cauza nivelurilor înalte de LDH provenite din eritrocite. ⁽¹⁻³⁾

- Au fost efectuate studii pentru a determina nivelul interferenței de la diferiți compuși.

Au fost testate următoarele nivele ale lactat dehidrogenazei (LDH) : 200 U/L și 700 U/L.

Nu este definită nicio interferență semnificativă printr-o recuperare $\leq \pm 10\%$ din valoarea inițială.

Bilirubină neconjugată: Nicio interferență semnificativă până la 30.0 mg/dL (513 $\mu\text{mol/L}$).

Bilirubină conjugată: Nicio interferență semnificativă până la 29.5 mg/dL (505 $\mu\text{mol/L}$).

Trigliceride: Nicio interferență semnificativă până la 3146 mg/dL (35.6 mmol/L).

Acid ascorbic: Nicio interferență semnificativă până la 20.0 mg/dL.

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

Acetaminofen: Nicio interferență 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 nefiabale. ⁽⁶⁾

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽⁷⁻⁸⁾

- Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 28 zile

Frecvența calibrării: 6 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit și după o operație de întreținere.

Aceste performanțe au fost obținute cu ajutorul analizorului ELITech Selectra ProM. Rezultatele pot varia dacă se utilizează un alt instrument sau o procedură manuală.

Performanțele aplicațiilor nevalidate de ELITech nu sunt garantate și trebuie definite de utilizator.

☞ DECLARAREA INCIDENTULUI GRAV

Vă rugăm să notificați producătorul (prin intermediul distribuitorului dumneavoastră) și autoritatea competentă a Statului Membru din Uniunea Europeană în care este stabilit utilizatorul și/sau pacientul, cu privire la orice incident grav care a avut loc legat de dispozitiv. Pentru alte jurisdicții, declararea incidentului grav trebuie să fie în conformitate cu cerințele reglementare locale, statale și federale.

Prin raportarea unui incident grav, furnizați informații care pot contribui la siguranța dispozitivelor medicale *in vitro*.

☞ ASISTENȚĂ TEHNICĂ:






Contactați distribuitorul dumneavoastră local sau ELITech Clinical Systems SAS (ccsupport@elitechgroup.com).

☞ BIBLIOGRAFIE

1. Wu, A.H.B., Clinical guide to laboratory test, 4th Ed., (W.B. Saunders eds.), (2006), 648.
2. Sanhai W. R., Protein Isoforms : Isoenzymes and Isoforms, Clinical Chemistry: Theory, Analysis, Correlation, 5th Ed., Kaplan, L.A, Pesce, A.J., (Mosby Inc. eds.), (2010), 302 and appendix.
3. Panteghini, M. D., Enzymes, Tietz Fundamentals of Clinical Chemistry, 6th Ed., Burtis, C.A., Ashwood, E.R., Bruns, D.E. (W.B. Saunders eds.), (2008), 317.
4. Schumann, G. *et al.*, Clin. Chem. Lab. Med., (2002), **40**, 643.
5. Guder, W.G., *et al.*, Use of anticoagulants in diagnostic laboratory investigations and stability of blood, plasma and serum samples. (2002). WHO/DIL/LAB/99.1 Rev.2.
6. 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.
7. Young, D. S., Effects of preanalytical variables on clinical laboratory tests, 2nd Ed., AACC Press, (1997).
8. Young, D. S., Effects of drugs on clinical laboratory tests, 4th Ed., AACC Press, (1995).

☞ SIMBOLURI

Simbolurile utilizate sunt definite în standardul ISO 15223-1, cu excepția celor prezentate mai jos:

	Conținut
	Reactivul 1
	Reactivul 2
	Modificare față de versiunea anterioară
	Conformitate europeană

Notă

Doar pentru ref. **LLSL-0230**, utilizate cu software-ul Selectra TouchPro.

LLSL



LDH
720

0
PIT-LLSL



FTNA-LDLL-v8 (06/2020)

References :
LDLL-0230 4 x 28 mL

Kit composition :
R1 4 x 21 mL + R2 4 x 7 mL

CAUTION: Federal Law restricts this device to sale by or on the order of a licensed healthcare practitioner (Rx ONLY)

INTENDED USE

ELITech Clinical Systems CHOLESTEROL LDL SL 2G is an *in vitro* diagnostic reagent intended for the quantitative determination of Low Density Lipoprotein (LDL) Cholesterol in human serum and plasma samples using ELITech Clinical Systems Selectra Pro Series Analyzers. Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases. It is not intended for use in Point of Care settings.

CLINICAL SIGNIFICANCE (1-4)

Cholesterol, insoluble molecule, circulates associated with lipoproteins (HDL, LDL and VLDL). LDL (Low Density Lipoprotein) come from VLDL (Very Low Density Lipoprotein) hydrolysis by different lipolytic enzymes. LDL, which transport approximately 60% of total plasmatic cholesterol, are mainly taken up through specific receptors by extrahepatic and hepatic tissues. A positive association exists between the incidence of coronary heart disease and LDL cholesterol. LDL are atherogenic lipoproteins: LDL cholesterol increase is a major cause of apparition and evolution of atherosclerosis, in particular coronary atherosclerosis. Therefore, the treatment of elevated LDL cholesterol is the primary target of cholesterol-lowering therapy. An increase in LDL cholesterol may be seen in different pathological states including hyperlipoproteinemia types IIIa and IIIb, premature coronary heart diseases, hyperlipoproteinemia due to hepatic or renal disorder, to hypothyroidism, diabetes.

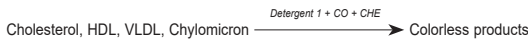
METHOD

Enzymatic. Colorimetric. End point.
Selective detergent

PRINCIPLE

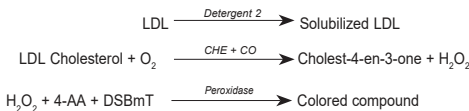
1st step:

When a sample is mixed with reagent R1, non-LDL lipoproteins are solubilized by detergent 1 and released cholesterol is subject to enzymatic reactions to be eliminated:



2nd step:

When reagent R2 is added, LDL is solubilized by detergent 2, then LDL cholesterol is measured by enzymatic reactions:



REAGENT COMPOSITION

Reagent 1 : R1		Reagent 2 : R2	
MES buffer, pH 6.3		MES buffer, pH 6.3	
Detergent 1	< 1.0 %	Detergent 2	< 1.0 %
Cholesterol esterase (CHE)(bacterial)	< 1500 U/L	N,N-bis(4-sulphobutyl)-m-	
Cholesterol oxidase (CO)(bacterial)	< 1500 U/L	toluidine-disodium(DSBmT)	< 1 mmol/L
Peroxidase (vegetable «horseradish»)	< 1300 ppg U/L	Preservative	
4-Amino-Antipyrine (4-AA)	< 0.1 %		
Ascorbate oxidase (vegetable)	< 3000 U/L		
Preservative			

MATERIAL REQUIRED BUT NOT PROVIDED

- Cholesterol LDL 2G Calibrator, ref.LDLL-0041.
- ELITROL I, control serum, ref.CONT-0080.
- ELITROL II, control serum, ref.CONT-0180.
- Normal saline solution (NaCl 9 g/L).
- General Laboratory equipment.

PRECAUTIONS AND WARNING

- This reagent is for professional *in vitro* diagnostic use only.
- Take normal precautions and adhere to good laboratory practice.
- Use clean or single use laboratory equipment only to avoid contamination.
- Do not freeze reagents.
- The reagents R1 and R2 are classified as hazardous.



Obtain Safety data sheet (SDS) before use for a proper handling.

WASTE MANAGEMENT

Disposal of all waste material should be in accordance with local, state and Federal regulatory requirements.

STABILITY OF REAGENTS

Store at 2-8 °C and protect from light.
Reagents are stable until the expiry date stated on the label.
On board stability: refer to § PERFORMANCE DATA.

PREPARATION

Reagents are ready for use.

REAGENT DETERIORATION

The reagent solutions should be clear. Cloudiness would indicate deterioration.

SAMPLES (1,3)

Specimen

- Serum or plasma in lithium heparin drawn from fasting patient (≥ 12 hours) are the required specimens. Separate from cells within 2 hours. To reduce biological variability, collection of samples should follow standardized conditions as recommended by NCEP.
- Venipuncture should be performed prior to the administration of drugs. Of particular note, venipuncture performed during an acetaminophen overdose situation, when N-acetyl-p-benzoquinone imine (NAPQI) an atypical metabolic breakdown product of acetaminophen, may be present, may lead to erroneously low LDL cholesterol results.
- Venipuncture performed during or immediately after administration of N-acetylcysteine (NAC), a drug used to treat acetaminophen overdose, or Metamizole may lead to erroneously low LDL Cholesterol results.

Storage

Store samples at 2-8 °C before analysis. Specimens are stable 7 days at 2-8 °C. For longer storage, freeze them at -70 °C or lower (frozen once).

REFERENCE VALUES (4)

The NCEP (American National Cholesterol Education Program) has established the following classification for LDL cholesterol levels according to the risk of developing coronary heart disease:

Risk Classification	Level (mg/dL)	Level (mmol/L)
Optimal	< 100	2.59
Near or above optimal	100 - 129	2.59 - 3.34
Borderline high	130 - 159	3.36 - 4.11
High	160 - 189	4.14 - 4.89
Very High	≥ 190	4.91

Note: It is recommended that each laboratory establishes and maintains its own reference values. The data given here are only an indication.

Conversion factor: mg/dL x 0.0259 = mmol/L

PROCEDURE

See application included in the barcode indicated at the end of the insert.

CALIBRATION

ELITech Clinical Systems Cholesterol LDL 2G Calibrator should be used for calibration. Its value is traceable to the reference method recommended by the CDC (Centers for Disease Control and Prevention).

Calibration frequency: refer to § PERFORMANCE DATA.

QUALITY CONTROL

To ensure adequate quality, control sera such as ELITROL I and ELITROL II should be used. These controls should be assayed together with patient samples, at least once a day and after each calibration. The control frequency 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, state, and/or federal guidelines.

CERTIFICATION

The reagent system has not been tested by the CRMLN (Cholesterol Reference Method Laboratory Network) .

PERFORMANCE DATA at 37 °C

A) On ELITech Clinical Systems Selectra ProM Analyzers

- Measuring range

Determined according to CLSI⁽⁵⁾ EP6-A protocol, the measuring range is from 15 to 380 mg/dL (0.39-9.83 mmol/L). Samples exceeding 380 mg/dL should be diluted 1:5 with NaCl 9 g/L solution (normal saline) and re-assayed. Use of this procedure extends the measuring range to 380 to 1900 mg/dL (9.83 to 49.14 mmol/L). This extended measuring range was confirmed in a study where a high concentration of Cholesterol LDL was spiked into native serum samples. The recovery observed did not exceed the expected recovery by > ± 10%.

The «dilute» function performs the sample dilution automatically. Results take the dilution into account.

- Limit of Detection (LoD) and Limit of quantification (LoQ)

Determined according to CLSI⁽⁶⁾ EP17-A protocol,

LoD = 1.5 mg/dL (0.04 mmol/L)
LoQ = 10.0 mg/dL (0.26 mmol/L)

- Precision

Determined according to CLSI⁽⁷⁾ EP5-A2 protocol.

	N	Mean		Within-run CV (%)	Total
		mg/dL	mmol/L		
Low level	80	96	2.48	1.2	1.9
Medium level	80	123	3.18	0.9	1.8
High level	80	150	3.88	1.8	2.3

- Correlation

A comparative study has been performed between ELITech Clinical Systems Selectra ProM Analyzer and another FDA-Approved system equipment (equivalent method) on 100 human serum samples according to CLSI⁽⁸⁾ EP9-A2 protocol.

The sample concentrations ranged from 16 to 370 mg/dL (0.41 to 9.57 mmol/L).

The parameters of linear regression are as follows:

Correlation coefficient: (r) = 0.998
Linear regression: y = 0.951 x + 1 mg/dL (0.03 mmol/L)

- Limitations / Interferences

- Do not report results outside of the usable range.
- Studies have been performed to determine the level of interference from different compounds according to CLSI⁽⁹⁾ EP7-A2 protocol and SFBC recommendations⁽¹⁰⁾. Recovery within ± 10% of initial value at LDL Cholesterol concentration of 100 mg/dL and 160 mg/dL.

<u>Conjugated Bilirubin</u> :	No significant interference up to 29.5 mg/dL (504 µmol/L).
<u>Unconjugated Bilirubin</u> :	No significant interference up to 30 mg/dL (513 µmol/L).
<u>Turbidity</u> :	No significant interference up to 614 mg/dL Triglyceride equivalent (6.94 mmol/L).
<u>Hemoglobin</u> :	No significant interference up to 500 mg/dL.
<u>Ascorbic acid</u> :	No significant interference up to 20 mg/dL (1136 µmol/L)

- In very rare cases, monoclonal gammopathies (multiple myeloma), in particular IgM type (Waldenstrom's macroglobulinemia) can cause unreliable results⁽¹¹⁾.

- Results may be falsely low when the sample is taken while levels of NAC, NAPQI (a metabolite of acetaminophen (paracetamol)) or Metamizole are significant.

- Many other substances and drugs may interfere. Some of them are listed in Young ^(12,13).

- 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: 28 days.

Recalibrate when reagent lots change, when quality control results fall outside the established range, and after a maintenance operation.

B) On ELITech Clinical Systems Selectra ProS Analyzers

- Measuring range

Determined according to CLSI⁽⁵⁾ EP6-A protocol, the measuring range is from 15 to 380 mg/dL (0.39-9.83 mmol/L). Samples exceeding 380 mg/dL should be diluted 1:5 with NaCl 9 g/L solution (normal saline) and re-assayed. Use of this procedure extends the measuring range to 380 to 1900 mg/dL (9.83 to 49.14 mmol/L). This extended measuring range was confirmed in a study where a high concentration of Cholesterol LDL was spiked into native serum samples. The recovery observed did not exceed the expected recovery by > ± 10%.

The «dilute» function performs the sample dilution automatically. Results take the dilution into account.

- Limit of Detection (LoD) and Limit of quantification (LoQ)

Determined according to CLSI⁽⁶⁾ EP17-A protocol,

$$\text{LoD} = 0.3 \text{ mg/dL (0.01 mmol/L)}$$

$$\text{LoQ} = 10.0 \text{ mg/dL (0.26 mmol/L)}$$

- Precision

Determined according to CLSI⁽⁷⁾ EP5-A2 protocol.

	N	Mean		Within-run CV (%)	Total
		mg/dL	mmol/L		
Low level	80	96	2.48	2.2	3.1
Medium level	80	122	3.16	1.0	2.4
High level	80	150	3.88	2.2	2.8

- Correlation

A comparative study has been performed between ELITech Clinical Systems Selectra ProS Analyzer and another FDA-Approved system equipment (equivalent method) on 100 human serum samples according to CLSI⁽⁸⁾ EP9-A2 protocol.

The sample concentrations ranged from 16 to 370 mg/dL (0.41 to 9.57 mmol/L).

The parameters of linear regression are as follows:

Correlation coefficient: (r) = 0.998

Linear regression: y = 0.982 x + 2 mg/dL (0.05 mmol/L)

- Limitations / Interferences

- Do not report results outside of the usable range.
- Studies have been performed to determine the level of interference from different compounds according to CLSI⁽⁹⁾ EP7-A2 protocol and SFBC recommendations⁽¹⁰⁾. Recovery within ± 10% of initial value at LDL Cholesterol concentration of 100 mg/dL and 160 mg/dL.

<u>Conjugated Bilirubin</u> :	No significant interference up to 29.5 mg/dL (504 µmol/L).
<u>Unconjugated Bilirubin</u> :	No significant interference up to 30 mg/dL (513 µmol/L).
<u>Turbidity</u> :	No significant interference up to 614 mg/dL Triglyceride equivalent (6.94 mmol/L).
<u>Hemoglobin</u> :	No significant interference up to 500 mg/dL.
<u>Ascorbic acid</u> :	No significant interference up to 20 mg/dL (1136 µmol/L)

- In very rare cases, monoclonal gammopathies (multiple myeloma), in particular IgM type (Waldenstrom's macroglobulinemia) can cause unreliable results⁽¹¹⁾.

- Results may be falsely low when the sample is taken while levels of NAC, NAPQI (a metabolite of acetaminophen (paracetamol)) or Metamizole are significant.

- Many other substances and drugs may interfere. Some of them are listed in Young ^(12,13).

- 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: 28 days.

Recalibrate when reagent lots change, when quality control results fall outside the established range, and after a maintenance operation.

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SYMBOLS

 IVD	In vitro diagnostic medical device	 Temperature limitation
 Consult instruction for use		 Batch code
 Manufacturer		 Use by
 REF	Catalogue number	 Content
 R1	Reagent 1	 European Conformity
 R2	Reagent 2	



LDL Cholesterol
360

0
FTNA-LDL

Modification from previous version

IMPORTANT NOTIFICATION

Adjustment of HDL CHOLESTEROL value in HDL LDL CALIBRATOR (ref. HLCA-0041)

Dear Selectra users,

The HDL CHOLESTEROL value in HDL LDL CALIBRATOR (ref. HLCA-0041) has been adjusted for the HDL CHOLESTEROL reagent (ref. CHDL-xxxx).

	Old value	New value
HDL CHOLESTEROL value in HLCA lot : <u>Lot 21-4019</u> R210463 ; R210642 ; R210775	33 mg/dL 0.85 mmol/L	36 mg/dL. 0.93 mmol/L

TouchPro users on Selectra PRO can scan the barcode in the value sheet LOT 21-4019 on the website :

https://www.elitechgroup.com/wp-content/uploads/sites/16/2022/05/21-4019_R210463_ADD05-22_2023-09.pdf

CHDL

CHDL - 0600	R1 2 x 90 mL + R2 1 x 60 mL
CHDL - 0250	R1 4 x 21 mL + R2 2 x 14 mL
☞ CHDL - 5090	R1 90 mL
☞ CHDL - 6060	R2 60 mL
☞ CHDL - 5021	R1 21 mL
☞ CHDL - 6014	R2 14 mL



FTRO-CHDL-v5 (04/2023) (PIT-CHDL-4-v5)

SCOPUL UTILIZĂRII

ELITech Clinical Systems HDL CHOLESTEROL este un reactiv de diagnostic in vitro destinat pentru determinarea cantitativă a Colesterolului HDL în probele de ser și plasmă umană pe analizoare automate sau semi-automate.

Acest dispozitiv de diagnostic in vitro este doar pentru uz profesional.

SEMNIFICAȚIE CLINICĂ⁽¹⁻³⁾

Colesterolul din ser este derivat din sursele alimentare sau este sintetizat endogen, în special în celulele hepatice și intestinale. Colesterolul este o componentă structurală importantă a membranelor celulare și a organelor. Acesta este un precursor al acizilor biliari, vitaminei D și hormonilor steroizi. Colesterolul, fiind solubil în apă, circulă în asociere cu lipoproteinele (HDL, LDL, VLDL și chilomicronii).

Moleculele HDL permit transportul colesterolului din celule în ficat unde poate fi catabolizat și eliminat. Astfel, s-a arătat că nivelele reduse de HDL reprezintă un factor de risc pentru bolile cardiace coronare.

În practică, măsurarea colesterolului HDL este necesară pentru a evalua predispoziția pacienților la risc cardiovascular ca parte a unui profil lipidic și pentru a monitoriza strategiile terapeutice asociate. Măsurarea colesterolului HDL este, de asemenea, importantă pentru a ajuta la diagnosticarea hiperlipoproteinemiilor.

LIMITAREA UTILIZĂRII

În cazul pacienților la care se observă lipoproteina, rezultatele colesterolului HDL pot fi discrepante între metodele de măsurare omogenă.⁽⁴⁾

Analiza cantitativă doar a Colesterolului HDL nu poate fi utilizată pentru diagnosticarea unei boli sau a unei patologii specifice.

Rezultatele trebuie interpretate în conjuncție cu alte rezultate ale testelor de diagnosticare, constatările clinice și istoricul medical al pacientului.

METODĂ ȘI PRINCIPIU⁽⁴⁾

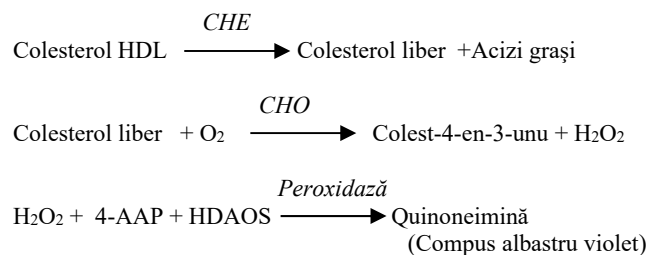
Inhibarea complexului de fosfați / PAP – Punct final

Pasul 1 :

În timp ce eșantionul este amestecat cu reactiv, surfactant și compușii de fosfor organic și anorganic blochează colesterolul non-HDL.

Pasul 2 :

Colesterolul din HDL este eliberat prin acțiunea colesterol-esterazei, apoi suferă o cascadă de reacții enzimatice care se termină cu o reacție de tip Trinder peroxidază / amino-antipirină:



CHE : Colesterol esterază

CHO : Colesterol oxidază

4-AAP = 4-Aminoantipirină

HDAOS : N-(2-Hidroxi-3-sulfopropil)-3.5-dimetoxianilină, sare de sodiu

COMPOZIȚIE

Reactivul 1: R1

Tampon, pH 6.85

N-(2-Hidroxi-3-sulfopropil)-3.5-dimetoxianilină, sare de sodiu

HDAOS \geq 0.5 mmol/L

Peroxidază \geq 8 000 U/L

Compuși de fosfor anorganic și organic

Reactivul 2: R2

Tampon, pH 8.15

Colesterol oxidază \geq 2 000 U/L

Colesterol esterază \geq 180 U/L

Peroxidază \geq 15 000 U/L

4-Aminoantipirină 2 mmol/L

Surfactant 0.6 % (m/m)

Azidă de sodiu < 0.1 % (m/m)

Conține și ascorbat oxidaza pentru performanță optimă.

MATERIALE NECESARE DAR NEFURNIZATE

- HLCA-0041 HDL LDL CALIBRATOR
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Soluție salină obișnuită (NaCl 9g/L)
- Aalizoare automate sau semi-automate.
- Echipamente generale de laborator (de ex. pipetă).
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Consultați Fișa cu date de Securitate (FDS) pentru o manipulare adecvată.
- Reactivul R2 conține azidă de sodiu care poate reacționa cu plumbul sau cuprul pentru a forma azide metalice cu potențial exploziv. În momentul eliminării acestor reactivi, spălați întotdeauna cu apă din abundență pentru a preveni acumularea de azide.
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Nu interschimbați fiolele de reactiv din truse diferite.

STABILITATE

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

A nu se utiliza după data de expirare indicată pe etichetele fiolelor.

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.
(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSULUI

- Produsul trebuie să fie limpede. Aspectul tulbure indică deteriorarea produsului.
- Nu utilizați produsul dacă există semne vizibile de contaminare sau deteriorare (de ex. materia cu particule).
- Deteriorarea containerului de reactiv poate afecta negativ performanța produsului. Nu utilizați reactivul dacă există dovezi fizice de deteriorare (de ex. scurgeri sau container perforat).

EȘANTIOANE

Specimene necesare (1,5)

- Ser.
- Plasmă (heparină de litiu)
- Utilizarea oricărui alt tip de specimen trebuie validată de laborator.

Avertismente și precauții

- Pentru determinarea unui profil lipic se recomandă utilizarea unei probe prelevate de la pacienți care fie au respectat o dietă (nu au ingerat nimic într-un interval orar) fie care nu au respectat o dietă. Repetarea profilului lipidic pentru o probă prelevată după utilizarea unei diete ar putea fi efectuată în cazurile în care se cunoaște un rezultat al trigliceridelor pentru o probă fără dieta > 400 mg / dL (4.5 mmol / L) sau hipertrigliceridemie.⁽⁶⁾
- Separați de celule în interval de 2 ore.⁽²⁾
- Eșantioanele trebuie colectate în conformitate cu Buna Practică de Laborator și liniile directe corespunzătoare care pot fi în vigoare.

Depozitare și stabilitate (1,5)

- 7 zile la 2-8 °C,
- înghețați la -70°C sau temperaturi mai mici (a se îngheța doar o dată)

VALORI DE REFERINȚĂ ⁽⁶⁾

Cele mai recente publicații recomandă adaptarea limitelor Colesterolul HDL ca parte a unei evaluări generale a riscului. La nivel de laborator, Federația Europeană de Chimie Clinică și Medicină de Laborator (EFLM) recomandă ca următoarele concentrații să fie raportate ca fiind anormale:

Colesterol HDL :

Ser, plasmă	mg/dL	mmol/L
Bărbați	≤ 40	≤ 1.0
Femei	≤ 45	≤ 1.2

Colesterol non-HDL:

Ser, plasmă	mg/dL	mmol/L
Probă fără a respecta o dietă	≥ 150	≥ 3.9
Probă după respectarea unei diete	≥ 145	≥ 3.8

Notă: Laboratoarele ar trebui să respecte recomandările aplicabile la nivel local pentru valorile de prag lipidice dacă acestea diferă de cele raportate mai sus.

☛ INSTALARE ȘI UTILIZARE

Pentru utilizare pe analizoare Selectra Pro:

- Consultați manualul operatorului :

- **Instrucțiuni speciale de programare:** Programarea instrucțiunilor speciale este obligatorie atunci când unele combinații de teste sunt efectuate împreună pe analizor. Consultați Instrucțiunile de utilizare pentru ACID SOLUTION & SYSTEM CLEANING SOLUTION pentru o programare adecvată (a se vedea PIT-SOL).

☛ PROCEDURĂ

Procedura manuală

lungime de unda : 578 nm
Drum optic: 1 cm
Raport probă/reactiv : 1:100
Temperatura: 37 °C
Citiți față de apă distilată.

	CALIBRARE	TEST
Reactiv R1	900 μL	900 μL
Calibrator	12 μL	
Eșantion		12 μL

Se amestecă și se citesc absorbantele (A1) după o incubare de 5 minute.

Apoi adauga :

Reactiv R2	300 μL	300 μL
------------	--------	--------

Se amestecă și se citesc absorbantele (A2) după o incubare de 2.5 minute.

Procedura automată

Acești reactivi pot fi utilizați pe mai multe analizoare automate. Pentru analizoarele ELITech tip Selectra, aplicațiile validate sunt disponibile la cerere. Pentru software-ul Selectra TouchPro, utilizați aplicația inclusă în codul de bare disponibil la sfârșitul acestui insert.



CALCUL

(A2 - A1 x Fdil) Proba

$$\frac{\quad}{\quad} \times n$$

(A2 - A1 x Fdil) Calibratorul

n = concentrație Calibratorul

Fdil = Factor de diluție = (Volum R1+volum proba)/(Volum R1 + Volum R2 + volum proba)

Factor de conversie: mg/dL x 0.0259 = mmol/L

CALIBRARE

HDL LDL CALIBRATOR este trasabil pentru metodei de referință recomandată de CDC (Centrele pentru Controlul și Prevenirea Bolilor).

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Se recomandă ca serurile pentru controlul calității precum ELITROL I și ELITROL II să fie utilizate pentru a monitoriza performanța analizei.

Controalele trebuie efectuate:

- Înainte de a analiza eșantioanele pacientului,
- Cel puțin o dată pe zi,
- după fiecare calibrare
- și/sau în conformitate cu cerințele laboratorului și de reglementare.

Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsurile corective necesare.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale. (vă rugăm să consultați Fișa cu date de securitate (FDS)).

PERFORMANȚE

Au fost obținute performanțe pe Selectra Pro, urmând recomandările tehnice CLSI, în condiții de mediu controlate.

- Interval de măsurare

5 - 200 mg/dL (0.13 - 5.17 mmol/L)

Nu raportați rezultatele care sunt în afara intervalului de măsurare.

- Limita de detecție (LoD) și Limita de cuantificare (LoQ)

LoD: 0 mg/dL (0.00 mmol/L)

LoQ: 5 mg/dL (0.13 mmol/L)

- Precizie

Datele privind imprecizia au fost obținute pe 2 analizoare Selectra Pro timp de 20 de zile (2 cicluri pe zi, teste efectuate de două ori).

Rezultatele reprezentative sunt prezentate mai jos.

	n	Medie		În interiorul ciclului	Total
		mg/dL	mmol/L		
				CV (%)	
Nivelul 1	80	31	0.80	1.2	1.8
Nivelul 2	80	53	1.37	0.9	1.5
Nivelul 3	80	85	2.20	1.7	2.1

- Corelație

A fost efectuat un studiu comparativ între reactivul HDL CHOLESTEROL pe un analizor Selectra Pro și un sistem similar disponibil în comerț pe eșantioane de ser uman 106.

Concentrațiile eșantioanelor au fost între 11 și 185 mg/dL (0.28 - 4.78 mmol/L).

Rezultatele sunt după cum urmează:

Coefficient de corelație: (r)=0.998

Regresie liniară: $y = 1.031x - 4$ mg/dL (0.10 mmol/L).

- Limitări/ Interferențe analitice

- Au fost efectuate studii pentru a determina nivelul interferenței de la diferiți compuși.

Au fost testate următoarele nivele ale Colesterolul HDL:

31 mg/dL și 54 mg/dL.

Nicio interferență semnificativă nu este definită de o recuperare $\leq \pm 4.2$ mg/dL a valorii inițiale la concentrația HDL de colesterol de 31 mg/dL (sau 13.6 %) și $\leq \pm 10$ % din valoarea inițială la concentrația HDL de colesterol de 54 mg/dL.

Bilirubină neconjugată: Nicio interferență semnificativă până la 30.0 mg/dL (513 μ mol/L)

Bilirubină conjugată: Nicio interferență semnificativă până la 29.5 mg/dL (505 μ mol/L)

Hemoglobină: Nicio interferență semnificativă până la 500 mg/dL

Turbiditate: Nicio interferență semnificativă până la 600 mg/dL (6.8 mmol/L) echivalent trigliceride.

Metil-dopa: Nicio interferență semnificativă până la 2.0 mg/dL

Acetaminofen: Nicio interferență semnificativă până la 30 mg/dL

Acid uric: Nicio interferență semnificativă până la 20.0 mg/dL (1190 μ mol/L)

Acid ascorbic: Nicio interferență semnificativă până la 19.8 mg/dL

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. ⁽⁷⁾

- Rezultatele pot fi reduse fals prin nivele semnificative în eșantion de NAC (N-Acetil-Cisteină), NAPQI (metabolit de acetaminofen (paracetamol)) sau metamizol.

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽⁸⁻⁹⁾

- Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 6 săptămâni.

Frecvența calibrării: 6 săptămâni

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit și după o operație de întreținere.

Aceste performanțe au fost obținute cu ajutorul analizorului ELITech Selectra Pro. Rezultatele pot varia dacă se utilizează un alt instrument sau o procedură manuală.

Performanțele aplicațiilor nevalidate de ELITech nu sunt garantate și trebuie definite de utilizator.



DECLARAREA INCIDENTULUI GRAV

Vă rugăm să notificați producătorul (prin intermediul distribuitorului dumneavoastră) și autoritatea competentă a Statului Membru din Uniunea Europeană în care este stabilit utilizatorul și/sau pacientul, cu privire la orice incident grav care a avut loc legat de dispozitiv. Pentru alte jurisdicții, declararea incidentului grav trebuie să fie în conformitate cu cerințele reglementare locale, statale și federale.

Prin raportarea unui incident grav, furnizați informații care pot contribui la siguranța dispozitivelor medicale *in vitro*.

ASISTENȚĂ TEHNICĂ:

Contactați distribuitorul dumneavoastră local sau ELITech Clinical Systems SAS (ccsupport@elitechgroup.com).

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

☞SIMBOLURI

Simbolurile utilizate în documentație sunt definite conform standardului ISO-15223-1 cu excepția celor prezentate în glosarul de simboluri disponibil pe site-ul ELITech. (Symbols glossary)

☞NOTĂ

- Selectra TouchPro : **CHDL-0250**

CHDL



HDL Cholesterol 2
341

0
PIT-CHDL

- **Instrucțiuni speciale de programare** : Vezi §
INSTALARE ȘI UTILIZARE



LPSL

	LPSL-0250	R1	2 x 8 mL	+	R2	2 x 6 mL
☞	LPSL-5088	R1	8 mL			
☞	LPSL-6161	R2	6 mL			

FTRO-LPSL-0250-v3 (06/2023) (PIT-LPSL-4-v3)



SCOPUL UTILIZĂRII

ELITech Clinical Systems LIPASE este un reactiv de diagnostic in vitro destinat pentru determinarea cantitativă a lipazei în probele de ser și plasmă umană pe analizoare automate

Acest dispozitiv de diagnostic in vitro este doar pentru uz profesional.

SEMNIFICAȚIE CLINICĂ⁽¹⁻²⁾

Lipaza este o enzimă digestivă pancreatică, care catalizează hidroliza legăturilor esterilor din trigliceride pentru a forma glicerol și acizi grași liberi. O creștere a activității lipazei serice poate fi observată în special în pancreatita acută, însă și în alte boli pancreatice, în patologiile intra-abdominale sau insuficiența renală. În timpul pancreatitei acute, nivelul lipazei serice începe să crească după câteva ore și poate fi crescut până la de 10 ori (atingând vârful după 24 de ore); aceasta revine la nivelul normal în interval de 8-14 zile.

Măsurarea activității lipazei este utilizată în special pentru a ajuta la diagnosticarea și monitorizarea pancreatitei acute, și poate ajuta și la diagnosticarea și urmărirea altor afecțiuni pancreatice

LIMITAREA UTILIZĂRII

Analiza cantitativă doar a lipazei nu poate fi utilizată pentru diagnosticarea unei boli sau a unei patologii specifice.

Rezultatele trebuie interpretate în conjuncție cu alte rezultate ale testelor de diagnosticare, constatările clinice și istoricul medical al pacientului.

METODĂ ȘI PRINCIPIU⁽²⁾

DGGR - Cinetică.

În prezența activatorilor specifici precum colipaza, ionii de calciu și acizii biliari, lipaza pancreatică separă substratul cromogen 1,2-O-dilauril-rac-glicero-3-acid glutaric-(6-metilrezorufină) ester (DGGR) în 1,2-O-dilauril-rac-glicerol și acid glutaric -(6-metilrezorufină) ester, care se descompune spontan în soluție alcalină pentru a forma acidul glutaric și metilrezorufina.

Creșterea absorbanței la 578 nm, datorită formării de metilrezorufină, este proporțională cu activitatea lipazei din eșantion.

Lipază pancreatică

DGGR \longrightarrow 1,2-O-dilauril-rac-glicerol + acid glutaric-(6-metilrezorufină) ester

Reacție spontană

acid glutaric-(6-metilrezorufină) ester \longrightarrow acid glutaric + metilrezorufină

COMPOZIȚIE

Reactivul 1: R1

Tampon Good pH 8.0

Azidă de sodiu < 0.1 % (m/m)

Reactivul 2: R2

DGGR 0.27 mmol/L

Conține și colipază, clorură de sodiu și săruri acide biliare pentru performanță optimă.

MATERIALE NECESARE DAR NEFURNIZATE

- CALI-0550 ELICAL 2
- CONT-0060 ELITROL I
- CONT-0160 ELITROL II
- Soluție salină obișnuită (NaCl 9g/L)
- Aalizoare automate.
- Echipamente generale de laborator (de ex. pipetă).
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Reactivul R2 este clasificat ca periculos.



ATENȚIE : Poate provoca o reacție alergică a pielii. A se purta mănuși de protecție/îmbrăcăminte de protecție/echipament de protecție a ochilor/echipament de protecție a feței. ÎN CAZ DE CONTACT CU PIELEA: Spălați cu multă apă și săpun. În caz de iritare a pielii sau de erupție cutanată: consultați medicul. Scoateți îmbrăcăminte contaminată și spălați-o înainte de reutilizare.

Procurați Fișa cu date de Securitate (FDS) înainte de utilizare, pentru o manipulare adecvată.

- Reactivul R1 conține azidă de sodiu care poate reacționa cu plumbul sau cuprul pentru a forma azide metalice cu potențial exploziv. În momentul eliminării acestor reactivi, spălați întotdeauna cu apă din abundență pentru a preveni acumularea de azide.

- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.

- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.

Nu interschimbați fiolele de reactiv din truse diferite.

STABILITATE

A se depozita la 2-8 °C și a se proteja împotriva luminii. A nu se îngheța.

A nu se utiliza după data de expirare indicată pe etichetele fiolelor.

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.
(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSULUI

- Produsul trebuie să fie limpede. Aspectul tulbure indică deteriorarea produsului.
- Nu utilizați produsul dacă există semne vizibile de contaminare sau deteriorare (de ex. materia cu particule).
- Deteriorarea containerului de reactiv poate afecta negativ performanța produsului. Nu utilizați reactivul dacă există dovezi fizice de deteriorare (de ex. scurgeri sau container perforat).

EȘANTIOANE

Specimene necesare ⁽³⁾

- Ser.
- Plasmă (heparină de litiu)
- Utilizarea oricărui alt tip de specimen trebuie validată de laborator.

Avertismente și precauții

Eșantioanele trebuie colectate în conformitate cu Buna Practică de Laborator și liniile directoare corespunzătoare care pot fi în vigoare.

Depozitare și stabilitate ⁽³⁾

- 7 zile la temperatura camerei
- 3 săptămâni la 2-8°C
- 1 an la -20°C

VALORI DE REFERINȚĂ ⁽⁴⁾

Ser, plasmă	U/L	μkat/L
Adulți	13 - 60	0.22 – 1.00

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

☞INSTALARE ȘI UTILIZARE

Pentru utilizare pe analizoare Selectra Pro:

- Consultați manualul operatorului :
- **Instrucțiuni speciale de programare: Programarea instrucțiunilor speciale este obligatorie atunci când unele combinații de teste sunt efectuate împreună pe analizor.** Consultați Instrucțiunile de utilizare pentru ACID SOLUTION & SYSTEM CLEANING SOLUTION pentru o programare adecvată (a se vedea PIT-SOL).

☞PROCEDURĂ

Pentru analizoarele ELITech Clinical Systems tip Selectra, aplicațiile sunt disponibile la cerere.

Lungime de undă 578 nm
Temperatura: 37 °C

Citiți față de un blank de reactiv

Reactiv R1	150 μL
Eșantion	3 μL
Amesteca și așteapta incubarea 4 minute și 43 de secunde.	
Reactiv R2	90 μL

Amesteca și după 77 de secunde de incubare, măsura modificarea absorbantei pe minut ($\Delta A/\text{min}$), timp de 159 de secunde.

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

In aplicatie, decalajul trebuie sa fie setat la:

- 2 U/L (-0.03 μkat/L)

CALCUL

ΔA Proba

_____ x n

n = concentrație Calibratorul

ΔA Calibratorul

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

CALIBRARE

ELICAL 2 este trasabil la măsurarea manuala.

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Se recomandă ca serurile pentru controlul calității precum ELITROL I și ELITROL II să fie utilizate pentru a monitoriza performanța analizei.

Controalele trebuie efectuate:

- Înainte de a analiza eșantioanele pacientului,
- Cel puțin o dată pe zi,
- după fiecare calibrare
- și/sau în conformitate cu cerințele laboratorului și de reglementare.

Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia măsurile corective necesare.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale. (vă rugăm să consultați Fișa cu date de securitate (FDS)).

PERFORMANȚE

Au fost obținute performanțe pe Selectra ProM, urmând recomandările tehnice CLSI, în condiții de mediu controlate.

- **Interval de măsurare**

5 - 300 U/L (0.08 - 5.00 μkat/L)

Eșantioanele care au concentrații mai mari vor fi automat diluate 1:10 cu soluție de NaCl 9 g/L și re-analizate. Această procedură extinde intervalul de măsurare până la 3 000 U/L (50.00 μkat/L).

Nu raportați rezultatele în afara acestui interval extins.

Pentru utilizatorii cu software Selectra TouchPro, funcția „dilute” efectuează automat diluarea probei. Rezultatele iau în considerare diluția.

- Limita de detecție (LoD) și Limita de cuantificare (LoQ)

LoD = 1 U/L (0.02 μ kat/L)

LoQ = 5 U/L (0.08 μ kat/L)

- Precizie

Datele privind imprecizia au fost obținute pe 2 analizoare Selectra ProM timp de 20 de zile (2 cicluri pe zi, teste efectuate de două ori).

Rezultatele reprezentative sunt prezentate mai jos.

	n	Medie		În interiorul ciclului	Total
		U/L	μ kat/L	CV (%)	
Nivelul 1	80	28	0.47	0.8	3.9
Nivelul 2	80	55	0.92	0.7	4.0
Nivelul 3	80	229	3.82	0.4	4.4

- Corelație

A fost efectuat un studiu comparativ între reactivul LIPASE pe un analizor Selectra ProM și un sistem similar disponibil în comerț pe eșantioane de ser uman 100.

Concentrațiile eșantioanelor au fost între 6 și 284 U/L. (0.10 - 4.73 μ kat/L)

Rezultatele sunt după cum urmează:

Coeficient de corelație: (r)=0.999

Regresie liniară: $y=1.063x + 1$ U/L (0.02 μ kat/L)

- Limitări/ Interferențe analitice

- Au fost efectuate studii pentru a determina nivelul interferenței de la diferiți compuși.

Au fost testate următoarele nivele ale lipazei : 30, 60 și 240 U/L.

Nu este definită nicio interferență semnificativă printr-o recuperare $\leq \pm 10\%$ din valoarea inițială.

Bilirubină neconjugată: Nicio interferență semnificativă până la 30.0 mg/dL (513 μ mol/L).

Bilirubină conjugată: Nicio interferență semnificativă până la 29.5 mg/dL (504 μ mol/L).

Hemoglobină : Nicio interferență semnificativă până la 50 mg/dL.

Trigliceride : Nicio interferență semnificativă până la 3 000 mg/dL (33.90 mmol/L).

Acid ascorbic: Nicio interferență semnificativă până la 20 mg/dL.

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

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

Nu utilizați probe hemolizate.

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglobulinemia Waldenstrom) poate duce la rezultate nefiabile. ⁽⁵⁾

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽⁶⁻⁷⁾

- Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 28 zile

Frecvența calibrării: 28 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit și după o operație de întreținere.

DECLARAREA INCIDENTULUI GRAV

Vă rugăm să notificați producătorul (prin intermediul distribuitorului dumneavoastră) și autoritatea competentă a Statului Membru din Uniunea Europeană în care este stabilit utilizatorul și/sau pacientul, cu privire la orice incident grav care a avut loc legat de dispozitiv. Pentru alte jurisdicții, declararea incidentului grav trebuie să fie în conformitate cu cerințele reglementare locale, statale și federale.

Prin raportarea unui incident grav, furnizați informații care pot contribui la siguranța dispozitivelor medicale *in vitro*.

ASISTENȚĂ TEHNICĂ

Contactați distribuitorul dumneavoastră local sau ELITech Clinical Systems SAS (ccsupport@elitechgroup.com).

BIBLIOGRAFIE

1. Dufour, D.R., *The Pancreas: Function and Chemical Pathology, Clinical Chemistry: Theory Analysis, Correlation*, 5th Ed., Kaplan, L.A., Pesce, A.J., (Mosby Inc. eds), (2010), 651 and appendix.
2. Panteghini, M. & Bais, R., *Enzymes, Tietz Fundamentals of Clinical Chemistry*, 6th Ed., Burtis, C.A., Ashwood, E.R., Bruns, D.E., (W.B. Saunders eds.), (2008), 317.
3. Guder, W.G., et al., *Use of anticoagulants in diagnostic laboratory investigations and stability of blood, plasma and serum samples*. (2002). WHO/DIL/LAB/99.1 Rev.2.
4. Wu, A.H.B., *Clinical guide to laboratory tests*, 4th Ed., (W.B. Saunders eds.), (2006), 676.
5. 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.
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7. Young, D.S., *Effects of drugs on clinical laboratory tests*, 4th Ed., AACC Press, (1995).

☞ SIMBOLURI

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ELITech Clinical Systems SAS

Zone Industrielle-61500 SEES Franța

www.elitechgroup.com

NOTĂ :

LPSL



Lipase
820

1
PIT-LPSL

- Vezi § **PROCEDURĂ** : Este necesara introducerea manuala

☞ - **Instrucțiuni speciale de programare** :
Vezi § **INSTALARE ȘI UTILIZARE**

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 :

- Os produtos seja estável 2 semanas a 2-8°C ou 10 semanas a -20°C.

- Esses produtos devem ser tampados imediatamente e firmemente para evitar contaminação e evaporação.

PROCEDIMENTO

Para usar HDL LDL CALIBRATOR, siga o procedimento descrito nas instruções de uso do reagente ELITech Clinical Systems utilizado.

LIMITAÇÕES

O uso de HDL LDL CALIBRATOR foi validado com o sistema ELITech (analisador e reagentes utilizados para a determinação quantitativa de colesterol HDL ou LDL (Ref. CHDL-XXXX or CLDL-XXXX)).

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 permitam a importação de dados para testes, calibradores e controles, use 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 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 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 seu distribuidor local ou com a ELITech Clinical Systems SAS. (CSsupport@elitechgroup.com).

ΕΛΛΗΝΙΚΑ - EL

ΠΡΟΒΛΕΠΟΜΕΝΗ ΧΡΗΣΗ

To en λόγω διαγνωστικό *in vitro* προορίζεται για την βαθμονόμηση αντιδραστηρίων της ELITech Clinical Systems, χρησιμοποιούμενο για τον ποσοτικό προσδιορισμό του χοληστερίνου HDL ή LDL.

To en λόγω διαγνωστικό *in vitro* προορίζεται για επαγγελματική χρήση.

ΣΥΣΤΑΣΗ

- Τα λυοφιλοποιημένα προϊόντα που ετοιμάζονται για ανθρώπινο ορό.

- Οι συγκεντρώσεις των HDL και LDL για τον συγκεκριμένο βαθμονομητή εξαρτώνται από την παρτίδα.

ΑΠΑΙΤΟΥΜΕΝΑ ΥΛΙΚΑ ΠΟΥ ΔΕΝ ΣΥΜΠΕΡΙΛΑΜΒΑΝΟΝΤΑΙ

- Αντιδραστήριο της ELITech Clinical Systems που χρησιμοποιείται για ποσοτικό προσδιορισμό χοληστερίνου HDL ή LDL. (Ref. CHDL-XXXX or CLDL-XXXX).

- Γενικός Εργαστηριακός Εξοπλισμός.

ΙΧΝΗΛΑΣΙΜΟΤΗΤΑ

Ο βαθμονομητής HDL LDL είναι ανιχνεύσιμος με την εγκεκριμένη μέθοδο αναφοράς του CDC (Κέντρο Ελέγχου Λοιμώξεων και Πρόληψης).

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 ρυθμίσεις CE. 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 συνήθειες 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

- Ανοίξτε προσεκτικά το φιαλίδιο, αποφεύγοντας την απώλεια της λυοφιλωμένης ουσίας.

- Προσθέστε ακριβώς 1 mL απεσταγμένου/αποιονισμένου νερού.

- Κλείστε με προσοχή το φιαλίδιο και διαλύστε το περιεχόμενο εντελώς ανακατεύοντας ελαφρά, αποφεύγοντας την δημιουργία αφρού.

- Να κρατηθεί σε θερμοκρασία δωματίου για 30 λεπτά πριν τη χρήση.

ΑΛΛΟΙΩΣΗ ΤΟΥ ΠΡΟΪΟΝΤΟΣ

- Μετά την ανασύσταση : Ο προϊόν μπορεί να παρουσιάσει 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 τη ανασύσταση :

- Αποθηκεύστε στους 2-8oC και προστατέψτε από το φως.

- Μην χρησιμοποιείτε μετά τις ημερομηνίες λήξης που αναφέρονται στις ετικέτες των φιαλιδίων.

Κατόπιν ανασύστασης :

- Τα προϊόντα είναι σταθερά 2 μέρες στους 2-8oC και για 10 μήνες στους -20oC.

- Στα εν λόγω προϊόντα πρέπει το πώμα να τοποθετείται αμέσως και σφικτά προς αποφυγή μόλυνσης και εξάμιση.

ΔΙΑΔΙΚΑΣΙΑ

Για την χρήση HDL LDL CALIBRATOR, ακολουθείστε την περιγραφόμενη διαδικασία στις οδηγίες χρήσης του αντιδραστηρίου της ELITech Clinical Systems που χρησιμοποιείται.

ΠΕΡΙΟΡΙΣΜΟΙ

Την χρήση HDL LDL CALIBRATOR έχει επικυρωθεί με τα συστήματα ELITech (Αναλυτές και αντιδραστήρια που χρησιμοποιούνται για τον ποσοτικό προσδιορισμό του χοληστερίνου HDL ή LDL (Ref. CHDL-XXXX or CLDL-XXXX)).

Η χρήση οποιουδήποτε άλλου συστήματος πρέπει να επικυρωθεί από το εργαστήριο

ΤΙΜΕΣ

Οι συγκεντρώσεις υποδεικνύονται στο φύλλο τιμών που συμπεριλαμβάνεται στο κιτ.

Για να επιτρέπεται η εισαγωγή δεδομένων, τεστ, βαθμονομητών και ορών ελέγχου στους χρήστες μηχανημάτων Selectra, χρησιμοποιήστε τον ανάλογο γραμμικό κώδικα διαβάσιμο 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 συμβάλουν στην ασφάλεια των *in vitro* ιατρικών μηχανημάτων.

ΤΕΧΝΙΚΗ ΒΟΗΘΕΙΑ

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

SYMBOLS/ 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, εκτός από αυτά που παρουσιάζονται παρακάτω.

	Contenu Content Contilene Conteúdo περιεχόμενο
	Calibrant Calibrator Calibrador Calibrador Βαθμονομητής
	Reconstituer avec x mL Reconstitute with x mL Reconstituir con x mL Reconstituir com x mL Ανασύσταση με x mL
	Ajouter précisément 1 mL d'eau distillée ou déionisée Add exactly 1 mL of distilled or deionised water Agregar exactamente 1 mL de agua destilada o de agua desionizada Acrescentar exactamente 1 mL água destilada ou desionizada Προσθέστε ακριβώς 1 mL απεσταγμένου/αποιονισμένου νερού
	Conservar à température ambiante pendant 30 minutes avant utilisation Keep at room temperature for 30 minutes before use Conservar a temperatura ambiente durante 30 minutos antes de utilizar 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 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 μέρες 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 εξάμιση.
	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
	Conformité Européenne European Conformity Conformidad Europea Conformidade Europeia Ευρωπαϊκή Συμμόρφωση



☞Referințe:
ALBU-0250
ALBU-0600
ALBU-0700

Compoziția 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.

☞SEMNIFICAȚIE CLINICĂ⁽¹⁻³⁾

Albumina este sintetizată în special de ficat și reprezintă aproximativ 50% din proteinele plasmatică. Funcția principală a albuminei este menținerea presiunii oncotice și transportul unui număr mare de compuși. Măsurarea albuminei serice sau plasmatică este indicată în special pentru a ajuta la diagnosticarea și monitorizarea bolilor cu pierdere de proteine sau sinteză scăzută (sindromul nefrotic, pierderea gastrointestinală, insuficiența hepatică), inflamația acută și cronică, și malnutriția severă.

☞METODĂ⁽⁴⁾

Verde de bromocresol (BCG). Punct final

PRINCIPIU⁽⁴⁾

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

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

☞COMPOZIȚIA 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 utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

☞AVERTISMENTE ȘI PRECAUȚII

- Acest dispozitiv de diagnostic *in vitro* (Reactiv și Standardul) este destinat numai pentru uz profesional.
- Standardul conține azidă de sodiu care poate reacționa cu plumbul sau instalațiile din cupru pentru a forma potențiale azide metalice explozive. În momentul eliminării acestui standard, spălați întotdeauna cu apă din abundență pentru a preveni acumularea de azide.
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Standardul trebuie să fie imediat închis cu capacul pentru a preveni contaminarea și evaporarea.
- Pentru mai multe informații, Fișa de date privind siguranța (SDS) este disponibilă la cerere pentru utilizatorul profesional.

☞STABILITATEA

A se depozita la 2-25°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii și Standardul sunt gata pentru utilizare.

☞DETERIORAREA PRODUSELOR

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

☞PROBE

Specimen⁽²⁾

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

Avertismente și precauții

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

Depozitare⁽¹⁾

- Analizați serul proaspăt sau stocați-le la 2-8°C mai puțin de 72 de ore.
- Stocate la -20°C, probele sunt stabile 6 luni. Pentru o depozitare mai îndelungată, probele sunt înghețate la -70°C.

☞VALORI DE REFERINȚĂ⁽¹⁾

Ser, plasmă:

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

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

ALBUMIN

☞ Referințe:
ALBU-0250
ALBU-0600
ALBU-0700

Compoziția 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

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems, aplicațiile sunt disponibile la cerere.
Lungime de undă 620 nm
Temperatură: 37°C
Citiți 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

Amestecați și citiți absorbanțele (A) după o incubare de 4 minute și 30 de secunde.

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

☞ CALCUL

A Sample
_____ x n n = calibrator/standard concentration
A Standard/
Calibrator

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

☞ CALIBRARE

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

Valorile concentrației Standardului Albumin 3.5 g/dL și calibratorului multiparametric ELICAL 2 sunt trasabile conform materialului de referință ERM-DA 470k.

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

☞ CONTROLUL CALITĂȚII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum ELITROL I și ELITROL II. Aceste controale trebuie efectuate și validate înainte ca probele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform reglementărilor locale.

☞ MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale.

☞ DATE DE PERFORMANȚĂ la 37°C 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 și 6.0 g/dL (de la 16 la 60 g/L).

- Limita de detecție (LoD) și 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⁾.

	n	Medie		În interiorul ciclului	Total
		g/dL	g/L		
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

- Corelație

A fost efectuat un studiu comparativ între un analizor ELITech Clinical Systems ProM și un sistem similar disponibil în comerț (metoda BCG) pe eşantioane de ser uman 100 determinată conform protocolului CLSI EP9-A2⁽⁸⁾.

Concentrațiile eşantioanelor au fost între 1.43 și 5.89 g/dL (14.3 – 58.9 g/L).

Rezultatele sunt după cum urmează:

Coeficient de corelație: (r)=0.997

Regresie liniară: y = 0.961x + 0.12 g/dL (1.2 g/L)

- Limitări și interferențe

- Nu raportați rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2⁽⁹⁾. Recuperarea este în intervalul ±10% din valoarea inițială a activității Albumina de 3.5 și 5.00 g/dL.

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

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

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

Trigliceride: Nicio interferență semnificativă până la 3000 mg/dL (33.90 mmol/L).

Acid ascorbic: Nicio interferență semnificativă până la 20.0 mg/dL.

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

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

Gamma globulină: Nicio interferență semnificativă până la 1500 mg/dL.

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

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽¹¹⁻¹²⁾

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

ALBUMIN

☞ Referințe:
 ALBU-0250
 ALBU-0600
 ALBU-0700

Compoziția 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

- **Stabilitatea la bord/Frecvența calibrării**

Stabilitatea la bord: 28 zile

Frecvența calibrării: 28 zile





Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit și după o operație de întreținere.

☞ **BIBLIOGRAFIE**

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

☞ **SIMBOLURI**

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

	Conținut
	Reactiv
	Standard
	Conformitate europeană
☞	Modificare față de versiunea precedentă

Notă

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



Albumin. 0
 101 PIT-ALBU

Referințe:

ALSL-0250	8 x 25 mL
ALSL-0455	4 x 55 mL
ALSL-0410	2 x 62,5 mL
ALSL-0430	4 x 62,5 mL
ALSL-0510	5 x 125 mL

Compoziția trusei:

R1	8 x 20 mL + R2 8 x 5 mL
R1	4 x 44 mL + R2 4 x 11 mL
R1	2 x 50 mL + R2 1 x 26 mL
R1	4 x 50 mL + R2 2 x 26 mL
R1	5 x 100 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 și plasmă.

SEMNIFICAȚIE CLINICĂ ^(1-3,6)

Alaninaminotransferaza (ALT), cunoscută și 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 și rinichi, și cele mai mici cantități în inimă și mușchii scheletici. Concentrația ALT este crescută când celulele hepatice sunt deteriorate (necroză celulară hepatică sau leziune de orice cauză). Într-adevăr, hepatita virală și toxică induce o creștere marcată a activității ALT în ser. Aportul de alcool, delirium tremens, și administrarea diverselor medicamente induc creșterea ușoară sau moderată a ALT. Concentrația ALT în ser este, de asemenea, crescută ușor în diverse afecțiuni precum: distrofia musculară, boala hemolitică, infarctul miocardic...

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

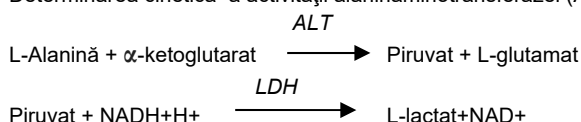
Nivelul ALT din ser poate fi scăzut în cazul deficienței de vitamina B6.

METODĂ ⁽⁴⁾

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

PRINCIPIU ⁽⁴⁾

Determinarea cinetică a activității alaninaminotransferazei (ALT).



LDH=lactat dehidrogenază

COMPOZIȚIA 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.
- Soluție salină obișnuită (NaCl 9 g/L).
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Acest reactiv este conceput doar pentru utilizarea în scopul diagnosticării *in vitro*.
- Acești reactivi conțin azidă de sodiu care poate reacționa cu plumbul sau instalațiile sanitare din cupru și poate forma azide metalice explozibile. În cazul aruncării acestor reactivi, spălați întotdeauna cu cantități mari de apă pentru a preveni formarea de azide.
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Nu interschimbați fiolele de reactiv din truse diferite.
- Pentru mai multe informații, consultați Fișa de date privind siguranța (SDS).

STABILITATEA REACTIVILOR

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA REACTIVILOR

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

AMBALAJ DETERIORAT

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

PROBE ^(1,5)

Specimen

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

Avertisment și precauții

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



Referințe:

ALSL-0250	8 x 25 mL
ALSL-0455	4 x 55 mL
ALSL-0410	2 x 62,5 mL
ALSL-0430	4 x 62,5 mL
ALSL-0510	5 x 125 mL

Compoziția trusei:

R1 8 x 20 mL + R2 8 x 5 mL
R1 4 x 44 mL + R2 4 x 11 mL
R1 2 x 50 mL + R2 1 x 26 mL
R1 4 x 50 mL + R2 2 x 26 mL
R1 5 x 100 mL + R2 1 x 127 mL



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

Depozitare

Eșantioanele sunt stabile timp de 3 zile la temperatura camerei și 7 zile la 2-8°C. Stabilitatea ALT este menținută mai bine la -70°C.

VALORI DE REFERINȚĂ (1,4)

Bărbați: ≤ 45 U/L

Femei: ≤ 34 U/L

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems.

Aplicațiile sunt disponibile la cerere

Lungime de undă 340 nm

Temperatură 37°C

Citiți pe reactivul maror.

Reactiv R1	240 μL
Proba	15 μL

Amestecați și așteptați 4 minute și 43 de secunde incubația.

Reactiv R2	60 μL
-------------------	-------

Amestecați și așteptați o incubație de 50 de secunde, măsurați modificarea absorbantei pe minut (ΔA/min.) timp de 159 de secunde.

- Cu software-ul Selectra TouchPro, utilizați aplicația 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, aplicația conține o alarmă specifică pentru a avertiza utilizatorii.

CALCUL

(ΔA) Proba x n n=concentrație 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 referință IFCC (6).

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați și DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I (control normal) și ELITROL II (control patologic). Aceste controale trebuie efectuate și validate înainte ca probele pacienților să fie testate. Frecvența controlului trebuie

să fie de cel puțin o dată pe zi, după fiecare calibrare, și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele locale și legale.

DATE DE PERFORMANȚĂ 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 și 450,0 U/L (de la 0,17 la 7,50 μkat/L). Probele care depășesc 450,0 U/L trebuie să fie diluate 1:10 cu soluție de NaCl 9 g/L (salină normală) și 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, funcția „reluare diluare” efectuează diluția automată a eșantionului. Rezultatele iau în considerare diluția.

- Limita de detecție (LoD) și 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).

	n	Medie		În interiorul ciclului	Total
		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

- Corelație

A fost efectuat un studiu comparativ între Analizorul Selectra ProM ELITech Clinical Systems și un alt echipament al unui sistem aprobat de FDA (metoda IFCC) pe 100 de eșantioane de ser uman conform protocolului CLSI EP9-A2(10).

Valorile acoperă domeniul de măsurare.

Parametrii regresiei liniare sunt după cum urmează:

Coeficient de corelație: (r)= 0,996

Regresie liniară: y= 1,017x + 0,6 U/L (0,01 μkat/L)

Referințe:

ALSL-0250	8 x 25 mL
ALSL-0455	4 x 55 mL
ALSL-0410	2 x 62,5 mL
ALSL-0430	4 x 62,5 mL
ALSL-0510	5 x 125 mL

Compoziția trusei:

R1 8 x 20 mL + R2 8 x 5 mL
R1 4 x 44 mL + R2 4 x 11 mL
R1 2 x 50 mL + R2 1 x 26 mL
R1 4 x 50 mL + R2 2 x 26 mL
R1 5 x 100 mL + R2 1 x 127 mL



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- Limitări și interferențe

- Eșantioanele hemolizate nu trebuie să fie utilizate deoarece hemoliza semnificativă poate crește concentrația ALT din cauza nivelului ridicat de ALT în eritrocite.

- Nu raportați rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2 ⁽¹¹⁾ al CLSL. Recuperarea este în intervalul ±10% din valoarea inițială a lipazei de 35,0 și 350,0 U/L.

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

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

Trigliceride: Nicio interferență semnificativă până la 2300 mg/dL (25,99 mmol/L).

Piruvat: Nicio interferență semnificativă până la 3,0 mg/dL.

Acid ascorbic: Nicio interferență semnificativă până la 20 mg/dL.

Acid acetilsalicilic: Nicio interferență semnificativă până la 200,0 mg/dL.

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

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

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young și Glick. ⁽¹³⁻¹⁴⁾

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

- Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 28 de zile

Frecvența calibrării: 28 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit, și după o operație de întreținere.

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







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SIMBOLURI

	Dispozitiv medical de diagnosticare in vitro.
	Consultați instrucțiunea de utilizare.
	Producător
	Limită de temperatură
	Număr de lot
	Data expirării
	Număr catalog
	Conținut
	Reactiv 1
	Reactiv 2
	Conformitate europeană

ALT/GPT 4+1 SL

Referințe:

ALSL-0250	8 x 25 mL
ALSL-0455	4 x 55 mL
ALSL-0410	2 x 62,5 mL
ALSL-0430	4 x 62,5 mL
ALSL-0510	5 x 125 mL

Compoziția trusei:

R1 8 x 20 mL + R2 8 x 5 mL
R1 4 x 44 mL + R2 4 x 11 mL
R1 2 x 50 mL + R2 1 x 26 mL
R1 4 x 50 mL + R2 2 x 26 mL
R1 5 x 100 mL + R2 1 x 127 mL



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Notă

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



ALT (GPT)
140

1
PIT-ALSL

:Modificare față de versiunea precedentă.

AMYLASE SL

Referințe:

AMSL-0230	6 x 20 mL
AMSL-0390	1 x 50 mL
AMSL-0400	6 x 50 mL

Compoziția trusei:

R 6 x 20 mL
R 1 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 și plasmă pentru diagnosticare *in vitro*.

SEMNIFICAȚIE CLINICĂ⁽¹⁻²⁾

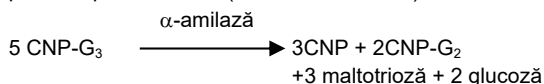
α -amilaza este o enzimă de origine pancreatică sau salivară care hidrolizează legăturile 1,4- α -glucozidice, ajutând astfel la digestia amidonului. Analiza amilazei serice este utilizată în special în diagnosticarea bolilor pancreatice (pancreatită acută sau cronică și complicațiile acestora, carcinoame).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

METODĂ⁽³⁾

Substrat: CNP-G₃ (2-cloro-4-nitrofenil- α -maltotriozidă)
 Enzimatică, cinetică

PRINCIPIU⁽³⁾

Substratul CNP-G₃ este hidrolizat prin acțiunea catalitică a α -amilazei pentru a produce CNP (2-cloro-4-nitrofenol).



CNP-G₂ = 2-cloro-4-nitrofenil- α -maltozidă

Rata de creștere a absorbanței este măsurată la 405 nm și este direct proporțională cu activitatea α -amilazei în probă,

COMPOZIȚIA 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-G ₃	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.
- Soluție salină obișnuită (NaCl 9 g/L).
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Această trusă de reactiv este concepută doar pentru utilizarea profesională în scopul diagnosticării *in vitro*.
- În contact cu acizi, degajă un gaz toxic.
- Reactivul conține azidă de sodiu, care poate reacționa cu plumbul sau instalațiile sanitare din cupru și poate forma azide metalice explozibile. În cazul aruncării acestor reactivi, spălați întotdeauna cu cantități mari de apă pentru a preveni formarea de azide.
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Saliva și transpirația conține amilază. Astfel, se recomandă purtarea mănușilor și a unei măști pentru a evita contaminarea reactivului.
- Fișa cu date de securitate disponibilă la cerere.

STABILITATEA REACTIVILOR

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.
 (Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA REACTIVILOR

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

AMBALAJ DETERIORAT

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

PROBE⁽⁴⁾

Specimen

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

Avertisment și precauții

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

Depozitare și stabilitate

Probele sunt stabile timp de 1 săptămână la temperatura camerei, 1 săptămână la 2-8°C, și 1 an la -20°C.

VALORI DE REFERINȚĂ⁽⁵⁾

Ser, plasmă (37°C): 31-107 U/L

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.



AMYLASE SL

Referințe:

AMSL-0230	6 x 20 mL
AMSL-0390	1 x 50 mL
AMSL-0400	6 x 50 mL

Compoziția trusei:

R 6 x 20 mL
R 1 x 50 mL
R 6 x 50 mL

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



PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems.

Aplicațiile sunt disponibile la cerere
Lungime de undă 405 nm
Temperatură 37°C
Citiți pe reactivul martor.

Reactiv R	300 µL
Probă	3 µL

Amestecați și după o incubare de 50 de secunde, măsurați modificarea absorbanței pe minut ($\Delta A/\text{min.}$) timp de 159 de secunde.

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

CALCUL

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

Factor de conversie: U/L x 0,0167 = $\mu\text{kat/L}$

CALIBRARE ⁽⁵⁾

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

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Pentru a asigura precizia analizelor, vor fi utilizate serurile de control precum ELITROL I (control normal) și ELITROL II (control patologic). Aceste controale trebuie efectuate și validate înainte ca probele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare și trebuie adaptată procedurilor de Controlul Calității fiecărui laborator și cerințelor reglementarilor în 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 calității trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele locale și legale.

DATE DE PERFORMANȚĂ 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 și 1500 U/L (de la 0,33 la 25,00 $\mu\text{kat/L}$). Probele care depășesc 1500 U/L trebuie să fie diluate 1:10 cu soluție de NaCl 9 g/L (salină normală) și re-analizate. Utilizarea acestei proceduri extinde intervalul de măsurare de la 1500 la 15000 U/L (de la 25,00 la 250,00 $\mu\text{kat/L}$).

Pentru utilizatorii Selectra TouchPro, funcția „diluare” efectuează diluția automată a probei. Rezultatele iau în considerare diluția.

- Limita de detecție (LoD) și Limita de cuantificare (LoQ)

Determinată conform protocolului CLSI EP17-A⁽⁷⁾.
LoD = 6 U/L (0,10 $\mu\text{kat/L}$).
LoQ = 13 U/L (0,22 $\mu\text{kat/L}$).

- Precizie

Determinată conform protocolului CLSI EP5-A2⁽⁸⁾.

	n	Medie		În interiorul ciclului	Total
		U/L	$\mu\text{kat/L}$	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

- Corelație

A fost efectuat un studiu comparativ între Analizorul Selectra ProM ELITech Clinical Systems și 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 și 1439 U/L (între 0,35 și 23,98 $\mu\text{kat/L}$).

Parametrii regresiei liniare sunt după cum urmează:

Coeficient de corelație: $(r)=0,999$

Regresie liniară: $y=0,976x - 1 \text{ U/L (0,02 } \mu\text{kat/L)}$

- Limitări și interferențe

- Nu raportați rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2⁽¹⁰⁾ al CLSL. Recuperarea este în intervalul $\pm 10\%$ din valoarea inițială a amilasa de 80 U/L și 1000 U/L.

Trigliceride: Nicio interferență semnificativă până la 3000 mg/dL (33,9 mmol/L).

Bilirubină neconjugată: Nicio interferență semnificativă până la 30,0 mg/dL (513 $\mu\text{mol/L}$).

Bilirubină conjugată: Nicio interferență semnificativă până la 29,5 mg/dL (504 $\mu\text{mol/L}$).

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

Acid ascorbic: Nicio interferență semnificativă până la 20,0 mg/dL.

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

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

- În cazuri foarte rare, gamopatiile monoclonale (mieloame multiple), în special de tipul IgM (macroglubulinemia Waldenstrom) poate duce la rezultate nefiabile. ⁽¹¹⁾

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽¹²⁻¹³⁾

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



AMYLASE SL

Referințe:

AMSL-0230	6 x 20 mL
AMSL-0390	1 x 50 mL
AMSL-0400	6 x 50 mL

Compoziția trusei:

R 6 x 20 mL
R 1 x 50 mL
R 6 x 50 mL

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


Stabilitatea la bord/Frecvența calibrării
Stabilitatea la bord: 28 de zile











Frecvența calibrării: 28 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit și după o operație de întreținere.

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

SIMBOLURI


	Dispozitiv medical de diagnosticare <i>in vitro</i> .
	Consultați instrucțiunea de utilizare.
	Producător
	Limită de temperatură
	Număr de lot
	Data expirării
	Număr catalog
	Conținut
	Reactiv
	Conformitate europeană

Notă

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


 Amylase IFCC
 165

 0
 PIT-AMSL

 Modificare față de versiunea precedentă.


AST/GOT 4+1 SL

Referințe:

ASSL-0250	8 x 25 mL
ASSL-0455	4 x 55 mL
ASSL-0410	2 x 62,5 mL
ASSL-0430	4 x 62,5 mL
ASSL-0510	5 x 125 mL

Compoziția trusei:

R1 8 x 20 mL + R2 8 x 5 mL
R1 4 x 44 mL + R2 4 x 11 mL
R1 2 x 50 mL + R2 1 x 26 mL
R1 4 x 50 mL + R2 2 x 26 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 și plasmă pentru diagnosticare *in vitro*.

SEMNIFICAȚIE CLINICĂ⁽¹⁻⁴⁾

Aspartat aminotransferaza (AST), cunoscută și 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, mușchii scheletici și rinichi.

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

Următoarele stări patologice sunt exemple ale afecțiunilor care duc, de asemenea, la o creștere a activității enzimatice: necroza celulelor ficatului sau leziunea de orice cauză (de exemplu aportul de alcool, delirium tremens, și administrarea diverselor medicamente induc creșterea moderată a AST), hepatita alcoolică, distrofia musculară și gangrena, mononucleoza infecțioasă, pancreatita acută, afecțiunile cardiace precum miocardita sau pericardita, emboliile pulmonare...

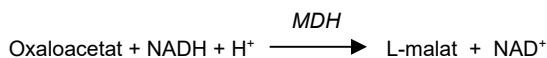
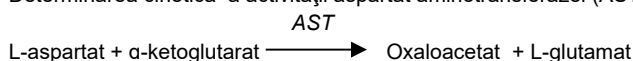
Nivelul AST în ser poate fi redus în cazul deficienței de vitamina B6.

METODĂ⁽⁵⁾

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

PRINCIPIU⁽⁵⁾

Determinarea cinetică a activității aspartat aminotransferazei (AST).



MDH=malat dehidrogenază

COMPOZIȚIA

Reactiv 1: R1

Tampon Tris, pH 7,80 (30°C)	100 mmol/L
L-aspartat	330 mmol/L
LDH	≥ 2000 U/L
MDH	≥ 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
- Soluție salină obișnuită (NaCl 9 g/L).
- Echipamente generale de laborator.
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Acest reactiv este conceput doar pentru utilizarea în scopul diagnosticării *in vitro*.
- Acești reactivi conțin azidă de sodiu care poate reacționa cu plumbul sau instalațiile sanitare din cupru și poate forma azide metalice explozibile. În cazul aruncării acestor reactivi, spălați întotdeauna cu cantități mari de apă pentru a preveni formarea de azide.
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Nu interschimbați fiolele de reactiv din truse diferite.
- Pentru mai multe informații, Fișa de date privind siguranța (SDS) este disponibilă la cerere pentru utilizatorul profesional.

STABILITATEA

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

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

PROBE^(2,6)

Specimen

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

Avertisment și precauții

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



AST/GOT 4+1 SL

Referințe:

ASSL-0250	8 x 25 mL
ASSL-0455	4 x 55 mL
ASSL-0410	2 x 62,5 mL
ASSL-0430	4 x 62,5 mL
ASSL-0510	5 x 125 mL

Compoziția trusei:

R1 8 x 20 mL + R2 8 x 5 mL
R1 4 x 44 mL + R2 4 x 11 mL
R1 2 x 50 mL + R2 1 x 26 mL
R1 4 x 50 mL + R2 2 x 26 mL
R1 5 x 100 mL + R2 1 x 127 mL



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

Depozitare și stabilitate

Eșantioanele sunt stabile timp de 24 de ore la temperatura camerei, 7 zile la 2-8°C, și 3 luni la -20°C.

VALORI DE REFERINȚĂ (2,3)

Ser. plasmă (37°C): <40 U/L

Valorile de referință pentru infanți sunt mai mari decât pentru adulți.

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems.

Aplicațiile sunt disponibile la cerere

Lungime de undă 340 nm

Temperatură 37°C

Citiți pe reactivul martor.

Reactiv R1	240 µL
Proba	15 µL

Amestecați și așteptați o incubație de 4 minute și 43 de secunde, apoi adăugați:

Reactiv R2	60 µL
-------------------	-------

Amestecați și așteptați o incubație de 50 de secunde, măsurând modificarea absorbăției per minut ($\Delta A/\text{min}$) timp de 159 de secunde.

- Cu software-ul Selectra TouchPro, utilizați aplicația 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, aplicația conține o alarmă specifică pentru a avertiza utilizatorii.

CALCUL

$(\Delta A) \text{ Proba} \times n$ $n = \text{concentrație calibrator}$

$(\Delta A) \text{ Calibrator}$

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 referință IFCC⁽⁶⁾.

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I și ELITROL II. Aceste controale trebuie efectuate și validate înainte ca probele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare, și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale.

DATE DE PERFORMANȚĂ 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 și 450,0 U/L (de la 0,17 la 7,50 µkat/L). Probele care depășesc 450,0 U/L trebuie să fie diluate 1:10 cu soluție de NaCl 9 g/L (salină normală) și 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, funcția „dilute” efectuează diluția automată a eșantionului. Rezultatele iau în considerare diluția.

- Limita de detecție (LoD) și 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⁾.

	n	Medie		În interiorul ciclului	Total
		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

- Corelație

A fost efectuat un studiu comparativ între Analizorul Selectra ProM ELITech Clinical Systems și un alt echipament al unui sistem aprobat de FDA (metoda IFCC fără piridoxal fosfat) pe 114 de eșantioane de ser uman conform protocolului CLSI EP9-A2⁽¹⁰⁾.

Valorile acoperă domeniul de măsurare.

Parametrii regresiei liniare sunt după cum urmează:

Coefficient de corelație: (r)=0,999

Regresie liniară: $y = 0,927 x - 0,3 \text{ U/L (0,01 } \mu\text{kat/L)}$.

- Limitări și interferențe

- Eșantioanele hemolizate nu trebuie să fie utilizate deoarece hemoliza semnificativă poate crește concentrația AST din cauza nivelurilor ridicate de AST în eritrocite.

- Nu raportați rezultatele în afara intervalului utilizabil.

Referințe:

ASSL-0250	8 x 25 mL
ASSL-0455	4 x 55 mL
ASSL-0410	2 x 62,5 mL
ASSL-0430	4 x 62,5 mL
ASSL-0510	5 x 125 mL

Compoziția trusei:

R1 8 x 20 mL + R2 8 x 5 mL
R1 4 x 44 mL + R2 4 x 11 mL
R1 2 x 50 mL + R2 1 x 26 mL
R1 4 x 50 mL + R2 2 x 26 mL
R1 5 x 100 mL + R2 1 x 127 mL



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

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2 ⁽¹¹⁾ al CLSL și recomandările SFBC⁽¹²⁾. Recuperarea este în intervalul ±10% din valoarea inițială a activității AST de 35,0 U/L și 350,0 U/L.

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

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

Trigliceride: Nicio interferență semnificativă până la 2400 mg/dL (27,12 mmol/L) echivalent trigliceride.

Piruvat: Nicio interferență semnificativă până la 3 mg/dl.

Acid ascorbic: Nicio interferență semnificativă până la 20 mg/dL.

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

Acetaminofen: Nicio interferență 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 substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽¹⁴⁻¹⁵⁾
- Rezultatele acestui studiu trebuie interpretate doar în conjuncție cu aste rezultate ale testelor de diagnosticare, constatările clinice și istoricul medical al pacientului.

Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 28 de zile

Frecvența calibrării: 28 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit, și după o operație de întreținere.

BIBLIOGRAFIE

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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).
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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 laboratory tests*, 4th Ed., AACC Press, (1995).

SIMBOLURI

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


	Conținut
	Reactiv 1
	Reactiv 2
	Conformitate europeană

Notă:

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


 ASAT (GOT)
180

 1
PIT-ASSL

: Modificare față de versiunea precedentă.



BILIRUBIN TOTAL & DIRECT 4+1

Referințe:

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

Compoziția 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



SCOPUL UTILIZĂRII

Pentru Bilirubină Totală: BILIRUBIN TOTAL 4+1 ELITech Clinical Systems este conceput pentru determinarea cantitativă a bilirubinei totale în serul uman și plasmă în cazul adulților și 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 și plasmă pentru diagnosticare *in vitro*.

SEMNIFICAȚIE CLINICĂ⁽¹⁻²⁾

Aproximativ 80-85% din bilirubina este produsă din fracțiunea hem a hemoglobinei eliberate de eritrocitele care îmbătrânesc în 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 și hidrolizată în tractul gastrointestinal.

Concentrația serului de bilirubină neconjugată crește în cazul supra-producerii de bilirubină (anemie hemolitică acută și cronică) și în cazul afecțiunilor metabolismului bilirubinei și defectelor de transport (aport afectat de celulele hepatice: sindromul Gilbert; defectele în reacția de conjugare: sindromul Crigler-Najjar). Excreția redusă (deteriorare hepatocelulară: hepatită, ciroză...; sindromul Dubin-Johnson și Rotor) și obstrucția fluxului biliar (cel mai adesea produsă de calculii biliari sau de tumori) induc o creștere importantă a bilirubinei conjugate și într-o măsură minoră o creștere a bilirubinei neconjugate (hiperbilirubinemia conjugată).

METODĂ⁽²⁾

Malloy-Evelyn modificată. Punct final.

PRINCIPIU⁽¹⁻²⁾

Acidul sulfanilic reacționează cu nitritul de sodiu pentru a forma acidul sulfanilic diazotat. În prezența acceleratorului (cetrimidă), bilirubina conjugată și neconjugată reacționează cu acidul sulfanilic diazotat pentru a forma azobilirubina (Bilirubina totală 4+1). În absența acceleratorului, doar bilirubina conjugată reacționează (Bilirubină directă 4+1). Creșterea absorbânței la 546 nm este proporțională cu concentrația bilirubinei.

Acidul sulfanilic + NaNO₂ → Acid sulfanilic diazotat

Bilirubină + Acid sulfanilic diazotat → Azobilirubină

COMPOZIȚIA 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
- Soluție salină obișnuită (NaCl 9 g/L)
- Echipamente generale de laborator.
- Analizor de biochimie echipat cu filtrele necesare. (Consultați § PROCEDURA).
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Acești reactivi sunt doar pentru utilizarea profesională, în scopul diagnosticării *in vitro*.
- Reactivii R1 conține acid sulfanilic. Poate provoca o reacție alergică.
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Nu interschimbați fiolele de reactiv din truse diferite.
- Fișa cu date de securitate disponibilă la cerere.

STABILITATEA

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

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

PROBE⁽³⁾

Specimen

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



BILIRUBIN TOTAL & DIRECT 4+1

Referințe:

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

Compoziția 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

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Avertisment și precauții

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

Depozitare și stabilitate

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

VALORI DE REFERINȚĂ ⁽⁴⁾

Ser, plasmă:

Bilirubină totală:

Adulți și 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 menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems,

aplicațiile sunt disponibile la cerere.

A) Bilirubină totală

Lungime de undă 546-700 nm

Temperatură: 37°C

Citiți pe reactivul martor.

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

Amestecați și citiți absorbanta (ΔA1) după o incubație de 4 minute 40 (proba martor), apoi adăugați:

Reactiv R2	60 μL
------------	-------

Amestecați și citiți absorbanta (ΔA2) după o incubație de 6 minute 30.

Cu software-ul Selectra TouchPro, utilizați aplicația inclusă în codul de bare disponibil la finalul acestei inserții.

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

B) Bilirubină directă

Lungime de undă 546 nm

Temperatură: 37°C

Citiți pe reactivul martor.

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

Amestecați și citiți absorbanta (A1) după o incubație de 4 minute 40 (proba martor), apoi adăugați:

Reactiv R2	60 μL
------------	-------

Amestecați și citiți absorbanta (A2) după o incubație de 50 de secunde.

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

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

CALCUL

A) Bilirubină totală

$(\Delta A2 - \Delta A1) \text{ Probă} \times \text{concentrație calibrator}$

$(\Delta A2 - \Delta A1) \text{ Calibrator}$

B) Bilirubină directă

$(A2 - A1) \text{ Probă} \times \text{concentrație calibrator}$

$(A2 - A1) \text{ Calibrator}$

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 referință SRM 916a (al Institutului Național de Standarde și Tehnologie).

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum ELITROL I (control normal) și ELITROL II (control patologic). Aceste controale trebuie efectuate și validate înainte ca probele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele locale, statale și federale.

DATE DE PERFORMANȚĂ la 37°C 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 și 25,00 mg/dL (de la 4,3 la 427,6 μmol/L). Probele care depășesc 25,00 mg/dL trebuie diluate 1:5 cu soluție de NaCl 9 g/l (soluție salină normală) și re-testate. Utilizarea acestei

BILIRUBIN TOTAL & DIRECT 4+1

Referințe:

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

Compoziția 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



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proceduri extinde intervalul de măsurare între 25,00 și 60,00 mg/dL (de la 427,6 la 1026,3 μmol/L).

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

- Limita de detecție (LoD) și 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⁾.

	n	Medie		În interiorul ciclului	Total
		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

- Corelație

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems și un alt echipament al sistemului aprobat de FDA (metoda DCA) pe 100 de probe de ser uman conform protocolului CLSI EP9-A2⁽⁸⁾.

Concentrațiile probelor au fost între 0,32 și 23,02 mg/dL (5,5 și 393,7 μmol/L).

Parametrii regresiiilor liniare sunt după cum urmează:

Coeficient de corelație: (r)=0,999

Regresie liniară: y= 0,948 x -0,11 mg/dL (1,9 μmol/L)

- Limitări și interferențe

- Nu raportați rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2⁽⁹⁾. Recuperarea este în intervalul ±15% din valoarea inițială a concentrației bilirubinei totale de 1,00 mg/dL și 15,00 mg/dL.

Trigliceride: Nicio interferență semnificativă până la 2100 mg/dL (23,73 mmol/L).

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

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

Acid ascorbic: Nicio interferență semnificativă până la 4 mg/dL.

Acid acetilsalicilic: Nicio interferență 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 substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽¹¹⁻¹²⁾

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

- Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 28 de zile

Frecvența calibrării: 28 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit și după o operație de întreținere.

B) Bilirubină directă

- Interval de măsurare

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

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

- Limita de detecție (LoD) și 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⁾.

	n	Medie		În interiorul ciclului	Total
		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

- Corelație

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems și un alt echipament al sistemului aprobat de FDA (metoda DCA) pe 100 de probe de ser uman conform protocolului CLSI EP9-A2⁽⁸⁾.

Concentrațiile probelor au fost între 0,09 și 10,52 mg/dL (1,5 și 179,9 μmol/L).

Parametrii regresiiilor liniare sunt după cum urmează:

Coeficient de corelație: (r)=0,998

Regresie liniară: y=0,926 x -0,03 mg/dL (0,5 μmol/L)

- Limitări și interferențe

- Concentrația acidului ascorbic mai mare de 0,5 mg/dL poate duce la rezultate fals pozitive ale bilirubinei directe.

- Nu raportați rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2⁽⁹⁾. Recuperarea este în intervalul ±15% din valoarea inițială a concentrației bilirubinei directe de 0,40 mg/dL și 4,00 mg/dL.

Trigliceride: Nicio interferență semnificativă până la 2000 mg/dL (22,60 mmol/L).

Hemoglobină: Nicio interferență semnificativă până la 125 mg/dL.

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



BILIRUBIN TOTAL & DIRECT 4+1

Referințe:

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

Compoziția 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



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Acid ascorbic: Nicio interferență semnificativă până la 0,5 mg/dL.

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

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

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽¹¹⁻¹²⁾

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

- Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 28 de zile

Frecvența calibrării: 28 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit și după o operație de întreținere.

SIMBOLURI

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

CONT	Conținut
R1	Reactiv 1
R2	Reactiv 2
CE	Conformitate europeană

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 :Modificare față de versiunea precedentă.



BILIRUBIN TOTAL & DIRECT 4+1

Referințe:

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

Compoziția 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

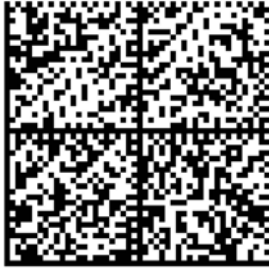
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BILIRUBINĂ DIRECTĂ 4+1:

NOTĂ IMPORTANTĂ

- Doar pentru ref. **BIDI-0250**, utilizată cu software-ul Selectra TouchPro.
- **Vezi ȘPROCEDURĂ:** 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



☞ Referințe:
CALA-0600
CALA-0250

Compoziția trusei:
R 2 x 125 mL + Std 1 x 5 mL
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 și urină.

SEMNIFICAȚIE CLINICĂ⁽¹⁻³⁾

În sânge, aproximativ 45% din calciul plasmatic este liber, 45% este legat de proteine, asociat în principal cu albumina și 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, contracția musculară și coagularea sângelui. Nivelurile de proteine serice sau albumina trebuie avute în vedere pentru interpretarea corespunzătoare a nivelurilor de calciu seric total. Hipocalcemia poate rezulta din insuficiența renală cronică cu hipoproteinemia și hiperfosfatemia, sau hipoparatiroidismul, sau deficiența 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 excepția tubulopatiilor renale.

METODĂ

Testul direct colorimetric complexometric (Arsenazo III).
Punct final.

PRINCIPIU⁽⁴⁾

La un pH ușor acid, ionii Ca²⁺ formează cu Arsenazo III (acid 2,7-bis(2-aronofenilazo))-1,8-dihidroxi-naftalen-3,6-disulfonic) un complex a cărui absorbanta este direct proporțională cu concentrația totală de calciu.

COMPOZIȚIA 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. (Consultați ȘI PROCEDURA).
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Acest dispozitiv de diagnostic *in vitro* (Reactiv și Standardul) este destinat numai pentru uz profesional.
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.

- Standardul trebuie să fie imediat închis cu capacul pentru a preveni contaminarea și evaporarea.
- Pentru mai multe informații, Fișa de date privind siguranța (SDS) este disponibilă la cerere pentru utilizatorul profesional.

STABILITATEA

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultați ȘI DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii și Standardul sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

- Reactivul și soluția standard trebuie să fie limpezi. Turbiditatea ar indica deteriorarea.
- Nu utilizați produsul dacă există semne vizibile de deteriorare biologică, chimică sau fizică.
- Nu utilizați reactivul dacă deteriorările ambalajului ar putea avea un efect asupra performanței produsului (scurgeri, folie perforată).

PROBE^(1,2,5)

Specimen

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

Avertismente și precauții

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

Depozitare

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

VALORI DE REFERINȚĂ^(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 funcție de ratele proteinei plasmatice.

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

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

☞ Referințe:
CALA-0600
CALA-0250

Compoziția trusei:
R 2 x 125 mL + Std 1 x 5 mL
R 12 x 20 mL



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

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems,

aplicațiile sunt disponibile la cerere.

Lungime de undă 660-700 nm

Temperatură: 37°C

Citiți pe reactivul maror.

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

Amestecați, așteptați 4 minute și 30 de secunde și apoi citiți absorbanta (A).

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

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

CALCUL

ΔA Proba

_____ x n n = concentrație calibrator/standard

ΔA Standard/
Calibrator

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

☞ CALIBRARE

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

Pentru referința CALA-0250: Pentru calibrare, utilizați calibratorul multiparametric ELICAL 2.

Valorile concentrației Standardului de calciu de 10 mg/dL și calibratorului multiparametric ELICAL 2 sunt trasabile conform Materialului Standard de Referință 956d (al Institutului Național de Standarde și Tehnologie).

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați și DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum ELITROL I și ELITROL II. Aceste controale trebuie efectuate și validate înainte ca probele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale.

DATE DE PERFORMANȚĂ la 37°C 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 și 15,00 mg/dL (de la 1,25 la 3,74 mmol/L).

b) Urină

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

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

- Limita de detecție (LoD) și 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

	n	Medie		În interiorul ciclului	Total
		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

	n	Medie		În interiorul ciclului	Total
		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

☞ - Corelație

a) Ser/Plasmă

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems și 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 și 15,53 mg/dL (1,33 și 3,87 mmol/L).

Parametrii regresii liniare sunt după cum urmează:

Coefficient de corelație: (r)=0,993

Regresie liniară: y=0,996x +0,43 mg/dL (0,11 mmol/L)

☞ Referințe:
CALA-0600
CALA-0250

Compoziția trusei:
R 2 x 125 mL + Std 1 x 5 mL
R 12 x 20 mL



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

b) Urină

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems și 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 și 17,99 mg/dL (0,39 și 4,49 mmol/L).

Parametrii regresii liniare sunt după cum urmează:

Coefficient de corelație: (r)=0,995

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

- Limitări și interferențe

- Nu raportați rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2⁽¹¹⁾.

a) Ser/Plasmă

Recuperarea este în intervalul $\pm 10\%$ din valoarea inițială a concentrației calciului de 8,00 mg/dL și 12,00 mg/dL.

Bilirubină neconjugată: Nicio interferență semnificativă până la 30,0 mg/dL (513 μ mol/L).

Bilirubină conjugată: Nicio interferență semnificativă până la 29,5 mg/dL (504 μ mol/L).

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

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

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

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

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

Acetaminofen: Nicio interferență 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 nefiabale.⁽¹²⁾

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young.⁽¹³⁻¹⁴⁾

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

b) Urină

Recuperarea este în intervalul $\pm 10\%$ din valoarea inițială a concentrației calciului de 4,00 mg/dL și 16,00 mg/dL.

Bilirubină conjugată: Nicio interferență semnificativă până la 29,5 mg/dL (504 μ mol/L).

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

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

Uree: Nicio interferență semnificativă până la 5000 mg/dL.

(832 mmol/L).

Acid uric: Nicio interferență semnificativă până la 100 mg/dL.

(5,9 mmol/L).

Magneziu: Nicio interferență semnificativă până la 1,0 mg/dL.

(4,1 mmol/L).

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

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young.⁽¹³⁻¹⁴⁾

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

- Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 28 de zile

Frecvența calibrării: 28 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit și după o operație de întreținere.

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CALCIUM ARSENAZO

☞ **Referințe:**

CALA-0600
CALA-0250

Compoziția trusei:






R 2 x 125 mL + **Std** 1 x 5 mL
R 12 x 20 mL



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SIMBOLURI

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

	Conținut
	Reactiv
	Standard
	Conformitate europeană
	Modificare față de versiunea precedentă

Notă:

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



Calcium New
245

0
PIT-CALA



Referințe:

CKSL-0230 4 x 25 mL
 CKSL-0410 2 x 62,5 mL
 CKSL-0430 4 x 62,5 mL

Compoziția trusei:

R1 4 x 20 mL + R2 4 x 5 mL
 R1 2 x 50 mL + R2 1 x 26 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 și plasmă pentru diagnosticare *in vitro*.

SEMNIFICAȚIE CLINICĂ⁽¹⁻⁴⁾

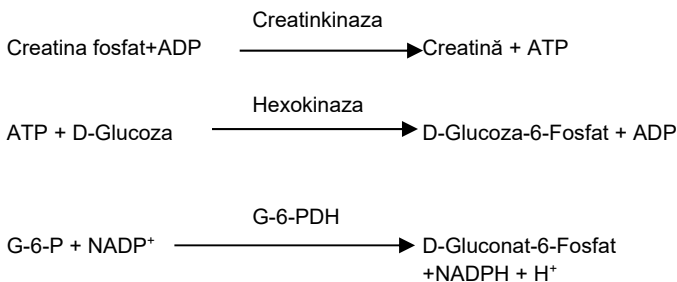
Creatinkinaza (CK) există în 3 forme citoplasmatic: CK-MM (în mușchiul striat și cardiac), CK-MB (doar în mușchiul cardiac), și CK-BB (în special în creier). Determinarea CK este utilizată pentru diagnosticarea și urmărirea bolilor musculare (în special distrofiile musculare) și ale leziunilor mușchiului 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 și quetiapina) și în unele cazuri hipotiroidismul, declanșează de asemenea creșterea activității CK.

METODĂ⁽⁵⁾

Metoda IFCC - cinetică. UV.

PRINCIPIU⁽⁵⁾



G-6-P: D-Glucoza-6-Fosfat

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

Creșterea concentrației NADPH este direct proporțională cu activitatea CK enzimatică.

COMPOZIȚIA 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 pentafoșfat	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.
- Soluție salină obișnuită (NaCl 9 g/L).
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

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



PERICOL: Poate dăuna fătului. Procurați instrucțiuni speciale înainte de utilizare. Purtați mănuși de protecție/îmbrăcăminte de protecție/echipament de protecție a ochilor/echipament de protecție a feței.

ÎN CAZ DE expunere sau de posibilă expunere: consultați medicul

- Reactivii conțin azidă de sodiu care poate reacționa cu plumbul sau instalațiile din cupru pentru a forma potențiale azide metalice explozive. În momentul eliminării acestor reactivi, spălați întotdeauna cu apă din abundență pentru a preveni acumularea de azide.
- Pentru mai multe informații, consultați Fișa de date privind siguranța (SDS).
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Nu interschimbați reactivii din truse diferite.

STABILITATEA

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

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

Referințe:

CKSL-0230 4 x 25 mL

CKSL-0410 2 x 62,5 mL

CKSL-0430 4 x 62,5 mL

Compoziția trusei:

R1 4 x 20 mL + R2 4 x 5 mL

R1 2 x 50 mL + R2 1 x 26 mL

R1 4 x 50 mL + R2 2 x 26 mL



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PROBE (1,5)

Specimen

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

Avertismente și precauții

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

Depozitare și stabilitate

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

VALORI DE REFERINȚĂ (5)

Bărbați < 171 U/L

Femei < 145 U/L

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems,

aplicațiile sunt disponibile la cerere.

Lungime de undă 340 nm

Temperatură: 37°C

Citiți pe reactivul martor.

Reactiv 1	240 µL
Proba	12 µL

Amestecați și așteptați 4 minute și 43 de secunde, apoi adăugați:

Reactiv 2	60 µL
------------------	-------

Amestecați și după o incubare de 130 de secunde, măsurați modificarea absorbției pe minut ($\Delta A/\text{min.}$) timp de 106 secunde.

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

CALCUL
 $\Delta A \text{ Proba} \times n \quad n = \text{concentrație calibrator}$
 $\Delta A \text{ Calibrator}$

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

CALIBRARE

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

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum ELITROL I (control normal) și ELITROL II (control patologic). Aceste controale trebuie efectuate și validate înainte ca probele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare, și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele de reglementare. Rezultatele trebuie să fie în intervalele definite. Dacă valorile sunt în afara intervalelor definite, fiecare laborator trebuie să ia

măsurii corective. Materialele pentru controlul calității trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale.

DATE DE PERFORMANȚĂ 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 și 1714 U/L (de la 0,17 la 28,57 µkat/L). Probele care depășesc 1714 U/L trebuie diluate 1:10 cu soluție de NaCl 9 g/L (soluție salină normală) și re-testate. Utilizarea acestei proceduri extinde intervalul de măsurare între 1714 și 17140 U/L (de la 28,57 la 285,67 µkat/L).

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

- Limita de detecție (LoD) și Limita de cuantificare (LoQ)

Determinată conform protocolului CLSI EP17-A⁽⁷⁾.

 $\text{LoD} = 1 \text{ U/L (0,02 } \mu\text{kat/L)}$
 $\text{LoQ} = 5 \text{ U/L (0,08 } \mu\text{kat/L)}$
- Precizie

Determinată conform protocolului CLSI EP5-A2⁽⁸⁾.

	n	Medie		În interiorul ciclului	Total
		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

- Corelație

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems și un alt echipament al sistemului aprobat de FDA (metoda IFCC) pe 100 de probe de ser uman conform protocolului CLSI EP9-A2⁽⁹⁾.

Concentrațiile probelor au fost între 11 și 1712 U/L (0,18 și 28,53 µkat/L).

Parametrii regresiiilor liniare sunt după cum urmează:

Coeficient de corelație: (r)=0,998

Regresie liniară: $y = 1,012 \times x + 2 \text{ U/L (0,03 } \mu\text{kat/L)}$

- Limitări și interferențe

- Probele hemolizate nu trebuie utilizate deoarece hemoliza semnificativă poate duce la concentrație fals crescută a CK din cauza eliberării adenilat kinazei.

- Nu raportați rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2⁽¹⁰⁾. Recuperarea este în intervalul $\pm 10\%$ din valoarea inițială a activității CK de 150 și 1200 U/L.

Trigliceride: Nicio interferență semnificativă până la 3000 mg/dL (33,9 mmol/L).



Referințe:

CKSL-0230 4 x 25 mL
 CKSL-0410 2 x 62,5 mL
 CKSL-0430 4 x 62,5 mL

Compoziția trusei:

R1 4 x 20 mL+R2 4 x 5 mL
 R1 2 x 50 mL+R2 1 x 26 mL
 R1 4 x 50 mL+R2 2 x 26 mL

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

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

Acid ascorbic: Nicio interferență semnificativă până la 20,0 mg/dL.

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

Acetaminofen: Nicio interferență 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 nefiabale. ⁽¹¹⁾

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽¹²⁻¹³⁾

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

- Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 28 de zile

Frecvența calibrării: 28 zile





Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit și după o operație de întreținere.

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SIMBOLURI

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

	Conținut
	Reactiv 1
	Reactiv 2
	Conformitate europeană

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



CK Total
390

0
PIT-CKSL

 Modificare față de versiunea precedentă.



Referințe:

CMSL-0230	4 x 25 mL
CMSL-0410	2 x 62,5 mL
CMSL-0430	4 x 62,5 mL

Compoziția trusei:

R1	4 x 20 mL + R2	1 x 20 mL
R1	2 x 50 mL + R2	1 x 26 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.

SEMNIFICAȚIE CLINICĂ⁽¹⁻²⁾

Creatinkinaza există în 3 forme citoplasmice: CK-MB (doar în mușchiul cardiac), CK-MM (în mușchiul striat și cardiac) și CK-BB (în special în creier).

Determinarea CK în ser este utilizată pentru diagnosticarea și urmărirea leziunilor musculare cardiace. În infarctul miocardic, ratele CK totale și 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 conține un anticorp care inhibă în mod specific subunitățile CK-M (și anume 100% din CK-MM și 50% din izoenzimele CK-MB). Activitatea rămasă, corespunzând activității fracției CK-B, este măsurată conform metodei de referință IFCC pentru măsurarea activității CK. Activitatea CK-MB este apoi obținută prin înmulțirea cu 2 a activității rămase.

COMPOZIȚIA 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 %

Concentrația anticorpului anti-CK-M conținut de reactivul 1 este suficient pentru a inhiba 2000 U/L din CK-M la 37°C.

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 utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

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



PERICOL: Poate dăuna fătului. Procurați instrucțiuni speciale înainte de utilizare. Purtați mănuși de protecție/îmbrăcăminte de protecție/echipament de protecție a ochilor/echipament de protecție a feței. ÎN CAZ DE expunere sau de posibilă expunere: consultați medicul.

- Reactivii conțin azidă de sodiu care poate reacționa cu plumbul sau instalațiile din cupru pentru a forma potențiale azide metalice explozive. În momentul eliminării acestor reactivi, spălați întotdeauna cu apă din abundență pentru a preveni acumularea de azide.
- Pentru mai multe informații, consultați Fișa de date privind siguranța (SDS).
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Nu interschimbați reactivii din truse diferite.

STABILITATEA REACTIVILOR

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

PREGĂTIREA ȘI STABILITATEA REACTIVULUI DE LUCRU

- Pregătire

Amestecați 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 20-25°C
2 săptămâni la 2-8°C

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor. (Consultați §DATE PRIVIND PERFORMANȚA).

DETERIORAREA REACTIVILOR

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

AMBALAJ DETERIORAT

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

Referințe:

 CMSL-0230 4 x 25 mL
 CMSL-0410 2 x 62,5 mL
 CMSL-0430 4 x 62,5 mL

Compoziția trusei:
R1 4 x 20 mL+ **R2** 1 x 20 mL
R1 2 x 50 mL+ **R2** 1 x 26 mL
R1 4 x 50 mL+ **R2** 2 x 26 mL


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PROBE ⁽⁶⁾
Specimen

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

Avertismente și precauții

Conform buneii practici de laborator, puncția venoasă trebuie să fie efectuată înainte de administrarea de medicamente.

Depozitare și stabilitate

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

VALORI DE REFERINȚĂ ⁽³⁻⁵⁾

Ser (37°C): 0-25 U/L

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

$$(CK-MB/CK \text{ totală}) \times 100 < 6\%$$

Următorii 3 factori sunt indicatori ai deteriorării mușchiului cardiac:

CK totală

Bărbați > 171 U/L

Femei > 145 U/L

CK-MB: > 25 U/L

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

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

PROCEDURĂ

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

Pentru Analizoarele Selectra ale ELITech Clinical Systems,

aplicațiile sunt disponibile la cerere.

ungime de undă 340 nm

Temperatură: 37°C

Citiți pe reactivul martor.

Reactiv de lucru	250 μL
Proba	10 μL

Amestecați și după o incubare de 130 de secunde, măsurați modificarea absorbției pe minut (ΔA/min.) timp de 159 secunde.

Cu software-ul Selectra TouchPro, utilizați aplicația 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:

$$\text{Activitate (U/L)} = \Delta A / \text{min.} \times 8 \ 254$$

c) Procent activitate CK-MB în eșantion:

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

$$\text{Factor de conversie: U/L} \times 0,0167 = \mu\text{kat/L}$$

CONTROLUL CALITĂȚII

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 calității trebuie efectuat și validat înainte ca eșantioanele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare, și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale.

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

 - **Interval de măsurare**

Reactivul este liniar între 15 și 600 U/L.

 - **Limita de detecție** ⁽⁷⁾

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

 - **Precizie**

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

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

 - **Corelație**

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

Concentrațiile eșantioanelor au fost între 11 și 1712 U/L (0,18 și 28,53 μkat/L).

Parametrii regresii liniare sunt după cum urmează:

Coeficient de corelație: (r)=0,9980

Regresie liniară: y=1,0007 x +1,3 U/L

 - **Limitări și interferențe** ^(2,7,8)

- Serurile hemolizate nu trebuie utilizate deoarece hemoliza semnificativă poate crește concentrația CK din cauza eliberării adenilat kinazei.

- metoda va măsura și 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 activității CK-BB, activitatea CK-MB va fi supraestimată.

Referințe:

CMSL-0230 4 x 25 mL
 CMSL-0410 2 x 62,5 mL
 CMSL-0430 4 x 62,5 mL

Compoziția trusei:

R1 4 x 20 mL+ **R2** 1 x 20 mL
R1 2 x 50 mL+ **R2** 1 x 26 mL
R1 4 x 50 mL+ **R2** 2 x 26 mL



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- Nu raportați rezultatele în afara intervalului utilizabil.
- Conform recomandărilor SFBC, au fost efectuate unele studii pentru a stabili nivelul interferenței din diferiți compuși:
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 interferență 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 nefiabale. ⁽⁹⁾
- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽¹⁰⁻¹¹⁾
- Rezultatele acestui studiu trebuie interpretate doar în conjuncție cu alte rezultate ale testelor de diagnosticare, constatările clinice și istoricul medical al pacientului.












- Stabilitatea la bord

Stabilitatea la bord: 7 zile

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

SIMBOLURI

	Dispozitiv medical de diagnosticare in vitro.
	Consultați instrucțiunea de utilizare.
	Producător
	Limită de temperatură
	Număr de lot
	Data expirării
	Număr catalog
	Conținut
	Reactiv 1
	Reactiv 2
	Conformitate europeană

Notă :

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

 CK-MB
400

 0
PIT-CMSL

 Modificare față de versiunea precedentă


Referințe:
FEFE-0230
FEFE-0600

Compoziția 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 deteriorarea cantitativ a fierului total în serul uman pentru diagnosticare *in vitro*.

SEMNIFICAȚIE CLINICĂ⁽¹⁻²⁾

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

METODĂ

Colorimetrică – Ferene
Punct final.

PRINCIPIU⁽¹⁻²⁾

Fierul este eliberat din transferină în pH-ul acid ca ion feric Fe³⁺. Acesta este apoi redus de acidul ascorbic în ion feros Fe²⁺ și formează eventual un complex colorat cu Ferene. Absorbanța la 578 nm de complex Fier - Ferene este proporțională cu concentrația fierului din eșantion.

pH acid, Acid ascorbic

Transferină – (Fe³⁺)₂ → 2 Fe²⁺ + Transferină

Fe²⁺ + 3 Ferene → Albastru de Ferene (complex de fier)

COMPOZIȚIA 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 utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

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



PERICOL: Provoacă iritarea pielii. Provoacă leziuni oculare grave. Purtați mănuși de protecție/îmbrăcăminte de protecție/echipament de protecție a ochilor/echipament de protecție a feței. 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: consultați medicul. Scoateți îmbrăcămintea contaminată și spălați-o înainte de reutilizare.

- Pentru mai multe informații, consultați Fișa de date privind siguranța (SDS).
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Standardul trebuie să fie imediat închis cu capacul pentru a preveni contaminarea și evaporarea.
- Nu interschimbați fiolele de reactiv din truse diferite.

STABILITATEA

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

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

PROBE^(1,3)

Specimen

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

Avvertisment și precauții

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



Referințe:
 FEFE-0230
 FEFE-0600

Compoziția 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

Depozitare

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

VALORI DE REFERINȚĂ (4)

Ser		
Nou-născuți	100-250 µg/dL	17,9-44,8 µmol/L
Infanți	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
Bărbați	65-175 µg/dL	11,6-31,3 µmol/L

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

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems.

Aplicațiile sunt disponibile la cerere

Lungime de undă 578-700 nm

Temperatură: 37°C

Citiți pe reactivul martor.

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

Amestecați și citiți absorbanta (A1) după o incubare de 4 minute 40.

Reactiv R2	60 µL	60 µL
-------------------	-------	-------

Amestecați și citiți absorbanta (A2) după o incubare de 6 minute 30.

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

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

CALCUL

(A2-A1) Proba x n n=concentrație calibrator/standard
 (A2-A1) Calibrator /Standard

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

CALIBRARE

Pentru referința FEFE-0600: Pentru calibrare, trebuie utilizat fie calibratorul multiparametric ELICAL 2 fie Standardul de fier de 100 µg/dL.

Pentru referința FEFE-0230: Pentru calibrare, utilizați calibratorul multiparametric ELICAL 2.

Valorile concentrației Standardului de fier de 10 µg/dL și calibratorului multiparametric ELICAL 2 sunt trasabile conform Materialului Standard de Referință SRM937 (al Institutului Național de Standarde și Tehnologie).

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

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I (control normal) și ELITROL II (control patologic). Aceste controale trebuie efectuate și validate înainte ca probele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare, și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele locale și legale.

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

- Interval de măsurare

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

- Limita de detecție (LoD) și 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)

Referințe:
FEFE-0230
FEFE-0600

Compoziția 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

- Precizie

Determinată conform protocolului CLSI EP5-A2⁽⁷⁾.

	n	Medie		În interiorul ciclului	Total
		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

- Corelație

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems și un alt echipament al sistemului aprobat de FDA (metoda colorimetrică Ferene) pe 99 de eșantioane de ser uman conform protocolului CLSI EP9-A2⁽⁸⁾.

Concentrațiile eșantioanelor au fost între 22 și 1048 µg/dL (3.9 și 187.7 µmol/L).

Parametrii regresiiilor liniare sunt după cum urmează:

Coefficient de corelație: (r)=1.000

Regresie liniară: $y=1,041 x - 2 \mu\text{g/dL}$
(0,4 µmol/L)

- Limitări și interferențe

- Nu raportați rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2⁽⁹⁾. Recuperarea este în intervalul ±10% din valoarea inițială a concentrației fierului de 40 µg/dL și 250 µg/dL.

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

Bilirubină conjugată: Nicio interferență semnificativă până la 29.5 mg/dL (504 µmol/L).

Trigliceride: Nicio interferență semnificativă până la 3000 mg/dL (33.90 mmol/L).

Acid ascorbic: Nicio interferență semnificativă până la 20 mg/dL .

Cupru: Nicio interferență semnificativă până la 500 µg/dL (78,7 µmol/L).

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

Acetaminofen: Nicio interferență 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 substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young.⁽¹¹⁻¹²⁾
- Rezultatele acestui studiu trebuie interpretate doar în conjuncție cu alte rezultate ale testelor de diagnosticare, constatările clinice și istoricul medical al pacientului.

- Stabilitatea la bord/Frecvența calibrării

Aceste date sunt definite pentru un volum de umplere de 14 ml într-un flacon de 25 ml pentru reactivul R1 și respectiv de 4 ml într-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

Frecvența calibrării: 14 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit, și după o operație de întreținere.

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- Young D.S., *Effects of drugs on clinical laboratory tests*, 4th edition, AACC Press (1995).

IRON FERENE

Referințe:
FEFE-0230
FEFE-0600






Compoziția 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



SIMBOLURI

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

	Conținut
	Reactiv 1
	Reactiv 2
	Standard
	Conformitate europeană


Notă:

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



Iron Ferene
510

0
FTCE-FEFE

 Modificare față de versiunea precedentă.

Referințe:

PASL-0230 4 x 25 mL
 PASL-0400 2 x 62,5 mL
 PASL-0420 4 x 62,5 mL

Compoziția trusei:

R1 4 x 20 mL + R2 4 x 5 mL
 R1 2 x 50 mL + R2 1 x 26 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*.

SEMNIIFICAȚIE 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 și placentă.

Rata ALP crește fiziologic pentru copii și adolescenți în perioadele creșterii active, precum și pentru femeile în al treilea trimestru de sarcină.

Creșterile marcate ale ratei ALP sunt observate în cazul obstrucției extra-hepatice (calculi biliari, tumori...) și bolile osoase precum boala Paget și cancerul osteogenic osos.

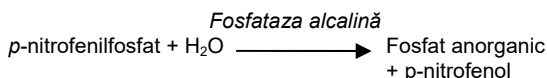
Activitatea PAL poate crește, de asemenea, moderat în cazul obstrucției intra-hepatice, hepatitei, cirozei, sau în cazul rahitismului, osteomalaciei, hiperparatiroidismului, vindecarea fracturilor osoase.

METODĂ⁽³⁻⁴⁾

Bazată pe metoda DGKC și SCE.
 Enzimatică. CINETICĂ.

PRINCIPIU⁽³⁻⁴⁾

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



COMPOZIȚIA 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 utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- 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. Purtați mănuși de



protecție/îmbrăcăminte de protecție/echipament de protecție a ochilor/echipament de protecție a feței.

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: consultați medicul.

- Reactivii conțin azidă de sodiu care poate reacționa cu plumbul sau instalațiile din cupru pentru a forma potențiale azide metalice explozive. În momentul eliminării acestor reactivi, spălați întotdeauna cu apă din abundență pentru a preveni acumularea de azide.
- Pentru mai multe informații, consultați Fișa de date privind siguranța (SDS).
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Nu interschimbați fiolele de reactiv din truse diferite.

STABILITATEA

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

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

PROBE^(1,2,5)

Specimen

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

Avertismente și precauții

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

Depozitare și stabilitate

- Activitatea ALP poate crește în cazul în care specimenul refrigerat (2-8°C) sau înghețat (-20°C) este pus la temperatura camerei.
- Dacă speciimenele sunt înghețate în scopul depozitării prelungite, mutați-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 2-8°C și 2 luni la -20°C.



Referințe:

PASL-0230 4 x 25 mL
 PASL-0400 2 x 62,5 mL
 PASL-0420 4 x 62,5 mL

Compoziția trusei:

R1 4 x 20 mL + R2 4 x 5 mL
 R1 2 x 50 mL + R2 1 x 26 mL
 R1 4 x 50 mL + R2 2 x 26 mL



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

VALORI DE REFERINȚĂ ⁽⁶⁾

Ser (37°C):

Bărbați <270 U/L
 Femei <240 U/L

Valorile de referință pentru copii și adolescenți în timpul creșterii oaselor sunt mai mari decât pentru adulți.

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems,

aplicațiile sunt disponibile la cerere.

Lungime de undă 405 nm

Temperatură: 37°C

Citiți pe reactivul martor.

Reactiv R1	200 µL
Proba	5 µL

Amestecați, așteptați 4 minute și 43 de secunde și adăugați:

Reactiv R2	50 µL
------------	-------

Amestecați și așteptați o incubație de 50 de secunde, măsurată variația absorbției pe minut ($\Delta A/\text{min.}$) timp de 133 secunde.

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

CALCUL

$\Delta A \text{ Proba} \times n$ n=concentrație calibrator

$\Delta A \text{ Calibrator}$

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.

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I și ELITROL II. Aceste controale trebuie efectuate și validate înainte ca eșantioanele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare, și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform liniilor directoare locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale.

DATE DE PERFORMANȚĂ 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 detecție ⁽⁷⁾

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

Precizie

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

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

Corelație

A fost efectuat un studiu comparativ pe analizorul Selectra XL ELITech Clinical Systems între procedura cu un reactiv și procedura cu doi reactivi pe 30 de eșantioane de ser.

Valorile au fost între 17 și 886 U/L.

Parametrii regresiei liniare sunt după cum urmează:

Coefficient de corelație: (r)=0,9999

Regresie liniară: $y=1,9800x + 3,19$ U/L

Limitări și interferențe ⁽⁷⁻⁸⁾

- Nu raportați rezultatele în afara intervalului utilizabil.

- Conform recomandărilor SFBC, au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși:

Bilirubină neconjugată: Nicio interferență semnificativă până la 36 mg/dL (615,8 µmol/L).

Bilirubină conjugată: Nicio interferență semnificativă până la 25 mg/dL (427,6 µmol/L).

Hemoglobină: Nicio interferență semnificativă până la 500 mg/dL (5 g/L).

Turbiditate: Nicio interferență 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 nefiabale. ⁽⁹⁾
- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽¹⁰⁻¹¹⁾
- Rezultatele acestui studiu trebuie interpretate doar în conjuncție cu alte rezultate ale testelor de diagnosticare, constatările clinice și istoricul medical al pacientului.

Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 14 zile

Frecvența calibrării: 7 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit, și după o operație de întreținere.



Referințe:

PASL-0230 4 x 25 mL
 PASL-0400 2 x 62,5 mL
 PASL-0420 4 x 62,5 mL

Compoziția trusei:

R1 4 x 20 mL + R2 4 x 5 mL
 R1 2 x 50 mL + R2 1 x 26 mL
 R1 4 x 50 mL + R2 2 x 26 mL







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- Young, D.S., *Effects of preanalytical variables on clinical laboratory tests*, 2nd Ed., AACC Press, (1997).
- 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.


	Conținut
	Reactiv 1
	Reactiv 2
	Conformitate europeană

Notă:

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



Alkaline Phosphatase 0
 120 PIT-PASL

 :Modificare față de versiunea precedentă.



Referințe:

TGML-0425
TGML-0515
TGML-0700
TGML-0427
TGML-0497
TGML-0517
TGML-0707

Compoziția trusei:

R 6 x 50 mL
R 6 x 100 mL
R 4 x 250 mL
R 6 x 50 mL + Std 1 x 5 mL
R 1 x 100 mL + Std 1 x 5 mL
R 6 x 100 mL + Std 1 x 5 mL
R 4 x 250 mL + Std 1 x 5 mL

Referințe:

TGML-0250
TGML-0455

Compoziția trusei:

R 12 x 20 mL
R 6 x 45 mL

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



SCOPUL UTILIZĂRII

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

SEMNIFICAȚIE CLINICĂ ⁽¹⁻²⁾

Trigliceridele constituie 95% din grăsimile depozitate în țesuturi și rolul lor principal este de a furniza energia pentru celulă. Acestea sunt sintetizate atât în intestin, din grăsimile dietetice și în ficat din carbohidrații dietetici, și sunt apoi transportate în sânge prin chilomicroni și VLDL.

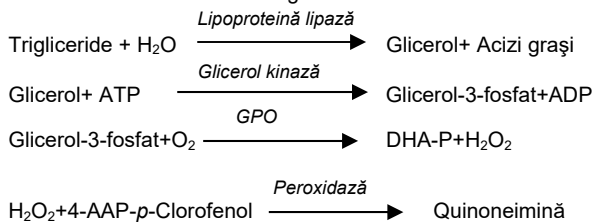
Nivelele înalte de trigliceride serice sunt asociate cu riscurile importante de ateroscleroză. Acestea pot fi cauzate de bolile precum diferitele afecțiuni ale metabolismului lipidic (hiperlipoproteinemia, deficiența activității lipazei, deficiența apolipoproteinei C-II), însă și de diabet, afecțiuni renale sau endocrine.

METODĂ ⁽³⁾

Enzimatică - colorimetrică. Punct final.

PRINCIPIU ⁽³⁾

Determinarea enzimatică a trigliceridelor conform următoarelor reacții:



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

COMPOZIȚIA

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, conține săruri de magneziu, FAD și surfactanți pentru performanță 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
- Soluție salină obișnuită (NaCl 9 g/L)
- Echipamente generale de laborator.
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Acest dispozitiv de diagnostic *in vitro* (Reactiv și Standardul) este destinat numai pentru uz profesional.
- Reactivul R și Standardul conține azidă de sodiu care poate reacționa cu plumbul sau instalațiile din cupru pentru a forma potențiale azide metalice explozive. În momentul eliminării acestor reactivi, spălați întotdeauna cu apă din abundență pentru a preveni acumularea de azide.
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Standardul trebuie să fie imediat închis cu capacul pentru a preveni contaminarea și evaporarea.
- Pentru mai multe informații, Fișa de date privind siguranța (SDS) este disponibilă la cerere pentru utilizatorul profesional.

STABILITATEA

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii și Standardul sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

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

PROBE ⁽⁴⁾

Specimen

- Ser sau plasmă heparinizată de litiu de la pacienții care țin post (≥12 ore).
- Nu utilizați eșantioane icterice sau hemolizate.
- A nu se utiliza alte specimene.

Referințe:	Compoziția 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

Referințe:	Compoziția trusei:
TGML-0250	R 12 x 20 mL
TGML-0455	R 6 x 45 mL

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Avertismente și precauții

- 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.
- Colectați mostrele în tuburi și tampoane fără glicerol.
- Separați de celule în termen de 2 ore.

Depozitare și stabilitate

- Eșantioanele sunt stabile între 5 și 7 zile, dacă sunt depozitate la 2-8°C, 3 luni de la -15°C până la -20°C și mai mulți ani la -70°C. Evitați înghețarea și dezghețarea repetate.

VALORI DE REFERINȚĂ (2)

NCEP (Programul Național American de Educație privind Colesterolul) a stabilit următoarea clasificare pentru nivelele de colesterol total, în funcție de riscul dezvoltării cardiopatiei coronariene:

Clasificarea riscurilor:

	<u>Nivel (mg/dl)</u>	<u>Nivel (mmol/L)</u>
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 menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems,

aplicațiile sunt disponibile la cerere.

Lungime de undă 505 nm

Temperatură: 37°C

Citiți pe reactivul maror.

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

Amestecați și citiți absorbantele (A) după o incubare de 11 minute și 30 secunde.

- Cu software-ul Selectra TouchPro, utilizați aplicația inclusă în codul de bare disponibil la finalul acestei inserții.
- **Reactivii Triglycerides SL și Triglyceride Mono SL New pot fi contaminați de reactivul Cholesterol HDL SL 2G.**

Pentru a evita contaminarea pe Selectra ProM și ProXL, programați incompatibilitățile 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, repetați orice rezultate absurde după programarea unei spăiri a acelor.

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

Pentru a evita contaminarea cuvetei pe instrumentele Selectra Pro, programați următoarele incompatibilități:

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 programați Lipase SL și Triglycerides SL în același ciclu. Asigurați-vă că instrumentul revine la statusul „stand-by” înainte de începerea unui ciclu care conține Lipase SL.

CALCUL

A Proba

_____ x n n = concentrație calibrator/standard

A Calibrator/
Standard

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

CALIBRARE

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

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

Valorile concentrației Standardului Triglycerides 200 mg/dL și calibratorului multiparametric ELICAL 2 sunt trasabile în raport metoda de referință ID-GC-MS (Diluția izotopică – Spectrometria de masă cromatografie de gaz - spectrometrie de masă).

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Pentru a verifica precizia testelor, vor fi utilizate serurile de control precum ELITROL I și ELITROL II. Aceste controale trebuie efectuate și validate înainte ca eșantioanele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare, și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform liniilor directe locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale.

Referințe:	Compoziția trusei:
TGML-0425	R 6 x 50 mL
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TGML-0455	R 6 x 45 mL

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DATE DE PERFORMANȚĂ 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 30 și 1000 mg/dL (0,34 – 11,30 mmol/L). Probele cu concentrații mai mari trebuie să fie diluate 1:5 cu soluție NaCl 9g/L (salină obișnuită) și re-evaluate. Utilizarea acestei proceduri extinde intervalul de măsurare până la 5 000 mg/dL (56,50 mmol/L.)

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

Precizie

Determinată conform protocolului CLSI EP5-A2⁽⁶⁾.

	Medie			În interiorul ciclului	Total
	n	mg/dL	mmol/L		
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

Corelație

A fost efectuat un studiu comparativ între un Analizor Selectra ProM ELITech Clinical Systems și un alt echipament al sistemului aprobat de FDA (metoda enzimatică și colorimetrică) pe 99 eșantioane de ser uman conform protocolului CLSI EP9-A2⁽⁷⁾.

Valorile au fost între 30 și 957 mg/dL (0,34 și 10,81 mmol/L).

Parametrii regresiiilor liniare sunt după cum urmează:

Coeficient de corelație: (r)=0,999

Regresie liniară: $y=1,019 \cdot x + 1$ mg/dL (0,10 mmol/L)

Limitări și interferențe

- Nu raportați rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2⁽⁸⁾. Recuperarea este în intervalul ±10% din valoarea inițială a concentrației trigliceridelor de 133 mg/dL și 266 mg/dL.

Bilirubină neconjugată: Nicio interferență semnificativă până la 15 mg/dL (257 μmol/L).

Bilirubină conjugată: Nicio interferență semnificativă până la 5,9 mg/dL (101 μmol/L)

Hemoglobină: Nicio interferență semnificativă până la 125 mg/dL.

Acid uric: Nicio interferență semnificativă până la 24,2 mg/dL (1440 μmol/L).

Acid ascorbic: Nicio interferență semnificativă până la 2,0 mg/dL. Concentrațiile peste nivelele terapeutice vor interfera și cauza rezultate eronate.

Metil-dopa: Nicio interferență 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 eșantionului de NAC (N-Acetil-Cisteină), NAPQI (metabolit de acetaminofen (paracetamol) sau metamizol).

- Multe alte substanțe și medicamente pot interfera. Unele dintre acestea sunt enumerate în reviste publicate de Young. ⁽¹⁰⁻¹¹⁾

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

Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 28 zile

Frecvența calibrării: 14 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit, și după o operație de întreținere.

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Referințe:	Compoziția trusei:
TGML-0250	R 12 x 20 mL
TGML-0455	R 6 x 45 mL

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☞ SIMBOLURI

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

CONT	Conținut
R	Reactiv
std	Standard
CE	Conformitate europeană
☞	Modificare față de versiunea precedentă

Notă

- Doar pentru ref. **TGML-0250/TGML-0455**, utilizată cu software-ul Selectra TouchPro.
- **Vezi ȘPROCEDURĂ:**
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 produto podem afetar o desempenho do produto. Não use o produto se houver evidência física de deterioração (por exemplo, vazamentos ou recipiente perfurado).

❖AMOSTRAS

Amstras ⁽²⁾

- Soro
- Plasma (heparina de lítio)

- Urina

- O uso de qualquer outro tipo de amostra deve ser validado pelo laboratório.

- 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.

Armaçamento e estabilidade ⁽⁴⁾

Soro / plasma

- 3-5 dias a 2-8 ° C

- 3-6 meses a -20 ° C

Urina (Alcalinizada)

- 3 dias em temperatura ambiente

Não refrigerar amostras de urina

❖VALORES DE REFERÊNCIAS ⁽¹⁾

<i>Soro / plasma</i>	mg/dL	μmol/L
Homens	3.5 - 7.2	208 - 428
Mulheres	2.6 - 6.0	155 - 357

<i>Urina (coleta de 24h)</i>	mg/24h	mmol/24h
	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 absorbâncias (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

(A) Amostra x n n = concentração do padrão/ (A) Padrão/ x n n = concentração do padrão/ calibrador 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*

150 - 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 μmol/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 \leq 10% do valor inicial.

Bilirrubina não conjugada: Nenhuma interferência significativa até 30 mg/dL (513 μmol/L).

- 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.

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 Waldenström) podem causar resultados não confiáveis.⁽⁵⁾

- Os resultados podem ser falsamente reduzidos em níveis significativos na amostra de NAC (*N*-acetil-cisteína), NAPQI (metabólito do acetaminofeno (paracetamol)) ou metanzolol.

- 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/dL (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*-acetil-cisteína), NAPQI (metabólito do acetaminofeno (paracetamol)) ou metanzolol.

- 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).

❖BIBLIOGRAFIE/BIBLIOGRAPHY BIBLIOGRAFÍA/BIBLIOGRAFIA

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SYMBLES/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



URIC ACID MONO SL

AUML-0427

AUML-0497

AUML-0507

AUML-0707

AUML-0420

AUML-0500

AUML-0250

AUML

R 6 x 50 mL + *Std* 1 x 5 mL

R 1 x 100 mL + *Std* 1 x 5 mL

R 6 x 100 mL + *Std* 1 x 5 mL

R 4 x 250 mL + *Std* 1 x 5 mL

R 6 x 50 mL

R 6 x 100 mL

R 12 x 20 mL



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⁾

- SéroM

- Plasma (héparine de lithium)

- Urine

- L'utilisation de toute autre type d'échantillon doit être validée par le laboratoire.

Alertissements 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⁾

SéroM/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⁾

<i>SéroM/plasma</i>	mg/dL	μmol/L
Hommes	3.5 - 7.2	208 - 428
Femmes	2.6 - 6.0	155 - 357

<i>Urine (recueil de 24 h)</i>	mg/24h	mmol/24h
	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 décroît 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

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.

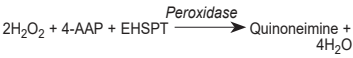
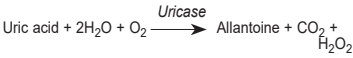
When uric acid concentration is abnormally high in urines, there is a risk of stone formation. In practice, the determination of uric acid in serum is indicated to help diagnose gout, for the follow-up of patients under radiation or chemotherapy, and sometimes to help diagnose pre-eclampsia. The determination 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.



EHSPT = N-Ethy-N-(2-Hydroxy-3-Sulfopropyl) *m*-Toluidine
4-AAP = Amino-4-antipirine

❖COMPOSITION

Reagent: R					
Buffer pH 7.00 (20-25°C)					
EHSPT	0.72	mmol/L			
Amino-4-antipirine	≥ 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).

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 (%)	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 (%)	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)

Correlation coefficient : (r) = 0.999
Linear regression: y = 1.044 x - 0.04 mg/dL (2 µmol/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 (Waldenström'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 metanzolol.

- 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 metanzolol.

- 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.

- 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 únicamente 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 cánceros 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.

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.

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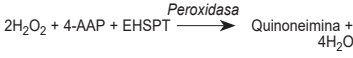
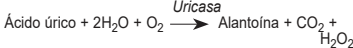
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❖LÍMITE DE UTILIZACIÓN

La cuantificación del ácido úrico no puede ser utilizado solo para diagnosticar una enfermedad o patología específicas.
Los resultados siempre deben compararse con los resultados de otras pruebas de diagnóstico, exámenes clínicos y el historial médico del paciente.

❖MÉTODO & PRINCIPIO ⁽⁴⁾



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 precauciones**
- 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⁾

<i>Suero/plasma</i>	mg/dL	µmol/L		
Hombres	3.5 - 7.2	208 - 428		
Mujeres	2.6 - 6.0	155 - 357		
<i>Orina (recolectada de 24h)</i>	mg/24h	mmol/24h		
	250 - 750	1.48 - 4.43		
	mg/dL* ⁽³⁾	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
Trazectoria óptica : 1 cm
Ratío 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

A Muestra *x* n n = concentración del estándar/
A Estándar / *l* *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



PIT-CHES-4-v18 (07/2020)

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.

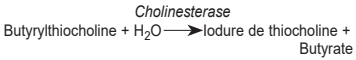
Une chute de 15-25 % se rencontre lors d'une intoxication faible, de 25-35 % lors d'une intoxication modérée, de 30 à 50 % lors d'une intoxication sévère par des composés organophosphorés, mais aussi chez des patients avec une hépatite chronique ou en phase aiguë. Une chute de 50 à 70 % se rencontre lors de cirrhose, de cancer avec métastases hépatiques.

MÉTHODE

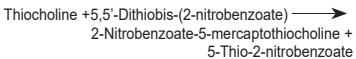
Enzymatique. Cinétique.

PRINCIPE ⁽⁴⁾

Sous l'action catalytique de la cholinestérase, l'iodure de butyrylthiocholine est hydrolysé en iodure de thiocholine :



Les thiols réagissent avec le 5,5'-Dithiobis-(2-nitrobenzoate) ou DNTB en donnant un produit coloré jaune, le 2-Nitrobenzoate-5-mercaptothiocholine :



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 référer 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 référer 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 référer 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

638 433

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 ($\Delta A/30$ 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)= $\Delta A/30$ 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 gammopathies 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 insecticides 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.

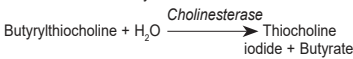
A 15-25 % decrease is observed in slight poisoning, a 25-35 % decrease in moderate poisoning, a 30-50 % decrease in serious poisoning by organophosphorus compounds, but also in patients with acute or chronic hepatitis. A 50-70 % decrease occurs in those with advanced cirrhosis and carcinoma metastases to the liver.

METHOD

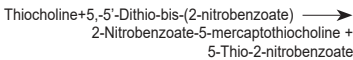
Enzymatic. Kinetic.

PRINCIPE ⁽⁴⁾

Under the catalytic action of cholinesterase, butyrylthiocholine iodide is hydrolysed in thiocholine iodide :



Thiols react with 5,5'-Dithiobis-(2-nitrobenzoate) or DNTB giving a yellow compound, 2-Nitrobenzoate-5-mercaptothiocholine :



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 measurs. 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) Triglicérides 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)

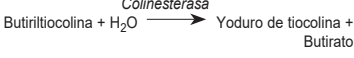
La colinesterasa sérica (CE) (pseudocolinesterasa o colinesterasa II, EC3.1.1.8) se encuentra principalmente en el hígado, pero también en la sustancia blanca del cerebro, el páncreas, el corazón y el suero. Su papel biológico es desconocido. La dosificación de la colinesterasa sirve como indicador en una posible intoxicación por inhalación o contacto con la piel por compuestos organofosforados (entre ellos ciertos insecticidas y gases neurotóxicos); 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 miorelajante. 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

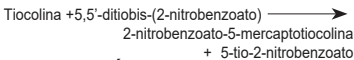
Enzimático. Cinético.

PRINCIPIO ⁽⁴⁾

Debido a la acción catalítica de la colinesterasa, el yoduro de butirilcolina se hidroliza a yoduro de tiocolina:



Los tioles reaccionan con el 5,5'-ditiobis-(2-nitrobenzoato) o DNTB dando un producto de color amarillo, el 2-nitrobenzoato-5-mercaptiotiocolina:



COMPOSICIÓN

Reactivo 1 : R1

Tampón fosfato, pH 7,40

5,5'-ditio-bis-2-nitrobenzoato 0,24 mmol/L

Reactivo 2 : R2

Yoduro de S-butilritiocolina

218 mmol/L

MATERIALES REQUERIDOS PERO NO INCLUIDOS

- CALL-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 (oduro de(propilcarbioniltoetil)trimetilamónio) .



- 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 :

Dissolver 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 :

Dissolver 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 población 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 deberá 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 butirilitiocolina) en 60 muestras de suero.

Los valores se distribuyen en el rango analítico.

Los parámetros de la regresión lineal son los siguientes :

Coefficiente 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 :
Bilirubina conjugada : Desviación negativa desde 17 mg/dL (300 μmol/L).
Bilirubina 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 gammopatías 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 neurotóxicos); em doenças hepáticas; ou antes de uma anestesia com succinilcolina, de modo a eliminar uma deficiência congênita dessas enzimas que poderiam conduzir a uma apneia prolongada devido a uma lenta degradação do miorrelaxante.

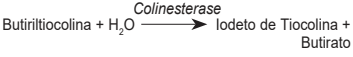
Uma redução de 15-25% pode ser observada na intoxicação ligeira, uma redução de 25-35% na intoxicação moderada, uma redução de 30-50% nas intoxicações graves por compostos organofosforados, mas também em pacientes com hepatite aguda ou crônica. Uma redução de 50-70% ocorre em pacientes com cirrose avançada e carcinoma e metástases para o fígado.

MÉTODO

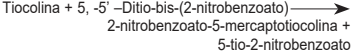
Enzimático. Cinético.

PRINCIPIO ⁽⁴⁾

Sob a ação catalítica de colinesterase, iodeto Butiriltiocolina é hidrolisado em Iodeto de Tiocolina.



Os tiois reagem com 5,5'-ditiobis- (2-nitrobenzoato) ou DNTB dando um composto amarelo, 2-nitrobenzoato-5-mercaptotiocolina.



COMPOSIÇÃO

Reactivo 1 : R1

Tampão fosfato, pH 7,40

5, 5'-ditiobis-2-nitrobenzoato 0,24 mmol/L

Reactivo 2 : R2

Iodeto de S-butilritiocolina

218 mmol/L

MATERIAIS NECESSÁRIO MAS NÃO FORNECIDOS

- CALL-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(propilcarbioniltoetil)trimetilamónio).



Informação de configuração importante : O Reagente CHOLESTEROL SL pode ser levemente contaminado pela MAGNESIUM XB em 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

(A) Amostra x n n = concentração do padrão/ Calibrador

(A) 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, o 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 das amostras automaticamente. Os resultados são tomados em consideração na diluição.

☛ **Limite de deteção (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 triglicéridos.

Ácido ascórbico: Nenhuma interferência significativa até 4.0 mg/dL.

Metilidopa : Nenhuma interferência significativa até 1.6 mg/dL.

Ácido úrico : Nenhuma interferência significativa até 23.7 mg/dL (1410 μmol/L).

- Não use amostras ictericas ou hemolisadas.

- Em casos muito raros, as gamopatias monoclonais (mieloma múltiplo), em particular, tipo IgM (macroglobulinemia de Waldenstrom) podem causar resultados não confiáveis.⁽⁹⁾

- Os resultados podem ser falsamente reduzidos em níveis significativos na amostra de NAC (*N*-acetilcisteína), NAPQI (metabólito do acetaminofeno (paracetamol)) ou metanzolol.

- Muitas outras substâncias e drogas podem interferir. Alguns deles estão referenciados em análises publicadas por Young.⁽⁷⁻⁶⁾

- **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 BIBLIOGRAFIA/BIBLIOGRAFIA

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6. 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.

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8. 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.

	Contient Content Contiene Conteúdo
	Réactif Reagent Reactivo Reagente
	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
	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 280	0 PIT-CHSL



CHOLESTEROL SL

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 structural 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.

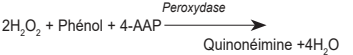
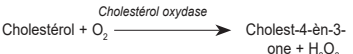
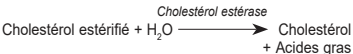
☛LIMITE D'UTILISATION

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.



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
Peroxidase ≥ 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 ses 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 hypertriglycéridémie > 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 aberrants après avoir programmé un lavage d'aiguille.

CHSL	CHSL-0497	CHSL-0507	CHSL-0707	CHSL-0250	CHSL-0455	CHSL-0500	CHSL-0700
R	1 x 100 mL	+	Std	1 x 5 mL			
R	6 x 100 mL	+	Std	1 x 5 mL			
R	4 x 250 mL	+	Std	1 x 5 mL			
R	12 x 20 mL						
R	6 x 45 mL						
R	6 x 100 mL						
R	4 x 250 mL						

CALCUL

(A) Echantillon x n n = concentration du standard/ Calibrant

(A) 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).

Frequéce 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.

☛- 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 :

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⁾

Xylydil Blue - End Point

Xylydil 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
Xylydil 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. ⁽³⁾

- **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⁾

<i>Serum/plasma</i>	mg/dL	mmol/L
	1.5 - 2.6	0.63 - 1.05

<i>Urine (24h - collection)</i>	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 urine 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:

<i>Software</i>	<i>Menu</i>	<i>Parameter</i>
TouchPro	Probe incompatibilities	incompatibility/ CHOLESTEROL - MAGNESIUM
Other	Needle incompatibility	CHOLESTEROL: MAGNESIUM

CALCULATION

^{ΔA} Sample x n = Calibrator/ standard
^{ΔA} 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. § 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
2.0 - 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.

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)

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).

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 3.0 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 (Waldenström'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⁾

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 únicamente 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 hipocalcemia y / o hipocalemia. 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 hipalbuminemia puede desencadenar una pseudohipomagnesemia, 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 Y PRINCIPIO ⁽⁵⁾

Bleu de Xylydil - 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 sodíca < 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. Para usuarios de Selectra ProM, los resultados toman en cuenta el factor de dilución.

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 precauciones ^(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⁾

<i>Suero/plasma</i>	mg/dL	mmol/L
	1.5 - 2.6	0.63 - 1.05
Orina		
<i>(recolectada de 24h)</i>	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
Relio 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

☛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:

Coefficiente 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:

Coefficiente 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.
Bilirrubina 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).
Tuvração: 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 (macroglubulinemia de Waldenstrom) podem causar resultados não confiáveis.⁽⁹⁾

- 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 signific 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).

☛BIBLIOGRAPHIE/BIBLIOGRAPHY

BIBLIOGRAFÍA/BIBLIOGRAFIA

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3. Kaplan, J.M. & First, M.R., *Renal Function, Clinical Chemistry: Theory, Analysis, Correlation*, 5ª Ed., Kaplan, L.A, Pesce, A.J., (Mosby Inc. eds.), (2010), 567 and appendix.

4. Bretauière, J.P., *et al., Clin_ Chem.*, (1976), **22**, 1614.

5. 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.

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7. Young, D.S., *Effects of drugs on clinical laboratory tests*, 4ª Ed., AACCPress (1995).

SYMBOLS/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.

	Contient	
	Contient	
CONT	Contiene	
	Conteúdo	
	Réactif R1	
R1	Reagent R1	
	Reactivo R1	
	Reagente R1	
	Réactif R2	
R2	Reagent R2	
	Reactivo R2	
	Reagente R2	
	Standard	
	Standard	
Std	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	
	Formité Européenne	
CE	European Conformity	
	Conformidade Europeia	
	Conformidade Europeia	



UREA UV SL

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/GIDH – Cinétique



GIDH = Glutamate déshydrogénase

☛COMPOSITION

Réactif 1 : R1

Tampou buffer, pH 7.60 (37 °C)

α-Cétoglutarate

Uréase ≥ 8 100 U/L

GIDH ≥ 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 - 48.3	2.88 - 8.21
Adultes (> 90 ans)	21.4 - 66.5	3.57 - 11.07

<i>Urine (recueil de 24h)</i>	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	1000 µL
(4 volumes de R1 + 1 volume de R2)	
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 ré



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 (macroglubulinemia 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 Contient Contiene Conteúdo
R	Réactif Reagent Reactivo Reagente
Std	Standard Standard Estándar Padrão
CE	Conformité Européenne European Conformity Conformidad Europea Conformidade Europeia

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 syndrome 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 diabète insipide ou de prise extrêmement importante de sel.

MÉTHODE ⁽⁴⁾

Thiocyanate de mercure. Colorimétrie.
 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 :



☛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 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 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

$$A_{\text{Echantillon}} \times n = n_{\text{concentration du standard/ calibrant}}$$

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 sont 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 Détection ⁽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 Chloro 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).
Bilirrubine conjugée: Aucune interférence significative jusqu'à 25 mg/dL (427,6 µmol/L).
Bilirrubine non-conjugée: 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 gammopathies 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.
Bilirrubine conjugée: 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
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 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.



☛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 (6)

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

$$A_{\text{Sample}} \times n \quad n = \text{calibrator/standard concentration}$$
$$A_{\text{Standard/ Calibrator}}$$

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 (mEq/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 positive 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 (Waldenström'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.

- Para más información, consulte la ficha de datos de seguridad (FDS).

☞ **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.

CONJUGADO 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).

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).

PREPARACION

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 empaque 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 precauciones**

- 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 (6)

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

Trajectory 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/ Calibrator	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.

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 gammopatías monoclonales (mieloma múltiple), en particular el tipo IgM (macroglubulinemia de Waldenström) pueden producir resultados poco confiables.(8)

- Para más información, consulte la ficha de datos de seguridad (FDS).

☞ **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 deberá tomar las medidas correctivas. Los materiales de control de calidad deben ser usados conforme a las directivas locales.

- **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.

☞ **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).

PREPARACION

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 empaque 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 precauciones**

- 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 (6)

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

Trajectory 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/ Calibrator	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.

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 gammopatías monoclonales (mieloma múltiple), en particular el tipo IgM (macroglubulinemia de Waldenström) pueden producir resultados poco confiables.(8)

- Para más información, consulte la ficha de datos de seguridad (FDS).

☞ **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 deberá tomar las medidas correctivas. Los materiales de control de calidad deben ser usados conforme a las directivas locales.

- **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.

☞ **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).

PREPARACION

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 empaque 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 precauciones**

- 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 (6)

Suero, plasma : 98 - 107 mEq/L

Orina, 24h :

Referințe:

GISL-0250
 GISL-0400
 GISL-0420

Compoziția trusei:

R1 8 x 20 mL + R2 8 x 5 mL
 R1 2 x 50 mL + R2 1 x 26 mL
 R1 4 x 50 mL + R2 2 x 26 mL



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 și plasmă.

SEMNIFICAȚIE CLINICĂ ⁽¹⁻³⁾

Gama glutamiltransferaza (γ -GT) este o enzimă legată de membrană prezentă în special în rinichi, pancreas, ficat și prostată. Această enzimă are un rol important în metabolismul glutationului și ia parte la transportul aminoacizilor în celule. Creșterea activității γ -GT este mai sensibilă decât fosfataza alcalină (ALP) în timpul unei afecțiuni a ficatului sau a căilor biliare. Cele mai mari creșteri sunt observate în cazurile de obstrucții 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 și hematoame, deoarece nivelele reflectă remiterea și recurența.

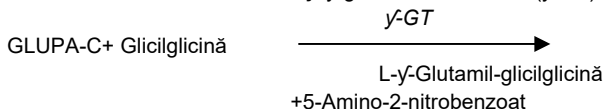
Creșteri mai moderate sunt observate în timpul hepatitei infecțioase, cirozei și steatozei hepatice. Alcool în ingestie cronică, unele medicamente precum antiepilepticele (fenobarbital, fenitoină) pot, de asemenea, crește rata γ -GT în ser.

METODĂ ⁽⁴⁾

Substrat Glupa-C – Standardizare conform metodei IFCC – Enzimatică. CINETICĂ.

PRINCIPIU ⁽⁴⁾

Determinarea cinetică a activității γ -glutamiltransferazei (γ -GT).



GLUPA-C: L- γ -Glutamil-3-carboxi-p-nitroanilidă.

Creșterea absorbantei la 405 nm datorită formării de 5-amino-2-nitrobenzoat este proporțională cu activitatea γ -GT.

COMPOZIȚIA
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
- Soluție salină obișnuită (NaCl 9 g/L).
- Echipamente generale de laborator.
- Nu utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Acest dispozitiv de diagnostic *in vitro* este destinat numai pentru uz profesional.
- Reactivii R1 și R2 conțin azidă de sodiu care poate reacționa cu plumbul sau instalațiile sanitare din cupru și poate forma azide metalice explozibile. În cazul aruncării acestor reactivi, spălați întotdeauna cu cantități mari de apă pentru a preveni formarea de azide.
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.
- Nu interschimbați fiolele de reactiv din truse diferite.
- Pentru mai multe informații, Fișa de date privind siguranța (SDS) este disponibilă la cerere pentru utilizatorul profesional.

STABILITATEA

A se depozita la 2-8°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor. (Consultați Ș DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

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

PROBE ⁽⁵⁾
Specimen

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

Avertisment și precauții

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

Depozitare și stabilitate

Serurile sunt stabile timp de 7 zile la 2-8°C și la temperatura camerei, și 1 an la -20°C.

VALORI DE REFERINȚĂ ⁽⁶⁾

	Bărbați	Femei
Ser, plasmă:	10-71 U/L	6-42 U/L



Referințe:

GISL-0250
 GISL-0400
 GISL-0420

Compoziția trusei:

R1 8 x 20 mL + R2 8 x 5 mL
 R1 2 x 50 mL + R2 1 x 26 mL
 R1 4 x 50 mL + R2 2 x 26 mL



VTLRO-GISL-v9 (08/2020)_VTL-GISL-4-v9

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems,

aplicațiile sunt disponibile la cerere

Lungime de undă: 405 nm

Temperatură: 37°C

Citiți pe reactivul martor.

Reactiv R1	220 µL
Proba	20 µL

Amestecați și așteptați 4 minute și 43 de secunde.

Reactiv R2	55 µL
-------------------	-------

Amestecați și așteptați 50 de secunde incubația, măsurati schimbarea absorbantei pe minut ($\Delta A/\text{min}$) timp de 159 de secunde.

Cu software-ul Selectra TouchPro, utilizați aplicația inclusă în codul de bare disponibil la finalul acestei inserții.

CALCUL

$\Delta A \text{ Proba} \times n$ n=concentrație calibrator

$\Delta A \text{ Calibrator}$

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⁾.

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

CONTROLUL CALITĂȚII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I și ELITROL II. Aceste controale trebuie efectuate și validate înainte ca eșantioanele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare, și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform liniilor directe locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele locale și legale.

DATE DE PERFORMANȚĂ 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 15 și 1200 U/L (0,25 și 20,00 µkat/L), care depășesc 1 200 U/L trebuie să fie diluate 1:10 cu soluție NaCl

9g/L (salină obișnuită) și re-evaluate. Utilizarea acestei proceduri extinde intervalul de măsurare până la 12 000 U/L (200,00 µkat/L).

Pentru utilizatorii Selectra TouchPro, funcția „diluare” efectuează diluția automată a eșantionului. Rezultatele iau în considerare diluția.

Limita de detecție (LoD) și 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⁾.

	n	Medie		În interiorul ciclului	Total
		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

Corelație

A fost efectuat un studiu comparativ între reactivul ELITech Clinical Systems și alt sistem concurent (metoda enzimatică standardizată IFCC) pe 94 de eșantioane de ser uman conform protocolului CLSI EP9-A2⁽¹⁰⁾.

Valorile au fost între 13,0 și 1169,7 U/L (între 0,22 și 19,50 µkat/L).

Parametrii regresii liniare sunt după cum urmează:

Coefficient de corelație: (r)=0,999

Regresie liniară: $y=0,900 x + 4,9 \text{ U/L}$ (0,08 µkat/L)

Limitări /interferențe

- Nu raportați rezultatele în afara intervalului utilizabil.

- Nu utilizați eșantioane vizibil turbide.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2⁽¹¹⁾ al CLSI. Recuperarea este în intervalul ±10% din valoarea inițială a activității γ-GT de 100,00 și 500,00 U/L.

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

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

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

Trigliceride: Nicio interferență semnificativă până la 926 mg/dL (10,46 mmol/L).

Glucoză: Nicio interferență semnificativă până la 540 mg/dL (29,97 mmol/L).

Acid acetilsalicilic: Nicio interferență semnificativă până la 200,00 mg/dL.



Referințe:

GISL-0250
 GISL-0400
 GISL-0420

Compoziția trusei:

R1 8 x 20 mL + R2 8 x 5 mL
 R1 2 x 50 mL + R2 1 x 26 mL
 R1 4 x 50 mL + R2 2 x 26 mL



VTLRO-GISL-v9 (08/2020)_VTL-GISL-4-v9

Acetaminofen: Nicio interferență semnificativă până la 30,0 mg/dL.

Metil-dopa: Nicio interferență semnificativă până la 1,0 mg/dL.

Doxacilină HCl: Nicio interferență semnificativă până la 20 mg/dL.

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

Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 14 de zile

Frecvența calibrării: 14 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit, și după o operație de întreținere.

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SIMBOLURI

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

	Conținut
	Reactiv 1
	Reactiv 2
	Conformitate europeană

Notă

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


 Gamma GT
 760

 1
 VTL-GISL

 Modificare față de versiunea precedentă.



TOTAL PROTEIN PLUS

Referințe:

PROB-0250 12 x 20 mL

PROB-0600 2 x 125 mL

PROB-0700 4 x 250 mL

Compoziția trusei:

R 12 x 20 mL

R 2 x 125 mL + Std 1 x 5 mL

R 4 x 250 mL + Std 1 x 5 mL



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.

SEMNIFICAȚIE CLINICĂ^(1,2)

În plasma umană, albumina este prezentă în procent de 50-60% din proteinele totale: restul fracției conține în special globuline (α 1, α 2, β și γ). Majoritatea proteinelor plasmatică sunt sintetizate de ficat, cu excepția imunoglobulinelor. Creșterea volumului plasmatic (sindromul de reținere a sării, intoxicația 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 concentrația albuminei sau imunoglobulinelor.

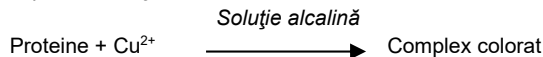
Astfel, insuficiența proteică severă (malabsorbția, maldigestia, insuficiența dietetică), bolile renale și hepatice, duc la hiperproteinemie. În cazul în care concentrația proteinelor totale este mai mică de 4g/dL, pot fi observate edemele. Hiperproteinemia poate fi observată, de exemplu, în cazul hiperimunoglobulinemiei (mielom multiplu, infecție).

METODĂ⁽³⁾

Biuret. Punct final.

PRINCIPIU⁽³⁾

Proteinele serice formează un complex colorat în prezența sării de cupru din soluția alcalină.



COMPOZIȚIA

Reactiv: R

Sulfat de cupru 6 mmol/L

Hidroxid de sodiu 490 mmol/L

Conține și ioduri de sodiu și tartrat de sodiu pentru performanță 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 utilizați materiale care nu sunt necesare, după cum este indicat mai sus.

AVERTISMENTE ȘI PRECAUȚII

- Acest dispozitiv de diagnostic *in vitro* (Reactiv și Standardul) este destinat numai pentru uz profesional.
- Reactivul R este clasificat ca periculos.



ATENȚIE: Poate fi coroziv pentru metale. Provoacă iritarea pielii. Provoacă o iritare gravă a ochilor. Nociv pentru mediul acvatic cu efecte pe termen lung. Purtați mănuși de protecție/îmbrăcăminte de protecție/echipament de protecție a

ochilor/echipament de protecție a feței. Evitați dispersarea în mediu.

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. Dacă iritarea ochilor persistă: consultați medicul. Absorbiți scurgerile de produs, pentru a nu afecta materialele din apropiere.

- Standardul conține azidă de sodiu care poate reacționa cu plumbul sau instalațiile din cupru pentru a forma potențiale azide metalice explozive. În momentul eliminării acestui standard, spălați întotdeauna cu apă din abundență pentru a preveni acumularea de azide.
- Standardul trebuie să fie imediat închis cu capacul pentru a preveni contaminarea și evaporarea.
- Pentru mai multe informații, consultați Fișa de date privind siguranța (SDS).
- Luați măsurile de precauție obișnuite și urmați buna practică de laborator.
- Utilizați doar echipamente de laborator curate sau de unică folosință pentru a evita contaminarea.

STABILITATEA

A se depozita la 2-25°C și a se proteja împotriva luminii. A nu se îngheța.

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

Stabilitatea la bord:

Stabilitatea la bord este specifică pentru fiecare analizor.

(Consultați § DATE PRIVIND PERFORMANȚA).

PREGĂTIRE

Reactivii și Standardul sunt gata pentru utilizare.

DETERIORAREA PRODUSELOR

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



TOTAL PROTEIN PLUS

Referințe:

PROB-0250 12 x 20 mL
 PROB-0600 2 x 125 mL
 PROB-0700 4 x 250 mL

Compoziția trusei:

R 12 x 20 mL
 R 2 x 125 mL + Std 1 x 5 mL
 R 4 x 250 mL + Std 1 x 5 mL



VTLRO-PROB-v12 (10/2020)_VTL-PROB-4-v12

PROBE (1,2,4)

Specimen

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

☞ Avertismente și precauții

- Conform bunei practici de laborator, prelevarea trebuie efectuată înainte de administrarea de medicamente.
- Probele trebuie să fie libere din hemoliză și lipemie.

Depozitare și stabilitate

Probele sunt stabile timp de 7 zile la 2-8°C și cel puțin 2 luni la -20°C. Pentru o depozitare mai îndelungată, înghețați eșantioanele la -70°C.

VALORI DE REFERINȚĂ (1,2,4)

Ser: Pacienți în ambulatoriu Pacienți în repaus
 6,4-8,3 g/dL 6,0-7,8 g/dL
 64-83 g/L 60-78 g/L

Plasmă:

Concentrațiile plasmei sunt mărite de la 0,2 la 0,4 g/dL (de la 2 la 4 g/L), în comparație cu concentrațiile serului (fibrinogen).

Notă: Intervalul menționat ar trebui să servească doar ca un ghid. Se recomandă ca fiecare laborator să verifice acest interval sau să stabilească un interval de referință pentru populația țintă.

☞ PROCEDURĂ

Pentru Analizoarele Selectra ale ELITech Clinical Systems,

aplicațiile sunt disponibile la cerere

Lungime de undă 546 nm

Temperatură: 37°C

Citiți pe reactivul martor.

	MARTOR	CALIBRARE	TEST
Reactiv R	300 µL	300 µL	300 µL
Apă distilată	3 µL		
Calibrator		3 µL	
Eșantion			3 µL

Amestecați și citiți absorbanta (A) după o incubare de 11 minute și 30 secunde.

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

Informații importante privind setarea:

Reactivul MAGNESIUM XYLIDYL poate fi slab contaminat cu TOTAL PROTEIN PLUS pe Selectra ProM și ProXL.

Pentru a evita contaminarea pe aceste instrumente, programați următoarele incompatibilități:

Software	Meniu	Parametru
TouchPro	Incompatibilități sondă	Incompatibilitate/PROTEINA-MAGNEZIU
Altele	Incompatibilitate ace	PROTEINĂ: MAGNEZIU

☞ CALCUL

A Proba

_____ x n n = concentrație calibrator/standard

A Calibrator/

Standard

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

CALIBRARE

Pentru referințele PROB-0600/PROB-0700: Pentru calibrare, trebuie utilizat calibratorul multiparametric ELICAL 2 sau Standardul proteină totală 6 g/dL.

Pentru referința PROB-0250: Pentru calibrare, utilizați calibratorul multiparametric ELICAL 2.

Valorile concentrației Standardului de proteina totală de 6 g/dL și calibratorului multiparametric ELICAL 2 sunt trasabile conform Materialului Standard de Referință 909c (al Institutului Național de Standarde și Tehnologie).

Frecvența de calibrare: Calibrarea este specifică pentru fiecare analizor. (Consultați § DATE PRIVIND PERFORMANȚA).

☞ CONTROLUL CALITĂȚII

Pentru a asigura calitatea adecvată, vor fi utilizate serurile de control precum ELITROL I și ELITROL II. Aceste controale trebuie efectuate și validate înainte ca probele pacienților să fie testate. Frecvența controlului trebuie să fie de cel puțin o dată pe zi, după fiecare calibrare și trebuie adaptată la procedurile de Controlul Calității fiecărui laborator și cerințele 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 calității trebuie utilizate conform reglementărilor locale.

MANAGEMENTUL DEȘEURILOR

Eliminarea tuturor deșeurilor trebuie să fie în conformitate cu cerințele de reglementare locale, statale și federale.

DATE DE PERFORMANȚĂ la 37°C 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 și 12,0 g/dL (de la 2,0 la 120,0 g/L).

- Limita de detecție (LoD) și 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).



Referințe:

PROB-0250 12 x 20 mL

PROB-0600 2 x 125 mL

PROB-0700 4 x 250 mL

Compoziția trusei:

R 12 x 20 mL

R 2 x 125 mL + Std 1 x 5 mL

R 4 x 250 mL + Std 1 x 5 mL



VTLRO-PROB-v12 (10/2020)_VTL-PROB-4-v12

- Precizie

 Determinată conform protocolului CLSI EP5-A2⁽⁷⁾.

	n	Medie		În	Total
		g/dL	g/L	interiorul ciclului	
				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

- Corelație

A fost efectuat un studiu comparativ între analizorul Selectra ProM ELITech Clinical Systems și un alt echipament al unui sistem aprobat de FDA (metoda Biuret) pe 100 probe de ser uman, conform protocolului CLSI EP9-A2⁽⁸⁾.

Concentrațiile probelor au fost între 0,27 și 11,25 g/dL (între 2,7 și 112,5 g/L).

Parametrii regresii liniare sunt după cum urmează:

Coeficient de corelație: (r)=0,997

Regresie liniară: $y=0,993x + 0,05$ g/dL
(0,5 g/L)

- Limitări și interferențe

- Nu raportați rezultatele în afara intervalului utilizabil.

- Au fost efectuate studii pentru a stabili nivelul interferenței din diferiți compuși conform protocolului CLSI EP7-A2⁽⁹⁾ al CLSL și recomandările SFBC. Recuperarea este în intervalul ±10% din valoarea inițială a concentrației proteinei totale de 4,00; 6,50 și 9,00 g/dL.

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

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

Glucoză: Nicio interferență semnificativă până la 507 mg/dL (28,14 mmol/L).

Turbiditate: Nicio interferență semnificativă până la 263 mg/dL (2,97 mmol/L) echivalent trigliceride.

Hemoglobină: Nicio interferență semnificativă până la 300 mg/dL.

Dextran: Induce rezultate fals ridicate la concentrații terapeutice.

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

- Stabilitatea la bord/Frecvența calibrării

Stabilitatea la bord: 14 zile

Frecvența calibrării: 14 zile

Recalibrați când loturile de reactiv se schimbă, când rezultatele controlului calității sunt în afara intervalului stabilit și după o operație de întreținere.

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7. *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition*. CLSI (NCCLS) document EP5-A2 (2004), **24** (25).
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TOTAL PROTEIN PLUS

Referințe:
PROB-0250 12 x 20 mL

PROB-0600 2 x 125 mL

PROB-0700 4 x 250 mL

Compoziția trusei:
R 12 x 20 mL


R 2 x 125 mL + **Std** 1 x 5 mL

R 4 x 250 mL + **Std** 1 x 5 mL


VTLRO-PROB-v12 (10/2020)_VTL-PROB-4-v12

SIMBOLURI

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

CONT	Conținut
R	Reactiv
Std	Standard
CE	Conformitate europeană
	Modificare față 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

Product Name:

EasyLyte and accessories per attachment


EasyElectrolytes and accessories per attachment

Model/Type:

EasyLyte Na/K, Na/K/Cl, Na/K/Li, Na/K/Cl/Li,
Na/K/Ca/pH, Na/K/Cl/Ca/Li

EasyElectrolytes Na/K/Cl, Na/K/Li

Manufacturer

 Medica Corporation
5 Oak Park Drive, Bedford, Massachusetts, 01730, USA

Representative


 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:



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 Maintenance 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
4405	EasyElectrolyte Na/K/Cl Demonstration Kit	21 07 11 02
4406	EasyElectrolyte Na/K/Li Demonstration Kit	21 07 11 02
4404	EasyElectrolyte Capillary Tube Kit	21 07 11 02
4306	EasyElectrolyte Sampler	21 07 11 02
6504	EasyBloodGas/EasyElectrolyte Pump Tube	21 07 11 02
6505	EasyStat/EasyBloodGas/EasyElectrolyte Printer Paper	21 07 11 02
4506	EasyElectrolyte Sensor Module	21 07 11 02
4507	EasyElectrolyte Valve Module	21 07 11 02
4508	EasyStat/EasyBloodGas/EasyElectrolyte Compression Plate	21 07 11 02
7302	Probe Wipers	21 07 11 02
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

EasyBloodGas™ analyzer
EasyLyte® analyzer

EasyElectrolytes® analyzer
EasyStat® analyzer

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

helena
Biosciences Europe

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.

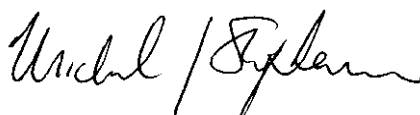
Product Code	Description	GMDN Classification Code
5267L	Thromboplastin L	55983

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

Tel +44 (0)191 482 8440
Fax +44 (0)191 482 8442
info@helena-biosciences.com
www.helena-biosciences.com

Helena Biosciences Europe
Queensway South, Team Valley Trading Estate,
Gateshead, Tyne and Wear, NE11 0SD,
United Kingdom

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.

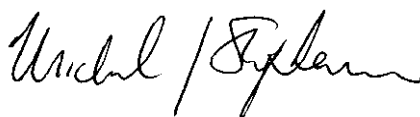
Product Code	Description	GMDN Classification Code
5185	Calibration Plasma	55995

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

Tel +44 (0)191 482 8440
Fax +44 (0)191 482 8442
info@helena-biosciences.com
www.helena-biosciences.com

Helena Biosciences Europe
Queensway South, Team Valley Trading Estate,
Gateshead, Tyne and Wear, NE11 0SD,
United Kingdom

Calibration Plasma <p>Istruzioni per l'uso</p>	it
SCOPO PREVISTO	es
Il kit Calibration Plasma è concepito per l'uso come materiale di calibrazione.	ru

Il Calibration Plasma può essere utilizzato come plasma di riferimento per il dosaggio dei fattori II, V, VII, VIII, IX, X¹, XI e XII², del fibrinogeno³, 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 dichiarati⁴. 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 INGHIRIRE. 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.																					
<p>Ogni kit contiene un Istruzioni per l'uso.</p> <p>Ogni kit contiene un inserto recante i valori di riferimento specifici per il lotto.</p> <p>MATERIALI NECESSARI, MA NON IN DOTAZIONE</p> <p>Il Calibration Plasma può essere utilizzato durante l'esecuzione di test su qualsiasi strumento di coagulazione meccanico o foto-otico in combinazione con tutti i reagenti idonei disponibili in commercio.</p> <p>CONSERVAZIONE, VITA UTILE E STABILITÀ</p> <p>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 ^o2 –8°C. Tutti gli altri fattori sono stabili per 4 ore a ^o2 –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.</p> <p>RACCOLTA E PREPARAZIONE DEI CAMPIONI</p> <p>Non applicabile.</p> <p>PROCEDURA</p> <p>Fare riferimento al manuale utente dello strumento appropriato per istruzioni dettagliate oppure contattare Helena Biosciences Europe per le note applicative specifiche dello strumento.</p> <p>INTERPRETAZIONE DEI RISULTATI</p> <p>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.</p> <p>LIMITAZIONI</p> <p>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.</p> <p>CONTROLLO QUALITÀ</p> <p>Ogni laboratorio deve definire un programma di controllo qualità. I plasmì 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.</p> <p>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</p> <p>VALORI DI RIFERIMENTO</p> <p>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.</p> <p>CARATTERISTICHE PRESTAZIONALI</p> <p>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.</p> <table> <tbody><tr> <th>Riproducibilità</th><td></td><td></td><td></td></tr> <tr> <th>Precisione tra i lotti</th><td></td><td></td><td></td></tr> <tr> <th><i>Parametro</i></th><th><i>n</i></th><th><i>Media</i></th><th><i>CV (%)</i></th></tr> <tr> <td>Fibrinogeno (g/L)</td><td>5</td><td>3.0</td><td>3.6</td></tr> <tr> <td>Fattore IX (%)</td><td>5</td><td>124.7</td><td>1.9</td></tr> <tr> <td>Proteina S (%)</td><td>5</td><td>98.5</td><td>2.8</td></tr> </tbody></table> <p>BIBLIOGRAFIA</p> <ol style="list-style-type: none">Babson AL and Flanagan ML (1975) Quantitative One Stage Assays for Factors V and X, <i>AJCP</i>, 64: 817-819. Hardisty RM <i>et al.</i> (1962) A One Stage Factor VIII Assay and Its Use on Venous and Capillary Plasma. <i>Thrombosis et Diathesis Haemorrhagica</i>, 7:215-229. Morse EE <i>et al.</i> (1971) Automated Fibrinogen Determination, <i>AJCP</i>, 55:671-676. Elodi S <i>et al</i> (1978) Some Sources of Error in the One-Stage Assay of Factor VIII, <i>Haemostasis</i>, 7:1-9. Thelin M (1968) Preparation and Standardization of a Stable AHF Plasma, <i>Thrombosis et Diathesis Haemorrhagica</i>, 19:423. Kirkwood TBL <i>et al.</i> (1977) Identification of Sources of Variation in Factor VIII Assay, <i>British Journal of Haematology</i>, 37:559-568. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, <i>AJCP</i>, 55:561-564. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, <i>AJCP</i>, 59:231-235.	Riproducibilità				Precisione tra i lotti				<i>Parametro</i>	<i>n</i>	<i>Media</i>	<i>CV (%)</i>	Fibrinogeno (g/L)	5	3.0	3.6	Fattore IX (%)	5	124.7	1.9	Proteina S (%)	5	98.5	2.8
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<i>Parametro</i>	<i>n</i>	<i>Media</i>	<i>CV (%)</i>																					
Fibrinogeno (g/L)	5	3.0	3.6																					
Fattore IX (%)	5	124.7	1.9																					
Proteina S (%)	5	98.5	2.8																					

Calibration Plasma <p>Instrucciones de uso</p>	es
USO PREVISTO	ru
El uso previsto del kit Calibration Plasma es como material de calibración.	

USO PREVISTO

El Calibration Plasma puede usarse como plasma de referencia cuando se valoran los factores II, V, VII, VIII, IX, X¹, XI, XII², fibrinógeno³, 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 indicados⁴. 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.

Una muestra de plasma de laboratorio.

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 destiliada o desionizada. Agite suavemente. Espere 20 minutos para que el producto se disuelva completamente.																					
<p>Cada kit contiene instrucciones de uso.</p> <p>Cada kit contiene valores de referencia específicos insertados del lote.</p> <p>ARTÍCULOS NECESARIOS NO SUMINISTRADOS</p> <p>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.</p> <p>ALMACENAMIENTO, CADUCIDAD Y ESTABILIDAD</p> <p>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 ^o2 –8°C. Todos los demás factores son estables durante 4 horas a ^o2 –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.</p> <p>RECOGIDA Y PREPARACIÓN DE LAS MUESTRAS</p> <p>No aplicable.</p> <p>PROCEDIMIENTO</p> <p>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.</p> <p>INTERPRETACIÓN DE LOS RESULTADOS</p> <p>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.</p> <p>LIMITACIONES</p> <p>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.</p> <p>CONTROL DE CALIDAD</p> <p>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.</p> <p>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</p> <p>VALORES DE REFERENCIA</p> <p>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.</p> <p>CARACTERÍSTICAS FUNCIONALES</p> <p>Las siguientes características de rendimiento han sido determinadas por Helena Biosciences Europe o sus representantes usando un instrumento de coagulación opto-mecánico.</p> <table> <tbody><tr> <th>Reproductibilidad</th><td></td><td></td><td></td></tr> <tr> <th>Precision inter-lote</th><td></td><td></td><td></td></tr> <tr> <th><i>Parámetro</i></th><th><i>n</i></th><th><i>Media</i></th><th><i>CV (%)</i></th></tr> <tr> <td>Fibrinógeno (g/L)</td><td>5</td><td>3.0</td><td>3.6</td></tr> <tr> <td>Factor IX (%)</td><td>5</td><td>124.7</td><td>1.9</td></tr> <tr> <td>Proteína S (%)</td><td>5</td><td>98.5</td><td>2.8</td></tr> </tbody></table> <p>BIBLIOGRAFÍA</p> <ol style="list-style-type: none">Babson AL and Flanagan ML (1975) Quantitative One Stage Assays for Factors V and X, <i>AJCP</i>, 64: 817-819. Hardisty RM <i>et al.</i> (1962) A One Stage Factor VIII Assay and Its Use on Venous and Capillary Plasma. <i>Thrombosis et Diathesis Haemorrhagica</i>, 7:215-229. Morse EE <i>et al.</i> (1971) Automated Fibrinogen Determination, <i>AJCP</i>, 55:671-676. Elodi S <i>et al</i> (1978) Some Sources of Error in the One-Stage Assay of Factor VIII, <i>Haemostasis</i>, 7:1-9. Thelin M (1968) Preparation and Standardization of a Stable AHF Plasma, <i>Thrombosis et Diathesis Haemorrhagica</i>, 19:423. Kirkwood TBL <i>et al.</i> (1977) Identification of Sources of Variation in Factor VIII Assay, <i>British Journal of Haematology</i>, 37:559-568. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, <i>AJCP</i>, 55:561-564. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, <i>AJCP</i>, 59:231-235.	Reproductibilidad				Precision inter-lote				<i>Parámetro</i>	<i>n</i>	<i>Media</i>	<i>CV (%)</i>	Fibrinógeno (g/L)	5	3.0	3.6	Factor IX (%)	5	124.7	1.9	Proteína S (%)	5	98.5	2.8
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УНИВЕРСАЛЬНЫЙ КАЛИБРАТОР <p>инструкция</p>	ru
НАЗНАЧЕНИЕ	
Комплект «Универсальный калибратор» предназначен для использования в качестве материала для калибровки.	

НАЗНАЧЕНИЕ

Калибратор в упаковке

Калибратор в упаковке

«Универсальный калибратор» может использоваться как референсная плазма, для определения факторов II, V, VII, VIII, IX, X¹, XI, XII², фибриногена³, фактора Виллебранда, 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 Пртеина С. Уровень значений сопоставим с рекомендациями ВОЗ⁴. 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 производится 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.

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 лиофилизована, 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).																	
<p>Каждый набор содержит инструкцию по применению.</p> <p>Паспорт с референсными значениями.</p> <p>НЕОБХОДИМЫЕ КОМПОНЕНТЫ, НЕ ВКЛЮЧЕННЫЕ В КОМПЛЕКТ ПОСТАВКИ</p> <p>Контрольные плазмы могут быть использованы с анализаторами, имеющими различный метод детекции (механический, оптический и т.д.) в сочетании с реагентами различных производителей.</p> <p>ХРАНЕНИЕ, СРОК ГОДНОСТИ И УСТОЙЧИВОСТЬ</p> <p>Невскрытые флаконы с лиофилизированной плазмой хранятся до истечения срока годности в условиях, указанных на этикетке. Разведенная плазма в закрытом флаконе может храниться при ^o2 –8°C в течение 4 часов. Значения для VIII фактора, фактор Виллебранда и КоФактор ристоцетина устойчивы в течение 2 часов при ^o2 –8°C. Неразведенный калибратор должен выглядеть, как светло-желтый сухой плотный лиофилизат. При повлении необычных признаков продукта, до использования обратитесь в компания Хелена.</p> <p>ОТБОР И ПОДГОТОВКА ОБРАЗЦОВ</p> <p>Не относится.</p> <p>ПРОЦЕДУРА</p> <p>«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.</p> <p>ИНТЕРПРЕТАЦИЯ РЕЗУЛЬТАТОВ</p> <p>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.</p> <p>ОГРАНИЧЕНИЯ</p> <p>Референсные значения могут варьировать между лабораториями в зависимости от используемых методов и коагулометров. По этой причине каждая лаборатория должна установить свои собственные нормативные параметры метода.</p> <p>КОНТРОЛЬ КАЧЕСТВА</p> <p>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</p> <p>НОРМАЛЬНЫЕ ПОКАЗАТЕЛИ</p> <p>Референсные значения могут варьировать между лабораториями в зависимости от используемых методов и коагулометров. По этой причине каждая лаборатория должна установить свои собственные значения.</p> <p>ЭКСПЛУАТАЦИОННЫЕ ХАРАКТЕРИСТИКИ</p> <p>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):</p> <table> <tbody><tr> <th>Вспроизводительность в пределах аналитической серии</th><td></td><td></td><td></td></tr> <tr> <th>Тест</th><th><i>n</i></th><th><i>Среднее</i></th><th><i>CV (%)</i></th></tr> <tr> <td>Фибриноген (г/Л)</td><td>5</td><td>3.0</td><td>3.6</td></tr> <tr> <td>Фактор IX (%)</td><td>5</td><td>124.7</td><td>1.9</td></tr> <tr> <td>Протеин S (%)</td><td>5</td><td>98.5</td><td>2.8</td></tr> </tbody></table> <p>ЛИТЕРАТУРА</p> <ol style="list-style-type: none">Babson AL and Flanagan ML (1975) Quantitative One Stage Assays for Factors V and X, <i>AJCP</i>, 64: 817-819. Hardisty RM <i>et al.</i> (1962) A One Stage Factor VIII Assay and Its Use on Venous and Capillary Plasma. <i>Thrombosis et Diathesis Haemorrhagica</i>, 7:215-229. Morse EE <i>et al.</i> (1971) Automated Fibrinogen Determination, <i>AJCP</i>, 55:671-676. Elodi S <i>et al</i> (1978) Some Sources of Error in the One-Stage Assay of Factor VIII, <i>Haemostasis</i>, 7:1-9. Thelin M (1968) Preparation and Standardization of a Stable AHF Plasma, <i>Thrombosis et Diathesis Haemorrhagica</i>, 19:423. Kirkwood TBL <i>et al.</i> (1977) Identification of Sources of Variation in Factor VIII Assay, <i>British Journal of Haematology</i>, 37:559-568. Goldenfarb MD (1971) Reproducibility in Coagulation Assays, <i>AJCP</i>, 55:561-564. Palkuti HA and Longberry JR (1973) A Precision Study of Coagulation Factor Assay Techniques, <i>AJCP</i>, 59:231-235.	Вспроизводительность в пределах аналитической серии				Тест	<i>n</i>	<i>Среднее</i>	<i>CV (%)</i>	Фибриноген (г/Л)	5	3.0	3.6	Фактор IX (%)	5	124.7	1.9	Протеин S (%)	5	98.5	2.8
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Declaration of Conformity

helena
Biosciences Europe

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.

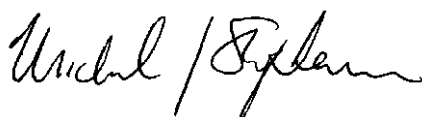
Product Code	Description	GMDN Classification Code
5556	Clauss Fibrinogen 50	55997

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:



Date: 12 Aug 2015

Tel +44 (0)191 482 8440

Fax +44 (0)191 482 8442

info@helena-biosciences.com

www.helena-biosciences.com

Helena Biosciences Europe

Queensway South, Team Valley Trading Estate,
Gateshead, Tyne and Wear, NE11 0SD,

United Kingdom

Clauss Fibrinogen 50



REF 5556
REF 5556H



Helena Biosciences Europe, Queensway South, Team Valley Trading Estate, Gateshead, Tyne and Wear, NE11 OSD, United Kingdom

Tel: +44 (0)191 482 8440

Fax: +44 (0)191 482 8442

Email: info@helena-biosciences.com

Web: www.helena-biosciences.com

HL-2-1771P 2012/03 (7)

<p>Clauss Fibrinogen 50 Instructions for use</p>	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 <i>in vitro</i> 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 immediately 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.	Reconstitue 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.
<p>Each kit contains instructions for use.</p> <p>Each kit contains lot specific reference values insert.</p>			

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 minutes⁵.

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 degradation 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		
<i>Fibrinogen (g/L)</i>	<i>n</i>	<i>CV (%)</i>	<i>Fibrinogen (g/L)</i>	<i>n</i>	<i>CV (%)</i>
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

REFERENCES

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- Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
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- Scully RE *et al.* (1980) Normal Reference Laboratory Values, *New England Journal Medicine*, **302**(37):37-48.
- Okuno T, Selenko V (1972) Plasma fibrinogen determination by automated thrombin time, *American Journal of Medical Technology*, **38**(6):196-201

<p>Clauss Fibrinogen 50 Fiche technique</p>	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 <i>in vitro</i> 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 e 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.		
<p>Chaque kit contient une fiche technique.</p> <p>Chaque kit contient valeurs de référence spécifiques du lot.</p>					
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	Conservé 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		
<i>Fibrinogène (g/L)</i>	<i>n</i>	<i>CV (%)</i>	<i>Fibrinogène (g/L)</i>	<i>n</i>	<i>CV (%)</i>
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

RÉFÉRENCES

- Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
- Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
- 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
- Scully RE *et al.* (1980) Normal Reference Laboratory Values, *New England Journal Medicine*, **302**(37):37-48.
- Okuno T, Selenko V (1972) Plasma fibrinogen determination by automated thrombin time, *American Journal of Medical Technology*, **38**(6):196-201

<p>Clauss Fibrinogen 50 Anleitung</p>	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 <i>in vitro</i> 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 Flaschen 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.		
<p>Jedes Kit enthält eine Gebrauchsanweisung.</p> <p>Jedes Kit enthält chargenspezifischen Referenzwerten.</p>					
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.				
PROBENTENNAHME 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		
<i>Fibrinogen (g/L)</i>	<i>n</i>	<i>CV (%)</i>	<i>Fibrinogen (g/L)</i>	<i>n</i>	<i>CV (%)</i>
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

REFERENZEN

- Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
- Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
- 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
- Scully RE *et al.* (1980) Normal Reference Laboratory Values, *New England Journal Medicine*, **302**(37):37-48.
- 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

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. Clauss¹ 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 orali². 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 disifibrinogenemia (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) <p>5 x 2 mL (REF 5556H)</p>	Ogni flacone contiene approssimativamente 200 (REF 5556) / 100 (REF 5556H) unità di Thrombin bovina con stabilizzatori.	Ricostituire ogni flacone con: <p>4 mL (REF 5556) <p>2 mL (REF 5556H) di acqua distillata. 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.</p></p>
Fibrinogen Calibrator	2 x 1 mL (REF 5556) <p>1 x 1 mL (REF 5556H)</p>	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) <p>1 x 25 mL (REF 5556H)</p>	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 silconizzato. 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 minuti³.

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 plasm 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				
<i>Fibrinogeno (g/L)</i>	<i>n</i>	<i>CV</i> (%)	<i>Fibrinogeno (g/L)</i>	<i>n</i>	<i>CV</i> (%)
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

RIFERIMENTI

- Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
- Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
- 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
- Scully RE *et al.* (1980) Normal Reference Laboratory Values, *New England Journal Medicine*, **302**(37):37-48.
- 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

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. Clauss¹ 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 orales². 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 disifibrinogenemia (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) <p>5 x 2 mL (REF 5556H)</p>	Cada vial contiene aproximadamente 200 (REF 5556) / 100 (REF 5556H) unidades de trombina bovina con estabilizadores.	Reconstituya cada vial con: <p>4 mL (REF 5556) <p>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.</p></p>
Fibrinogen Calibrator	2 x 1 mL (REF 5556) <p>1 x 1 mL (REF 5556H)</p>	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) <p>1 x 25 mL (REF 5556H)</p>	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 silconizado. 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. Decongelar rápidamente a *37°C antes de realizar la prueba. No conservar a *37°C durante más de 5 minutos³.

PROCEDIMIENTO

Consulta 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 directrix. 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					
Precision intra-ensayo	Precisión inter-ensayo				
<i>Fibrinógeno (g/L)</i>	<i>n</i>	<i>CV</i> (%)	<i>Fibrinógeno (g/L)</i>	<i>n</i>	<i>CV</i> (%)
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

REFERENCIAS

- Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
- Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
- 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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Тест-система "Определение фибриногена методом Клаусса 50"
инструкция

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 Клаусса¹ – простой метод количественного определения фибриногена, основанный на измерении времени образования густка. Метод проводится в разведенной плазме после добавления тромбинового реагента (> 30 МЕ/мл). Время образования густка пропорционально концентрации фибриногена. Уровень фибриногена может увеличиваться при воспалении, беременности или при приеме пероральных контрацептивов². Низкие значения могут наблюдаться при заболеваниях печени и ДВС. Изменение содержания фибриногена в плазме помогает диагностике врожденных дефицитных состояний, включая афibrinогенемию (полное отсутствие фибриногена), гипофибриногемию (концентрация фибриногена менее 1 мг/мл) и дисфибриногемию (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 mL (Кат. № 5556) <p>5 x 2 mL (Кат. № 5556H)</p>	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 mL (Кат. № 5556) <p>1 x 1 mL (Кат. № 5556H)</p>	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 mL (Кат. № 5556) <p>1 x 25 mL (Кат. № 5556H)</p>	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

Невыскртые 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 anticoагулянтom (3,2% или 3,8% цитрат натрия) в соотношении 9 + 1. После центрифугирования при 1500 г, 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 минут³.

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 r/l)^{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 r/l.

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 r/l (без дополнительных разведений плазмы).

Воспроизводимость					
в пределах аналитической серии	между разными аналитическими сериями				
<i>Фибриноген (r/l)</i>	<i>n</i>	<i>CV</i> (%)	<i>Фибриноген (r/l)</i>	<i>n</i>	<i>CV</i> (%)
1.24	5	4.88	1.02	10	6.17
3.01	5	3.58	3.62	10	3.75

СПИСОК ЛИТЕРАТУРЫ

- Clauss A (1957) Gerinnungsphysiologische Schnell-methode zur bestimmung des Fibrinogens, *Acta Haematol*, **17**:237-246
- Shaw TS (1977) Assays for Fibrinogen and its Derivatives CRC, *Crit. Rev. Clin. Lab. Sci*, **8**:145-192.
- 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
- Scully RE *et al.* (1980) Normal Reference Laboratory Values, *New England Journal Medicine*, **302**(37):37-48.
- Okuno T, Selenko V (1972) Plasma fibrinogen determination by automated thrombin time, *American Journal of Medical Technology*, **38**(6):196-201

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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.

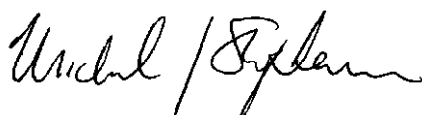
Product Code	Description	GMDN Classification Code
5392	Thrombin Time	55987

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

Signed:



Date: 06 Aug 2015

Tel +44 (0)191 482 8440
Fax +44 (0)191 482 8442
info@helena-biosciences.com
www.helena-biosciences.com

Helena Biosciences Europe
Queensway South, Team Valley Trading Estate,
Gateshead, Tyne and Wear, NE11 0SD,
United Kingdom

<div></div> <div>Thrombin Time</div>
Istruzioni per l'uso

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 polibrene¹, gli studi sulla miscelazione di plasma normale² o il dosaggio della reptilasi³, 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.

Component	Contiene	Descrizione	Preparazione
Thrombin Time	10 x 1 mL (REF 5392H) <p>10 x 2 mL (REF 5392)</p> <p>10 x 5 mL (REF 5377)</p>	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: <p>1 mL - REF 5392H</p> <p>2 mL - REF 5392</p> <p>5 mL - REF 5377</p> <p>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.</p>
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.
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RACCOLTA E PREPARAZIONE DEI CAMPIONI

Nel corso dell’intera procedura è necessario utilizzare plastica o vetro silicizzato. 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 minuti⁴.

PROCEDURA

- Raccogliere e preparare il campione di sangue conformemente alle istruzioni riportate nel paragrafo "Raccolta dei campioni e preparazione".
- Ricostituire il plasma di controllo seguendo le indicazioni fornite nell’inserito contenuto nella confezione di ciascun controllo.
- Preparare il reagente da utilizzare nella procedura conformemente alle istruzioni di ricostituzione riportate nel paragrafo "Composizione".
- 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

- Pipettare 0,2 mL di plasma del paziente o di plasma di controllo in una provetta di reazione.
- Incabare a *37°C per 3 minuti.
- 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.
- 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 Time⁵. Inoltre, i livelli terapeutici di eparina possono eliminare completamente la coagulazione nei test del Thrombin Time, sebbene la neutralizzazione con protamina solfato o polibrene dovrebbe correggere il Thrombin Time¹.

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			
<i>Campione</i>	<i>n</i>	<i>Formazione del coagulo (secondi)</i>	<i>CV (%)</i>	<i>Formazione del coagulo (secondi)</i>	<i>CV (%)</i>
Normali	10	12,5	1,43	12,5	1,29

BIBLIOGRAFIA

- Laposata *et al.*The Clinical Haemostasis Handbook, Yearbook Medical Publishers Inc., p219, 1989
- Thompson AR and Harker LA. Manual of Haemostasis and Thrombosis. 3rd Ed., F.A. Davis Co., p62, 1983
- DeMott WR. Laboratory Test Handbook, 2nd Ed., Jacobs D.S. et al Eds., Lexi-Comp Inc., p432-433, 1990.
- 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
- Gastineau DA *et al.* (1991) Inhibitor of the Thrombin Time in Systemic Amyloidosis: A Common Coagulation Abnormality, *Blood*, **77**:2637-40

<div></div> <div>Thrombin Time</div>
Istrucciones de uso

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 polibreno¹, los estudios de mezcla de plasma normal² o el ensayo de la reptilasa³ 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) <p>10 x 2 mL (REF 5392)</p> <p>10 x 5 mL (REF 5377)</p>	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: <p>1 mL - REF 5392H</p> <p>2 mL - REF 5392</p> <p>5 mL - REF 5377</p> <p>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.</p>
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.
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RECOGIDA Y PREPARACIÓN DE LAS MUESTRAS

Debe usarse siempre plástico o vidrio silicizado. 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 minutos⁴.

PROCEDIMIENTO

- Recoja y prepare la muestra de sangre de acuerdo con las instrucciones esbozadas en "Recogida y preparación de muestras".
- Reconstituya el plasma control de acuerdo con el prospecto incluido con cada control.
- Prepare el reactivo para su uso en el procedimiento de acuerdo con las instrucciones de reconstitución en la sección "Composición".
- 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

- Pipetee 0,2 mL del plasma del paciente o el plasma control en un tubo de reacción.
- Incube a *37°C durante 3 minutos.
- 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.
- 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 inibidor circulante que prolonga el Thrombin Time⁵. Además, los niveles terapéuticos de heparina 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 Time¹.

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			
<i>Muestra</i>	<i>n</i>	<i>Formación del coágulo (segundo)</i>	<i>CV (%)</i>	<i>Formación del coágulo (segunda)</i>	<i>CV (%)</i>
Normales	10	12,5	1,43	12,5	1,29

BIBLIOGRAFÍA

- Laposata *et al.*The Clinical Haemostasis Handbook, Yearbook Medical Publishers Inc., p219, 1989
- Thompson AR and Harker LA. Manual of Haemostasis and Thrombosis. 3rd Ed., F.A. Davis Co., p62, 1983
- DeMott WR. Laboratory Test Handbook, 2nd Ed., Jacobs D.S. et al Eds., Lexi-Comp Inc., p432-433, 1990.
- 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
- Gastineau DA *et al.* (1991) Inhibitor of the Thrombin Time in Systemic Amyloidosis: A Common Coagulation Abnormality, *Blood*, **77**:2637-40

<div></div> <div>Тест-система "Тромбиновое время"</div>
инструкция

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 полибреном¹, исследования на смешивание нормальной плазмы² или рептилазное исследование³ для установления различия между гипofибриногемией 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 производится в соответствии с местными правилами.

СОСТАВ

Состав	Содержимое набора	Описание	Приготовление
Тест-система «Тромбиновое время»	10 x 1 мл (Кат. № 5392H) <p>10 x 2 мл (Кат. № 5392)</p> <p>10 x 5 мл (Кат. № 5377)</p>	Каждый флакон содержит лиофилизированный препарат из бычьего тромбина с биферами и стабилизаторами. Восстановленный реагент содержит ≤10 NIH ЕД/мл тромбина. Реагентом должна быть лиофилизированная тромбоцитная пробка.	Восстановите реагент с рекомендуемым объемом очищенной воды: <p>1 мл для - кат № 5392H</p> <p>2 мл для - кат. № 5392</p> <p>5 мл для - кат. № 5377</p> <p>Дайте постоять 5 минут, затем перемешайте путем переморачивания и поместите в пластиковую пробирку. Восстановленный реагент должен представлять собой чистый бесцветный раствор.</p>

<p>В каждом наборе имеется инструкция по применению.</p>	
НЕОБХОДИМЫЕ КОМПОНЕНТЫ, НЕ ВКЛЮЧЕННЫЕ В КОМПЛЕКТ ПОСТАВКИ	
<p>Может использоваться любой высококачественный механическое, оптико-механического или фотооптического прибор, который может проверять время свертывания тромбина.</p>	
ХРАНЕНИЕ, СРОК ГОДНОСТИ И УСТОЙЧИВОСТЬ	
<p>Невыскртые флаконы остаются стабильными до истечения срока годности при хранении в условиях, указанных на флаконе или этикетке набора.</p>	
<p>Тест-система «Тромбиновое время»</p> <p>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.</p> <p>Срок хранения реагента в фотооптическом приборе Sysmex CA1500 не должен превышать 7 дней.</p>	

<p>ОТБОР И ПОДГОТОВКА ОБРАЗЦОВ</p>	
<p>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 centrifугирования при 1500 г 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°C⁴.</p>	
ПРОЦЕДУРА	
<ol style="list-style-type: none">Проведите забор и подготовку пробы крови в соответствии с указаниями документа ЗАБОР И ПОДГОТОВКА ОБРАЗЦОВ. Восстановите контрольную плазму в соответствии с приложенным листком-вкладышем. Подготовьте реагент к использованию в порядке, указанном в инструкции по восстановлению в разделе СОСТАВ. 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

- С помощью пипетки поместите 0,2 мл плазмы пациента или контрольной плазмы в реакционную пробирку.
- Инкубируйте 3 минуты при температуре *37°C.
- С помощью пипетки поместите 0,1 мл тест-системы «Тромбиновое время» в реакционную пробирку, содержащую плазму пациента или контрольную плазму, и одновременно включите таймер.
- Закфиксируйте 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 Байосайенс 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 средней ±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 время⁵. Также терапевтические дозы гепарина могут полностью прекратить свертывание в тесте на тромбиновое время, хотя нейтрализация сульфатом протамина или полибреном должна скорректировать тромбиновое время¹.

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 Байосайенс 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 Байосайенс Европ" или ее представителями:

Изучение повторяемости					
	Внутрианалитическая сходимость	Внутрианалитическая сходимость			
<i>Образец</i>	<i>Число образцов</i>	<i>Время свертывания (секунды)</i>	<i>CV (%)</i>	<i>Время свертывания (секунды)</i>	<i>CV (%)</i>
нормальным	10	12,5	1,43	12,5	1,29

ЛИТЕРАТУРА

- Laposata *et al.*The Clinical Haemostasis Handbook, Yearbook Medical Publishers Inc., p219, 1989
- Thompson AR and Harker LA. Manual of Haemostasis and Thrombosis. 3rd Ed., F.A. Davis Co., p62, 1983
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- 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
- Gastineau DA *et al.* (1991) Inhibitor of the Thrombin Time in Systemic Amyloidosis: A Common Coagulation Abnormality, *Blood*, **77**:2637-40

Declaration of Conformity

helena
Biosciences Europe

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.

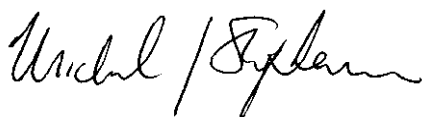
Product Code	Description	GMDN Classification Code
5186	Routine Control N	30590

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

Tel +44 (0)191 482 8440
Fax +44 (0)191 482 8442
info@helena-biosciences.com
www.helena-biosciences.com

Helena Biosciences Europe
Queensway South, Team Valley Trading Estate,
Gateshead, Tyne and Wear, NE11 0SD,
United Kingdom

Declaration of Conformity

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Biosciences Europe

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.

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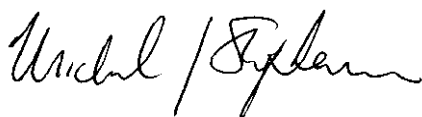
Product Code	Description	GMDN Classification Code
5187	Routine Control A	30590

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:



Date: 28 Jul 2015

Tel +44 (0)191 482 8440
Fax +44 (0)191 482 8442
info@helena-biosciences.com
www.helena-biosciences.com

Helena Biosciences Europe
Queensway South, Team Valley Trading Estate,
Gateshead, Tyne and Wear, NE11 0SD,
United Kingdom

Declaration of Conformity

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Biosciences Europe

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.

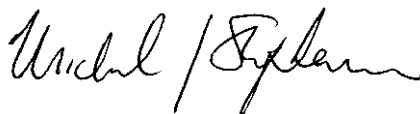
Product Code	Description	GMDN Classification Code
5183	Routine Control SA	30590

I, the undersigned declare that the devices registered against the above GMDN Classification Code conforms to the said Directives.

Full Name: M.J. Stephenson

Title: Managing Director

Signed:



Date: 28 Jul 2015

Tel +44 (0)191 482 8440
Fax +44 (0)191 482 8442
info@helena-biosciences.com
www.helena-biosciences.com

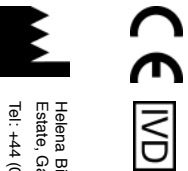
Helena Biosciences Europe
Queensway South, Team Valley Trading Estate,
Gateshead, Tyne and Wear, NE11 0SD,
United Kingdom

Coagulation Control Plasmas

REF 5186
REF 5187
REF 5183
REF 5482

Routine Control N
Routine Control A
Routine Control SA
Routine Coagulation Control Set

Helena
Biosciences Europe



Helena Biosciences Europe, Queensway South, Team Valley Trading Estate, Gateshead, Tyne and Wear, NE11 0SD, United Kingdom
Tel: +44 (0)191 482 8440
Fax: +44 (0)191 482 8442
Email: info@helena-biosciences.com
Web: www.helena-biosciences.com

HL-2-0482P 2016/01 (16)

Coagulation Control Plasmas

en

INTENDED PURPOSE

The Coagulation Control Plasma 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 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 a donated human plasma.
5183	Routine Control - SA	10 x 1 mL	Prepared from a donated 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 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 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 6 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 routine 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 reagent, diluent substrates and laboratory to laboratory variations. Each laboratory should establish an expected range for the particular instrument used.

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	PT CV (%)	aPTT CV (%)
Sample	n		
Routine Control N	5	2.63	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*, 37:555-568
2. 37:555-568 MD (1971) Reproducibility in Coagulation Assays. *AJOP* 55:561-564.
3. Pallott HA and Longbery JH (1979) A Precision Study of Coagulation Factor Assay Techniques. *AJOP* 59:231-235.

fr

Plasmas de contrôle de coagulation

Fiche technique

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 prolongés et nettement prolongés dans les déterminations du PT et du TCA, Le fibrinogène, le TCT et l'ATIII ont été dosés et ils sont préparés à partir de plasma humain normal.

AVERTISSEMENTS ET PRECAUTIONS

Les réactifs du kit sont à usage diagnostique *in vitro* uniquement. - NE PAS INGESTER. Porter un équipement de protection individuelle appropriée lors de la manipulation de tous les composants du kit. Consulter la fiche de données de sécurité du produit pour obtenir les précautions et les conseils de production le cas échéant. Éliminer les déchets conformément aux réglementations locales.

Un dépositage des produits sanguins a été réalisé et a donné un résultat négatif (sauf indication contraire sur la boîte du kit ou sur le carton) quant à la présence de: Hépatite B Antigène (HbsAg) HIV 1 Anticorps anti-HIV-2 Anticorps anti-HIV-2 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	Préparé à partir de plasma humain adonné.
5183	Routine Control - SA	10 x 1 mL	Préparées à partir de plasma humain adonné.
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 déionisée. 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-optiques 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 6 heures entre 2-8°C ou 4 semaines à -20°C en cas de congélation instantanée. Conserver le produit.

PRÉLEVEMENT 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 PT, le TCA et le fibrinogène. Le Routine Control A et le Routine Control SA ont été standardisés pour donner des temps PT et TCA prolongés et très prolongés respectivement. Les valeurs prévues spécifiques du kit 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, le réactif et le système de mesure. Les valeurs de référence de référence. Le laboratoire doit déterminer avec chaque prévue pour chaque système instrument-réactif.

CONTRÔLE QUALITÉ

Chaque laboratoire doit établir un programme de contrôle qualité. Les plasmas de contrôle, normale et anormale, doivent être testés avant chaque lot de réactifs 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 valides.

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 PERFORMANCE

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

Échantillon	n	Precision Intra-assay	PT CV (%)	aPTT CV (%)
Routine Control N	5	2.63	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*, 37:555-568
2. Goldstein MD (1971) Reproducibility in Coagulation Assays. *AJOP* 55:561-564.
3. Pallott HA and Longbery JH (1979) A Precision Study of Coagulation Factor Assay Techniques. *AJOP* 59:231-235.

Kontrollplasma für die Gerinnung

Anleitung

VERWENDUNGSZWECK

Das Coagulation Control Plasma-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, T2 und ATIII 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 verwenden für andere Zwecke. Bei der Verwendung dieses Produkts sind die entsprechenden Sicherheitsmaßnahmen zu beachten. Lesen Sie die Bedienungsanleitung des Produkts für weitere Informationen. Die Einzelkomponenten sind für die Verwendung im Labor vorgesehen. Lesen Sie die Bedienungsanleitung des Produkts für weitere Informationen. Die Blutprodukte wurden untersucht und sind für folgende Gene ohne Befund (soweit nicht anderweitig auf der Verpackung oder dem Etikett angegeben): Hepatitis-B-Antikörper (HbsAg) HIV-1-Antikörper 1 HIV-2-Antikörper 2

Das Produkt wird als Arzneimittel klassifiziert. Lesen Sie die Bedienungsanleitung des Produkts für weitere Informationen. 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	Adoniertem Humanplasma hergestellt.
5183	Routine Control - SA	10 x 1 mL	Adoniertem 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 einen Gebrauchsanweisung.

Jedes Fläschchen enthält 1 mL gepuffertes, lyophilisiertes Humanplasma.

Vorbereitung: Reconstituieren jedes Fläschchen des Kontrollplasma mit 1 mL destilliertem oder entionisiertem Wasser. Rekonstruieren. Lichtschirmen. Zum vollständigen Auflösen 10 Minuten stehen lassen und vor Gebrauch gut mischen.

ERFORDERLICHE, ABER NICHT MITGELIEFTE 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 dem auf der Verpackung oder Fläschchen angegebenen Lagerbedingungen bis zum aufgedruckten Verfallsdatum stabil. Einmal reconstituieren, sind die Kontrollen für 6 Stunden bei 2-8°C oder 4 Wochen bei -20°C, wenn schockgefroren, verschlossen aufbewahren.

PROBENTNAHME UND VORBEREITUNG

Entfällt.

VORGEHENSWEISE

Jedes 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 Rechnung mit Kontrollen enthalten.

ENSICHERUNGSMASSNAHMEN

Die mit Coagulation Control Plasmas erhaltenen Resultate hängen von mehreren Faktoren ab, die stark mit dem Gerät, dem verwendeten Reagenzien, möglichen Substraten und Unterschieden zwischen den Labors in Verbindung stehen. Jedes Labor sollte daher für jedes Geräte-Reagenzien-System einen eigenen Normalwertbereich erstellen.

QUALITÄTSKONTROLLE

Jedes Labor muss für eine eigene Qualitätskontrolle sorgen. Normale und pathologische Kontrollplasmas müssen vor jeder Analyse getestet werden. Die Werte von Kontrollen können variieren. Jedes Labor sollte daher für jedes Geräte-Reagenzien-System einen eigenen Normalwertbereich erstellen. Jedes Labor sollte daher für jedes Geräte-Reagenzien-System einen eigenen Normalwertbereich erstellen. Jedes Labor muss für eine eigene Qualitätskontrolle sorgen. Normale und pathologische Kontrollplasmas müssen vor jeder Analyse getestet werden. Die Werte von Kontrollen können variieren. Jedes Labor sollte daher für jedes Geräte-Reagenzien-System einen eigenen Normalwertbereich erstellen.

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

International Business Manager

**Helena Biosciences Europe**

Queensway South, Team Valley Trading Estate,
Gateshead, Tyne and Wear, NE11 0SD, United Kingdom

Tel +44 (0)191 482 8440
Fax +44 (0)191 482 8442

info@helena-biosciences.com
www.helena-biosciences.com

Declaration of Conformity

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Biosciences Europe

HL-7-DC-0814 Rev. 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
5560	APTT Si L Minus	55981

I, the undersigned, declare that the devices registered against the above GMDN Classification Code conforms to the said Directives.

Full Name: C.J. Sandercock

Title: QA and Regulatory Affairs Officer

Signed:



Date: 24 Nov 2020



Helena Biosciences Europe,
Gateshead, Tyne and Wear,
NE11 0SD, United Kingdom
Tel +44 (0)191 482 8440

info@helena-biosciences.com

www.helena-biosciences.com

EC REP

Prince Technologies B.V.
Waanderweg 62,
7812 HZ Emmen,
The Netherlands

APTT Si L Minus



REF 5562
REF 5560
REF 5559

CE IVD EC REP Prince Technologies B.V.
Waanderweg 62, 7812 HZ Emmen,
The Netherlands

Helena Biosciences Europe, Queensway South, Team Valley Trading Estate, Gateshead, Tyne and Wear, NE11 OSD, United Kingdom
Tel: +44 (0)191 482 8440
Email: info@helena-biosciences.com
Web: www.helena-biosciences.com

HL-2-P-1787 Rev. 8

APTT Si L Minus Instructions for use

INTENDED PURPOSE
The APTT Si L Minus kit is intended for carrying out clot based haemostasis assays.

For use in the determination of activated partial thromboplastin times (aPTT), and related coagulation procedures using phospholipid extract and a near-colloidal particle activator. The test system can be used on manual, semi-automated and automated methods. From its origins through the work of Langdell and coworkers¹, and later modified by Proctor and Rapaport², the aPTT is used to detect disorders in the intrinsic coagulation system, which involves coagulation factors VIII, IX, XI, XII, prekallikrein, and high molecular weight kininogen. The aPTT is also used in assays which quantitate these factors and is routinely used for pre-surgical screening and monitoring of heparin therapy³. Commercially available reagents typically use one of three activators: kaolin, silica, or ellagic acid. In the basic screening test, the aPTT indirectly measures the formation of thrombin by its action on fibrinogen forming the fibrin clot. In the test, citrated test plasma is mixed with aPTT reagent for a specified period of time (typically 5 minutes) at 37°C followed by the addition of pre-warmed (37°C) calcium chloride (0.025 M). Timing is begun from the time of addition of calcium chloride. The time required for clot formation is the aPTT. Clot detection can be by mechanical, manual (filt tube), or photo-optical measurement.

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.

Component	Content	Description	Preparation
APTT Si L Minus	5 x 5 mL (REF 5562) 10 x 5 mL (REF 5560) 10 x 10 mL (REF 5559)	Reagent contains a near colloidal particle activator (magnesium-aluminium-silicate) for optimum sensitivity to factor deficiencies and to heparin. The reagent also contains phospholipids with buffer and stabilisers.	Bring to room temperature prior to use. Mix well by swirling or inversion prior to use.
Calcium Chloride: 0.025M	5 x 5 mL (REF 5562) 10 x 5 mL (REF 5560) 10 x 10 mL (REF 5559)	The reagent is a 0.025 M solution of calcium chloride.	The reagent is ready for use as packaged.

Each kit contains instructions for use.

ITEMS REQUIRED BUT NOT PROVIDED

Any high quality electro-mechanical or photo-optical coagulation instrument designed for performing activated partial thromboplastin times 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. Store at 2° –8°C. DO NOT FREEZE. Stable for 30 days after opening. Avoid prolonged heating.

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. This will minimise the neutralisation of the lupus inhibitor⁴. Erroneous results may be caused by contamination with tissue fluids or stasis. Avoid agitation, air bubbles or foaming. For the effects of commonly administered drugs, refer to Young, *et al.*⁵.

PROCEDURE

Manual Method

1. Prewarm well mixed APTT Si L Minus and 0.025 M Calcium Chloride to 37°C.
2. Prewarm 0.1 mL test plasma in duplicate to 37°C for 2 minutes.
3. Forcibly add 0.1 mL prewarmed APTT Si L Minus to plasma and start timer. Incubate for exactly 5 minutes at 37°C.
4. Add 0.1 mL prewarmed 0.025 M Calcium Chloride.
5. Note time for clot formation. Report result as aPTT time (seconds).

Automated Method

Refer to the appropriate instrument operator manual for detailed instructions or contact Helena Biosciences Europe for instrument specification notes.

INTERPRETATION OF RESULTS

The results of the aPTT test should be reported to the nearest 1/10 of a second. The normal range (usually X ± 2 standard deviations) for each individual laboratory should be established. Results greater than the upper limits of the normal range should be considered abnormal and follow-up testing should be performed. Any aPTT values less than the lower limits of the normal range should be repeated on a new blood sample. Short aPTT values may be seen in association with *in vivo* thrombosis (e.g. deep vein thrombosis and disseminated intravascular coagulation).

Heparin monitoring

When monitoring heparin therapy, it is important to construct an *in vitro* reference curve which reflects the average heparin response, since individual patients respond differently to heparin. In general, one can consider the therapeutic range for heparin to be 0.2 to 0.5 units/mL^{3,6}.

The following precautions should be considered when monitoring heparin therapy:

1. Time of collection is important, since heparin has an *in vivo* half-life of only 1.5 hours⁷.
2. Release of platelet factor 4 (heparin neutralising factor) caused by platelet aggregation or damage during collection, should be avoided. Careful blood collection, proper centrifugation and prompt removal of the platelet poor plasma from the cells will help minimise the release of platelet factor 4.
3. Baseline data on each patient's aPTT should be established before therapy, to determine the respective patient aPTT as it relates to the normal range established by the laboratory.
4. Different clot detection systems (mechanical, photo-optical, etc.) show variable sensitivities to heparin. The same test system should be used when monitoring heparinised patients.
5. Heparin response curves should be reestablished when lot numbers of reagent change and at periodic intervals with the same lot number.
6. The curve should also be constructed using the same heparin employed in therapy, to eliminate variables connected with heparins from different sources (e.g. porcine mucosa or bovine lung).

LIMITATIONS

Expected values for the aPTT 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 specimen storage are all very important. Plasma sample collection and storage conditions should be standardised and carefully controlled. Unexpected results should be confirmed by additional tests. Platelet fragments present in a specimen may cause the release of phospholipids, and thus the neutralisation of any lupus inhibitor present in the specimen. The use of specimens with small plasma volumes should be avoided due to possible physiological pH changes. Testing could be affected by several drugs⁸. An increase in the aPTT results may be caused by the administration of diphenhydantoin, heparin, warfarin and radiographic agents⁸. Decreased aPTT values may be seen during the use of oral contraceptives, or male estrogen therapy²⁰. Thus, laboratories should establish their own expected values for patients and well defined performance standards for the control.

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 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 reference ranges.

PERFORMANCE CHARACTERISTICS

The following performance characteristics have been determined by Helena Biosciences Europe or their representatives using a photo-optical coagulation instrument. Each laboratory should establish its own performance data.

Reproducibility

Sample	Intra-assay precision			Inter-assay precision		
	n	CLOT formation (seconds)	CV (%)	n	CLOT formation (seconds)	CV (%)
Routine Control N	10	33,0	0,36	100	32,9	2,41
Routine Control SA	10	77,9	0,31	100	78,3	0,77

% Factor	Factor VIII (seconds)	Factor IX (seconds)	Factor XI (seconds)
<1	85,7	70,9	92,4
10	45,9	44,4	50,7
40	34,2	33,9	34,4
100	28,8	28,8	28,8

Heparin (IU/mL)	Clot formation (seconds)
0	29,9
0,2	70,0
0,4	174,0

BIBLIOGRAPHY

1. Langdell R, Wagner R, Brinkhous K (1953) Effect of Antihemophilic Factor on One Stage Clotting Tests, *J. Lab. Clin. Med.* **41**: 637
2. Proctor R, Rapaport S (1961) The Partial Thromboplastin Time with Kaolin, *Am. J. Clin. Path.* **36**: 212
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10. Crowell EB Jr, Clatanoff DV, Kiekhof W (1971) The effect of oral contraceptives on factor VIII levels, *Lab. Clin. Med*, **77**: 551-7

APTT Si L Minus Fiche technique

UTILISATION

Le kit APTT Si L Minus est destiné à la réalisation des analyses de l'hémostase basées sur la formation de caillots.

Utilisé dans la détermination du temps de céphaline activé (TCA), et pour des méthodes de coagulation connexes en utilisant des extraits de la phospholipide additionnés à particules semi-colloïdales comme activateur. Il est possible d'utiliser en général l'un de ces trois activateurs: kaolin, silice ou acide ellagique. Dans le test de base, le TCA mesure de façon indirecte la formation de thrombine par son action sur le fibrinogène aboutissant à la formation d'un caillot fibrineux. Dans la détermination, le plasma citraté à analyser est mélangé avec le réactif TCA pendant une durée concrète (en général 5 minutes) à 37°C, puis du chlorure de calcium (0,025 M) préchauffé à 37°C est ajouté. Le chromatographe commence au moment de l'ajout du chlorure de calcium. Le temps nécessaire à la formation du caillot est le TCA. Il est possible de détecter la coagulation par une technique mécanique, manuelle (tube incliné) ou avec un instrument photo-optique.

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 réglementations locales.

COMPOSITION

Composant	Contient	Description	Préparation
APTT Si L Minus	5 x 5 mL (REF 5562) 10 x 5 mL (REF 5560) 10 x 10 mL (REF 5559)	Contient un activateur à particules semi-colloïdales (magnésium-aluminiumsilicate) pour une sensibilité optimale aux déficits de facteurs et à l'héparine. Le réactif contient aussi le phospholipide avec le tampon et les agents de stabilisation.	Ramenez-le à température ambiante avant de l'utiliser. Mélangez bien en remuant ou en inversant avant d'utiliser.
Calcium Chloride: 0.025M	5 x 5 mL (REF 5562) 10 x 5 mL (REF 5560) 10 x 10 mL (REF 5559)	Le réactif est une solution de chlorure de calcium à 0,025 M.	Le réactif est prêt à l'emploi.

Chaque kit contient une fiche technique.

MATÉRIEL NÉCESSAIRE NON FOURNI

Il est possible d'utiliser un instrument de coagulation électromécanique ou photo-optique de haute qualité conçu pour déterminer le temps de céphaline active.

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. Conservez-les à 2° –8°C. SANS LE CONGELER. Stable pendant 30 jours après ouverture. Évitez des réchauffements prolongés.

PRÉLEVÈMENT ET PRÉPARATION DES ÉCHANTILLONS

Utiliser tout au long du prélèvement du plastique ou du verre silicisé. 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 car la neutralisation de la l'inhéteur lupique serait réduite⁴. Il est possible d'obtenir des résultats erronés en cas de contamination avec du liquide tissulaire ou en cas de stase. Éviter d'agiter et de former des bulles d'air ou de l'écume. Se référer à Young, *et al.*⁵ pour connaître les effets des médicaments couramment administrés.

PROCÉDURE

Méthode Manuelle

1. Préchauffez le mélange d'APTT Si L Minus et de chlorure de calcium à 0,025 M à 37°C.
2. Préchauffez 0,1 mL de plasma à analyser, en dosage double, à 37°C pendant 2 minutes.
3. Ajoutez énergiquement 0,1 mL d'APTT Si L Minus préchauffé au plasma et lancez le coagulomètre. Laissez incuber pendant 5 minutes exactement à 37°C.
4. Ajoutez 0,1 mL de chlorure de calcium à 0,025 M préchauffé.
5. Notez le temps de formation de caillots. Exprimez les résultats TCA en secondes.

Méthodes Automatisées

Consultez le manuel d'utilisation de l'instrument approprié pour obtenir des instructions détaillées ou contactez Helena Biosciences Europe pour obtenir des notes d'application spécifiques à l'instrument.

INTERPRÉTATION DES RÉSULTATS

Les résultats de TCA doivent être relevés en arrondissant au dixième de seconde. Il appartient à chaque laboratoire de déterminer ses valeurs usuelles (en général, temps moyen ± 2 écarts-types). Des résultats dépassant la limite supérieure des valeurs usuelles doivent être considérés comme anormaux et il est nécessaire de réaliser des études plus approfondies. Si les valeurs du TCA sont inférieures à la limite inférieure des valeurs usuelles, répéter l'analyse avec un nouvel échantillon de sang. Un TCA raccourci a été trouvé en association avec des thromboses *in vivo* (par exemple, thrombose veineuse profonde et coagulation intravasculaire disséminée).

Surveillance de l'héparine

Lors de la surveillance de l'héparinothérapie, il est important de créer une courbe de référence *in vitro* qui reflète la moyenne réponse à l'héparine, étant donné que chaque patient répond différemment à l'héparine. On considère en général que la plage thérapeutique de l'héparine se situe entre 0,2 et 0,5 unités/mL^{3,6}.

Les précautions suivantes doivent être prises en considération lors de la surveillance de l'héparinothérapie:

1. Le moment du prélèvement est important, étant donné la demi-vie *in vivo* de l'héparine n'est que de 1,5 heure⁷.
2. Il convient d'éviter que du facteur plaquettaire 4 ne soit libéré (facteur neutralisant l'héparine) en raison de l'agrégation plaquettaire ou de la rupture de la structure lors du prélèvement. Un prélèvement de sang correct, une centrifugation appropriée et un enlèvement rapide de plasma pauvre en plaquettes des globules rouges aide à réduire la libération de facteur plaquettaire 4.
3. Les valeurs initiales du TCA de chaque patient doivent être établies avant la thérapie afin de déterminer le TCA patient respectif puisqu'il se rapporte aux valeurs usuelles établies par le laboratoire.
4. La sensibilité à l'héparine varie en fonction du système de détection de coagulation (mécanique, photo-optique, etc.). Il est nécessaire d'utiliser le même système d'analyse pour la surveillance des patients sous héparine.
5. Les courbes de réponse à l'héparine doivent être déterminées de nouveau lorsque le numéro de lot de réactif change et à des intervalles périodiques avec le même numéro de lot.
6. La courbe de réponse à l'héparine doit être déterminée en utilisant la même héparine tout au long de la thérapie afin d'éliminer les variations dues aux différentes sources d'héparine (par exemple, muqueuse porcine ou poumon bovin).

LIMITES

Les valeurs prévues du TCA 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 ainsi que 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 normalisées et soigneusement contrôlées. Tout résultat hors intervalle doit être confirmé par des analyses supplémentaires. La présence de fragments de plaquettes dans un échantillon peut entraîner la libération de phospholipides et, par conséquent, la neutralisation de tout inhibiteur lupique présent dans l'échantillon. Il convient d'éviter d'utiliser des petits volumes de plasma en raison des potentielles variations physiologiques du pH. L'analyse peut être affectée par divers médicaments⁸. Un TCA allongé peut être dû à l'administration de diphenhydantoin, d'héparine, de warfarine et de substances radiologiques^{8,9}. Un TCA raccourci peut être observé en cas d'utilisation de contraceptifs oraux ou chez les sujets sous oestrogénothérapie^{9,10}. Il appartient donc à chaque laboratoire d'établir ses propres valeurs attendues pour les patients et de déterminer ses normes de performances pour le contrôle.

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 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 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 photo-optique. Chaque laboratoire doit établir ses propres données de performance.

Reproductibilité

Échantillon	Précision intra-série			Précision Inter-séries		
	n	Formation du caillot (seconde)	CV (%)	n	Formation du caillot (seconde)	CV (%)
Routine Control N	10	33,0	0,36	100	32,9	2,41
Routine Control SA	10	77,9	0,31	100	78,3	0,77

% Facteur	Facteur VIII (secondes)	Facteur IX (secondes)	Facteur XI (secondes)
<1	85,7	70,9	92,4
10	45,9	44,4	50,7
40	34,2	33,9	34,4
100	28,8	28,8	28,8

Héparine (IU/mL)	Formation du caillot (seconde)
0	29,9
0,2	70,0
0,4	174,0

BIBLIOGRAPHIE

1. Langdell R, Wagner R, Brinkhous K (1953) Effect of Antihemophilic Factor on One Stage Clotting Tests, *J. Lab. Clin. Med.* **41**: 637
2. Proctor R, Rapaport S (1961) The Partial Thromboplastin Time with Kaolin, *Am. J. Clin. Path.* **36**: 212
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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. Young DS *et al.* Effects of Drugs on Clinical Laboratory Tests, 3rd ed., AACF Press, Washington, D.C., 1990
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10. Crowell EB Jr, Clatanoff DV, Kiekhof W (1971) The effect of oral contraceptives on factor VIII levels, *Lab. Clin. Med*, **77**: 551-7

APTT Si L Minus Anleitung

VERWENDUNGSZWECK

Das APTT Si L Minus-Kit ist für koagulometrische Gerinnungstests vorgesehen.

Zur Bestimmung der aktivierten partiellen Thromboplastinzeit (aPTT) und ähnlichen Gerinnungsverfahren mit Extrakt von Phospholipid und mit nahezu kolloiden Partikeln als Aktivator. Das Testsystem kann mit manuellen, halbautomatischen oder automatischen Methoden angewendet werden. Der APTT-Test wurde durch die Arbeit von Langdell und Mitarbeitern konzipiert¹ und später durch Proctor und Rapaport modifiziert², die aPTT wird zum Nachweis von Funktionsstörungen im intrinsischen Gerinnungssystem verwendet, zu welchem die Gerinnungsfaktoren VIII, IX, XI, XII, Präkallikrein und hochmolekulares Kininogen gehören. Die aPTT wird auch bei Tests verwendet, die diese Faktoren quantifizieren, und routinemäßig bei der OP-Vorbereitung und dem Monitoring der Heparintherapie verwendet³. Kommerziell erhältliche Reagenzien enthalten üblicherweise einen von drei Aktivatorn: Kaolin, Siliziumdioxid oder Ellagsäure. Bei einem Standard-Screening-Test misst die aPTT indirekt durch ihr Einwirken auf Fibrinogen die Thrombinbildung und damit der Bildung eines Fibringerinnsels. Das zu testende Citratplasma wird im Testansatz mit aPTT-Reagenz bei 37°C über einen bestimmten Zeitraum (üblicherweise 5 Minuten) gemischt und danach vorgewärmtes (37°C) Calciumchlorid (0,025 M) zugegeben. Mit Zugabe des Calciumchlorids wird die Zeit gestoppt. Die Zeit, die es zur Gerinnelbildung braucht, wird als aPTT bezeichnet. Nachweis der Gerinnelbildung kann mechanisch, manuell (Kippmethode) oder lichtoptisch erfolgen.

WARNHINWEISE UND VORSICHTSMASSNAHMEN

Die in diesem Kit enthaltenen Reagenzien sind ausschließlich für die Verwendung von *in-vitro*-Diagnosen vorgesehen. NICHT VERSCHLÜCKEN. Tragen Sie beim Umgang mit sämtlichen Komponenten des Kits geeignete Schutzausrüstung. Beachten Sie gegebenenfalls die Verweise auf entsprechende Gefahren- und Vorbeugeklärungen in der Produktsicherheitserklärung. Entsorgen Sie die Komponenten gemäß den örtlichen Vorschriften.

ZUSAMMENSETZUNG

Komponente	Inhalt	Beschreibung	Vorbereitung
APTT Si L Minus	5 x 5 mL (REF 5562) 10 x 5 mL (REF 5560) 10 x 10 mL (REF 5559)	Das Reagenz enthält einen Aktivator aus nahezu kolloiden Partikeln (MagnesiumAluminium-Silikat), mit dem eine optimale Sensitivität gegenüber Faktor-Mangelzuständen und Heparin erreicht wird. Außerdem enthält das Reagenz Phospholipid mit Puffer und Stabilisatoren.	Bringen Sie es vor der Verwendung auf Raumtemperatur. Vor dem Gebrauch gut mischen durch Verwirbeln oder Umdrehen.
Calcium Chloride: 0.025M	5 x 5 mL (REF 5562) 10 x 5 mL (REF 5560) 10 x 10 mL (REF 5559)	Das Reagenz besteht aus einer 0,025 M Calciumchlorid-Lösung.	Das Reagenz ist gebrauchsfertig verpackt.

Jedes Kit enthält eine Gebrauchsanweisung.

ERFORDERLICHE, ABER NICHT MITGELIEFERTERTE ARTIKEL

APTT Si L Minus <p>Istruzioni per l'uso</p>
SCOPO PREVISTO
Il kit APTT Si L Minus è concepito per l'esecuzione di dosaggi di emostasi basati sulla presenza di coaguli.

Da utilizzare nella determinazione dei tempi di tromboplastina parziale attivata (aPTT), e nelle procedure di coagulazione correlate, con l'impiego di estratto di fosfolipide e particelle paracoloidale come attivatore. Il sistema di test può essere utilizzato con metodi manuali, semiautomatici e automatici.
Sii dalle origini, grazie all'opera di Langdell e dei suoi collaboratori¹, modificati successivamente da Proctor e Rapaport², il aPTT viene utilizzato per rilevare i disordini del sistema intrinseco della coagulazione, in cui intervengono i fattori della coagulazione VIII, IX, XI e XII, la precalcireina e il chininogeno ad alto peso molecolare. L'aPTT viene utilizzato anche nei dosaggi che quantificano questi fattori e viene abitualmente utilizzato per lo screening prechirurgico e il monitoraggio della terapia eparinica³. I reagenti disponibili in commercio impiegano solitamente uno dei 3 attivatori seguenti: caolino, silice o acido ellagico. Nel test di screening di base, il aPTT misura indirettamente la formazione di trombina grazie alla sua azione sul fibrinogeno che forma il coagulo di fibrina. Nel test, il plasma citrato di prova viene miscelato con il reagente per aPTT per un intervallo di tempo specifico (solitamente di 5 minuti) a 37°C, seguito dall'aggiunta di calcio cloruro (0,025 M) preriscaldato (37°C). La misurazione del tempo ha inizio al momento dell'aggiunta del calcio cloruro. Il tempo necessario per la formazione del coagulo corrisponde al aPTT. Il rilevamento del coagulo può avvenire per misurazione meccanica, manuale (inclinazione della provetta) o foto-ottica.

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 le relative indicazioni precauzionali e di pericolo, laddove pertinente, fare riferimento alla dichiarazione di sicurezza del prodotto. Smanitare i componenti conformemente alle normative locali vigenti.

COMPOSIZIONE

	Componente	Contiene	Descrizione	Preparazione
APTT Si L Minus	5 x 5 mL (REF 5562) <p>10 x 5 mL (REF 5560) <p>10 x 10 mL (REF 5559)</p></p>		Il reagente contiene un attivatore di particelle paracoloidale (silicato di magnesio ed alluminio) per una maggior sensibilità nei confronti di deficit di fattori e dell'eparina. Il reagente contiene inoltre un fosfolipide con tampon e stabilizzatori.	Prima dell'uso portare a temperatura ambiente. Miscelare accuratamente con il vortex o capovolgere più volte prima di utilizzare il reagente.
Calcium Chloride: 0,025M	5 x 5 mL (REF 5562) <p>10 x 5 mL (REF 5560) <p>10 x 10 mL (REF 5559)</p></p>		Il reagente è costituito da una soluzione 0,025 M di calcio cloruro.	Il reagente è in confezione pronta all'uso.
	Ogni kit contiene un Istruzioni per l'uso.			

MATERIALI NECESSARI, MA NON IN DOTAZIONE

È possibile utilizzare qualsiasi strumento di coagulazione elettromeccanico o foto-ottico di alta qualità idoneo alla determinazione dei tempi di tromboplastina parziale attivata.

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. Conservare a una temperatura compresa tra 2° -8°C. NON CONGELARE. Il reagente rimane stabile per 30 giorni dopo l'apertura. Evitare il riscaldamento prolungato.

RACCOLTA E PREPARAZIONE DEI CAMPIONI

Nel corso dell'intera procedura è necessario utilizzare plastica o vetro silicizzato. 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 mesi. Decongelare rapidamente a 37°C prima di eseguire i test. Non conservare a 37°C per oltre 5 minuti⁴. Ciò ridurrà al minimo la neutralizzazione del lupus inibitore. La contaminazione con liquidi tissutali o la stasi possono dare luogo a risultati erronei. Evitare l'agitazione, le bolle d'aria o la formazione di schiuma. Per gli effetti dei farmaci comunemente somministrati fare riferimento a Young *et al.*⁵.

PROCEDURA

Metodo Manuale

- Miscelare accuratamente APTT Si L Minus e il calcio cloruro a 0,025 M quindi preriscaldare a 37°C.
- Preriscaldare 0,1 mL di plasma di test, in doppio, a 37°C.
- Aggiungere forzatamente 0,1 mL di reagente APTT Si L Minus preriscaldato al plasma e avviare il cronometro. Incubare per esattamente 5 minuti a 37°C.
- Aggiungere 0,1 mL di calcio cloruro preriscaldato a 0,025 M.
- Prendere nota del tempo necessario per la formazione di coaguli. Riportare il risultato come tempo aPTT in 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 dei test aPTT devono essere registrati con un'approssimazione di 1/10 di secondo. Per ogni singolo laboratorio dovrebbe essere stabilito il range normale (di solito X ± 2 deviazioni standard). I risultati maggiori dei limiti superiori del range normale devono essere considerati anormali e devono pertanto essere eseguiti test di follow-up. I valori di aPTT minori dei limiti inferiori del range normale devono essere ripetuti su un nuovo campione di sangue. Valori di aPTT breve possono essere osservati in concomitanza con una trombosi *in vivo* (ossia trombosi delle vene profonde e coagulazione intravascolare disseminata).

Monitoraggio dell'eparina

In caso di monitoraggio della terapia eparinica, è importante costruire una curva di riferimento *in vitro* che rifletta la risposta media all'eparina, in quanto i singoli pazienti rispondono all'eparina in modo diverso. In generale, il range terapeutico per l'eparina può essere considerato compreso tra 0,2 e 0,5 unità/ml^{3,6}.

Durante il monitoraggio della terapia eparinica, è necessario adottare le misure precauzionali illustrate di seguito:

- Il tempo di raccolta è importante, in quanto l'eparina possiede un'emivita *in vivo* di appena 1,5 ore⁷.
- È necessario evitare il rilascio del fattore piastrinico 4 (fattore di neutralizzazione dell'eparina) causato dall'aggregazione delle piastrine o eventuali danni durante la raccolta. Un'attenta raccolta del sangue, una centrifugazione adeguata e una tempestiva rimozione del plasma povero di piastrine dalla cellule contribuiscono a ridurre al minimo il rilascio del fattore piastrinico 4.
- I dati di base sull'aPTT di ciascun paziente devono essere definiti prima della terapia, per determinare il rispetto aPTT correlato al range normale stabilito dal laboratorio.
- I diversi sistemi di rilevamento del coagulo (meccanica, foto-ottici, ecc.) mostrano sensibilità variabili all'eparina. Durante il monitoraggio dei pazienti eparinizzati è necessario utilizzare lo stesso sistema di test.
- Le curve di risposta all'eparina devono essere determinate nuovamente con il cambiamento dei numeri di lotto del reagente e ad intervalli periodici con lo stesso numero di lotto.
- La curva deve essere costruita utilizzando anche la stessa eparina impiegata in terapia, per eliminare le variabili collegate alle eparine provenienti da fonti diverse (ad es. mucosa suina o polmone bovino).

LIMITAZIONI

I valori previsti per il test dell'aPTT variano 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, nonché il tempo e il metodo di conservazione dei campioni sono tutti fattori estremamente importanti. Le condizioni di raccolta e conservazione dei campioni di plasma devono essere standardizzate ed attentamente controllate. I risultati imprevisti devono essere confermati da ulteriori test. I frammenti di piastrine presenti in un campione possono causare il rilascio di fosfolipidi e pertanto la neutralizzazione di un eventuale lupus inibitore contenuto nel campione stesso. Deve essere evitato l'utilizzo di campioni con piccoli volumi plasmatici in ragione delle possibili variazioni fisiologiche di pH. I test possono essere influenzati da svariate farmaci⁸. Un aumento dei risultati dell'aPTT può essere attribuito alla somministrazione di difenilidantoina, eparina, warfarin e agenti radiografici^{9,10}. Una riduzione dei valori di aPTT può essere osservata durante l'impiego di contraccettivi orali o nelle terapie estrogeniche maschili^{9,10}. Pertanto, i laboratori dovranno determinare i propri valori previsti per i pazienti e precisi standard preestazionali per il controllo.

CONTROLLO QUALITÀ

Ogni laboratorio deve definire un programma di controllo qualità. I plasm 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 previsti, 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 5301	Speciality Assayed Control N
REF 5302	Speciality Assayed Control A

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 foto-ottico. Ciascun laboratorio dovrà pertanto elaborare i propri dati preestazionali.

Riproducibilità						
	Precisione intra-dosaggio		Precisione tra i dosaggi			
<i>Campione</i>	<i>n</i>	<i>Formazione del coagulo (secondi)</i>	<i>CV (%)</i>	<i>n</i>	<i>Formazione del coagulo (secondi)</i>	<i>CV (%)</i>
Routine Control N	10	33,0	0,36	100	32,9	2,41
Routine Control SA	10	77,9	0,31	100	78,3	0,77
% Fattore	Fattore VIII (secondi)	Fattore IX (secondi)	Fattore XI (secondi)			
<1	85,7	70,9	92,4			
10	45,9	44,4	50,7			
40	34,2	33,9	34,4			
100	28,8	28,8	28,8			
Eparina (IU/mL)	Formazione del coagulo (secondi)					
0	29,9					
0,2	70,0					
0,4	174,0					

BIBLIOGRAFIA

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APTT Si L Minus <p>Instrucciones de uso</p>
USO PREVISTO
El uso previsto del kit APTT Si L Minus es realizar ensayos de hemostasia basados en la coagulación.

Para usar en la determinación de los tiempos de tromboplastina parcial activada (TTPa), y procedimientos de coagulacion relacionados usando extracto de fosfolipido con de particulas casi-coloidai como activador. El sistema de prueba puede usarse con métodos manuales, semiautomaticos y automatizados. Desde su definición por parte de Langdell et al¹ y tras diversas aportaciones de Proctor y Rapaport², el TTPa se utiliza para detectar trastornos del sistema de coagulación intrínseco, que implica a los factores de coagulación VIII, IX, XI, XII, precalcireina y cininógeno de alto peso molecular. El TTPa se usa también en ensayos que cuantifican estos factores y se usa rutinariamente para el cribado prequirúrgico y la monitorización del tratamiento con heparina³. Los reactivos disponibles comercialmente usan normalmente uno de tres activadores: caolin, silice o ácido elágico. En la prueba de cribado básica, el TTPa mide indirectamente la formación de trombina por su acción sobre el fibrinógeno que forma el coágulo de fibrina. En la prueba, el plasma de prueba citratado se mezcla con reactivo de TTPa durante un período de tiempo especificado (normalmente 5 minutos) a 37°C seguido por la adición de cloruro cálcico (0,025 M) precalentado (37°C). La temporización comienza desde el momento de la adición de cloruro cálcico. El tiempo necesario para la formación del coágulo es el TTPa. La detección de coágulos puede hacerse mediante medición mecánica, manual (tubo inclinado) o fotográfica.

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
APTT Si L Minus	5 x 5 mL (REF 5562) <p>10 x 5 mL (REF 5560) <p>10 x 10 mL (REF 5559)</p></p>		El reactivo contiene un activador de partículas casi-coloidales (magnesio-aluminosilicato) que permite una sensibilidad óptima frente a los déficits de factor y frente a la heparina. El reactivo contiene asimismo un fosfolipido con tampon y estabilizadores.	Antes de utilizar, esperar a que alcance la temperatura ambiente. Antes de utilizar mezclar bien mediante agitación suave o inversión.
Calcium Chloride: 0,025M	5 x 5 mL (REF 5562) <p>10 x 5 mL (REF 5560) <p>10 x 10 mL (REF 5559)</p></p>		El reactivo es una solución de cloruro cálcico 0,025 M.	El reactivo viene envasado listo para usar.
	Cada kit contiene instrucciones de uso.			

ARTÍCULOS NECESARIOS NO SUMINISTRADOS

Puede usarse cualquier instrumento de coagulación electromecánico o foto-óptico diseñado para realizar pruebas de tiempos de tromboplastina parcial activada.

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. Conservar a una temperatura entre 2° -8°C. NO CONGELAR. Tras sua apertura, el producto es estable durante 30 días. Evitar un calentamiento prolongado.

RECOGIDA Y PREPARACIÓN DE LAS MUESTRAS

Debe usarse siempre plástico o vidrio siliccionado. 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. Decongelar rápidamente a 37°C antes de realizar la prueba. No conservar a 37°C durante más de 5 minutos⁴. Esto minimizará la neutralización del inhibidor lupus. Pueden producirse resultados erróneos por contaminación con líquidos tisulares o estasia. Evitar la agitación, las burbujas de aire o la formación de espuma. Para comprobar los efectos de los fármacos que se suelen administrar, consultar Young, *et al.*⁵.

PROCEDIMIENTO

Método Manual

- Precalentar a 37°C el APTT Si L Minus y el cloruro cálcico 0,025 M bien mezclados.
- Precalentar 0,1 mL de plasma problema, por duplicado, a 37°C durante 2 minutos.
- Añadir 0,1 mL de APTT Si L Minus precalentado al plasma y activar el temporizador. Incubar durante exactamente 5 minutos a 37°C.
- Añadir 0,1 mL de cloruro cálcico 0,025 M precalentado.
- Anotar el momento de la formación del coágulo. Registrar el resultado como tiempo TTPa (en segundos).

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 TTPa deben comunicarse a la décima de segundo más próxima. Cada laboratorio debe establecer el intervalo normal (habitualmente, X ± 2 desviaciones estándar). Los resultados mayores que los límites superiores del intervalo normal deben considerarse anormales y deben realizarse pruebas de seguimiento. Cualquier valor de TTPa menor que los límites inferiores del intervalo normal deben repetirse en una nueva muestra de sangre. Pueden verse valores de TTPa cortos en asociación con la trombosis *in vivo* (p. ej., trombosis venosa profunda y coagulación intravasculatr diseiminada).

Monitorización de la heparina

Cuando monitorice el tratamiento con heparina, es importante construir una curva de referencia *in vitro* que refleje el promedio de respuesta de la heparina, porque los pacientes individuales responden de forma diferente a la heparina. En general, se puede considerar el intervalo terapéutico para la heparina como de 0,2 a 0,5 unidades/ml^{3,6}.

Deben considerarse las siguientes precauciones a la hora de monitorizar el tratamiento con heparina:

- El momento de la recogida es importante, porque la heparina tiene una semivida *in vivo* de sólo 1,5 horas⁷.
- Debe evitarse la liberación de factor 4 plaquetario (factor neutralizador de heparina) ocasionada por la agregación plaquetaria o por daños durante la recogida. Una recogida de sangre cuidadosa, una buena centrifugación y una eliminación rápida del plasma pobre en plaquetas de las células, contribuirán a minimizar la liberación de factor 4 plaquetario.
- Deben establecerse datos basales sobre los TTPa de cada paciente antes del tratamiento para determinar el TTPa respecto del paciente ya que se relaciona con el intervalo normal establecido por el laboratorio.
- Sistemas de detección de coágulos distintos (mecánica, fotoópticos, etc.) muestran sensibilidades variables a la heparina. Debe utilizarse el mismo sistema de prueba a la hora de monitorizar pacientes heparinizados.
- Deben reestablecerse las curvas de respuesta a la heparina cuando cambien los números de lote de los reactivos y a intervalos periódicos con el mismo número de lote.
- Debe construirse también la curva usando la misma heparina empleada en el tratamiento para eliminar las variables relacionadas con las heparinas de fuentes diferentes (p. ej., mucosa porcina o pulmón bovino).

LIMITACIONES

Los valores esperados para la prueba de TTPa 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. Los fragmentos plaquetarios presentes en una muestra pueden ocasionar la liberación de fosfolípidos y, con ello, la neutralización de cualquier inhibidor lupus presente en la muestra. Debe evitarse el uso de muestras con volúmenes pequeños de plasma debido a posibles cambios fisiológicos de pH. Las pruebas pueden verse afectadas por diversos fármacos⁸. Un aumento en los resultados de TTPa puede estar causado por la administración de difenilhidantoina, heparina, warfarina y agentes radiográficos^{8,9}. Se puede comprobar un descenso en los valores de TTPa mientras se usan contraceptivos orales o tratamientos con estrógenos para hombres^{9,10}. Por ello, los laboratorios deben establecer sus propios valores esperados para pacientes y estándares de rendimiento bien definidos para el control.

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 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 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 foto-óptico. Cada laboratorio debe establecer sus propios datos de rendimiento.

Riproducibilidad						
	Precisión intra-ensayo		Precisión inter-ensayo			
<i>Muestra</i>	<i>n</i>	<i>Formación del coágulo (segundo)</i>	<i>CV (%)</i>	<i>n</i>	<i>Formación del coágulo (segundo)</i>	<i>CV (%)</i>
Routine Control N	10	33,0	0,36	100	32,9	2,41
Routine Control SA	10	77,9	0,31	100	78,3	0,77
% Factor	Factor VIII (segundo)	Factor IX (segundo)	Factor XI (segundo)			
<1	85,7	70,9	92,4			
10	45,9	44,4	50,7			
40	34,2	33,9	34,4			
100	28,8	28,8	28,8			
Heparina (IU/mL)	Formación del coágulo (segundo)					
0	29,9					
0,2	70,0					
0,4	174,0					

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Тест-система "Активированное частичное тромбoplastиное время (кремниевый активатор L минус)" ИНСТРУКЦИЯ
HAЗНАЧЕНИЕ
Комплект АРТТ Si L Minus предназначен для выполнения анализов гемостаза на основе кровяного сгустка.

Используется для определения активированного частичного тромбoplastиногo времени (АЧТВ) и сопутствующих процессов коагуляции с использованием фосфорилидного экстракта и активатора оксиколоидных частиц. Тестовая система может использоваться в ручном, полуватоматическом и автоматическом режиме. Самостоятельно возникновение, в работе Лангделла и его коллег¹ и позднее переработанный Проктором и Рапалортом² показатель АЧТВ используется для определения нарушений у врожденной системы коагуляции, которая включает факторы коагуляции VIII, IX, XI, XII, прекалликреин и высокомолекулярный кининоген. АЧТВ также используется в анализах для подсчета данных факторов и обычно используется для скрининга и мониторинга гепариновой терапии перед хирургическими вмешательствами. Антифосфолипидные антитела и неспецифичные ингибиторы (волчаноподобные антикоагулянты) могут стать причиной пролонгированных значений АЧТВ. Однако признаю, что данный эффект связан с концентрацией ингибитора и является последовательным³. Реагенты доступные в торговой сети обычно используют один из трех активаторов: каолин, кремь или эллаговую кислоту. В базовом скрининговом исследовании активированное частичное тромбoplastиное время косвенно измеряет образование тромбина путем воздействия на фибриноген, формирующий фибриновые тромбы. В исследовании цитратная тестируемая плазма смешивается с реагентом АЧТВ в течение указанного промежутка времени (обычно 5 минут) при температуре 37°C, после чего добавляется предварительно подогретый хлорид кальция (0,025 M). Отсчет времени начинается со времени добавления хлорида кальция. Время, требуемое для образования тромбов, является АЧТВ. Определение тромбов может происходить путем механического, фотооптического измерения или вручную (наклонная пробирка).

ПРЕДУПРЕЖДЕНИЯ И МЕРЫ ПРЕДОСТОРОЖНОСТИ

Содержащиеся в данном наборе реагенты предназначены только для *in vitro* диагностики– НЕ ПРИНИМАТЬ ВНИТУРЬ! При работе со всеми компонентами набора использовать соответствующие средства индивидуальной защиты. В случае необходимости см. свідетельство 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	Содержание набора	Описание	Приготовление
АЧТВ (кремниевый активатор L минус)	5 x 5 mL (Kat. № 5562) <p>10 x 5 mL (Kat. № 5560) <p>10 x 10 mL (Kat. № 5559)</p></p>	Реагент содержит активатор оксиколоидных частиц (силикат магния-алюминия) для оптимальной чувствительности к дефициту фактора и к гепарину. Реагент также содержит фосфолипиды с буфером.	Доведите до комнатной температуры перед использованием. Хорошо перемешайте вращательными движениями или путем переворачивания перед использованием.
Хлорид кальция 0,			

Declaration of Conformity

helena
Biosciences Europe

HL-7-0674DC 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.

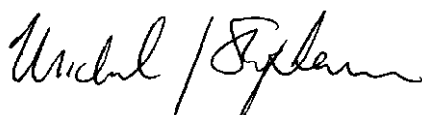
Product Code	Description	GMDN Classification Code
5552	Auto Blue D-Dimer 400	47346

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: 11 Aug 2015

Tel +44 (0)191 482 8440

Fax +44 (0)191 482 8442

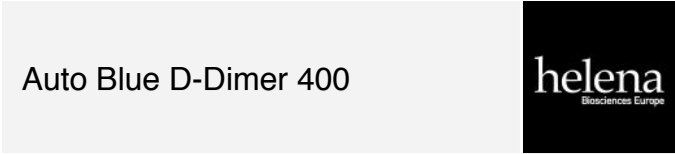
info@helena-biosciences.com

www.helena-biosciences.com

Helena Biosciences Europe

Queensway South, Team Valley Trading Estate,
Gateshead, Tyne and Wear, NE11 0SD,

United Kingdom




REF 5551

REF 5552

REF 5554



	Helena Biosciences Europe, Queensway South, Team Valley Trading Estate, Gateshead, Tyne and Wear, NE11 OSD, United Kingdom
	Tel: +44 (0)191 482 8440
	Fax: +44 (0)191 482 8442
	Email: info@helena-biosciences.com
	Web: www.helena-biosciences.com

HL-2-1802P 2015/10 (4)



Auto Blue D-Dimer 400

Instructions for Use

INTENDED PURPOSE

The Auto Blue D-Dimer 400 kit is intended for carrying out immunoturbidimetric based haemostasis assays.

D-dimer containing moieties are formed by plasmin degradation of factor XIIIa cross-linked fibrin. Elevated levels of D-dimer are found in clinical conditions such as deep vein thrombosis (DVT), pulmonary embolism (PE) and disseminated intravascular coagulation (DIC)¹⁻³. Laboratory measurements of fibrin degradation products, including D-dimer, have significance in the initial assessment of these conditions.

Auto Blue D-Dimer 400 is a turbidimetric assay that utilises antibody coated latex particles. In the presence of D-dimer, the particles aggregate and turbidity increases. The increase in scattered light is proportional to the amount of D-dimer in the sample. The latex particles are coated with a monoclonal antibody that reacts with fibrin D-dimer or fragment D of fibrin. The antibody has no cross reactivity with fibrinogen⁴. This allows for the determination of D-dimer in human plasma. Auto Blue D-Dimer 400 is an immunoturbidimetric assay used for the quantitative determination of the fibrin degradation products that contain D-dimer in 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

Important: The reagents are lot-specific. Lots are not interchangeable.

Component	Content	Description	Preparation
D-Dimer Blue Latex	1 x 3 mL (REF 5551) <p>2 x 3 mL (REF 5552)</p> <p>4 x 3 mL (REF 5554)</p>	Latex particles coated with anti-D-dimer monoclonal antibody.	Ready to use. The latex may sediment during storage. Mix thoroughly before use.
D-Dimer Blue Buffer	1 x 7 mL (REF 5551) <p>2 x 7 mL (REF 5552)</p> <p>4 x 7 mL (REF 5554)</p>	Containing buffer and preservatives.	Ready to use.
D-Dimer Diluent	1 x 7 mL (REF 5551) <p>1 x 7 mL (REF 5552)</p> <p>2 x 7 mL (REF 5554)</p>	Containing buffer and preservatives.	Ready to use.
D-Dimer Calibrator	1 x 1 mL (REF 5551) <p>1 x 1 mL (REF 5552)</p> <p>2 x 1 mL (REF 5554)</p>	Lyophilised human plasma enriched with D-dimer.	Reconstitute each vial of the appropriate calibrator with 1 mL of D-Dimer Diluent. Swirl gently. Allow to stand for 15 minutes for complete dissolution and mix well before use.

Each kit contains instructions for use.

Each kit contains lot specific reference values insert.

ITEMS REQUIRED BUT NOT PROVIDED

Analysér operable at 350-600 nm.

Helena Biosciences Europe supplies the following controls available for use with this product:

REF 5509 D-Dimer Control HL

The reagents contained in these kits are also available as separate items:

REF 32097SA D-Dimer Calibrator

REF 32096SA D-Dimer Diluent

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.

D-Dimer Blue Latex Once opened, the reagent is stable for 4 weeks at *2 –*8°C or 2 weeks at *20°C.

D-Dimer Blue Buffer Once opened, the reagent is stable for 4 weeks at *2 –*8°C or 2 weeks at *20°C.

D-Dimer Diluent Store at *2 –*8°C and use within 4 weeks of opening.

D-Dimer Calibrator Once reconstituted, the reagent is stable for 12 hours at *4 –*25°C.

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 minutes⁵. Plasma should be kept at *2 –*8°C or *18 –*24°C. Testing should be completed within 24 hours of sample collection, or plasma can be stored frozen at -20°C or -70°C for 24 months⁶. Thaw quickly at *37°C prior to testing. Do not keep at *37°C for more than 5 minutes.

PROCEDURE

Preparation of Standard Curve

Use the lot-specific value for D-Dimer Calibrator to determine the exact D-dimer concentration in each standard dilution. Users must construct a standard curve each time a new kit lot is used, after any instrument change or service, or every 6 months, and if D-Dimer Control H/L (REF 5509) is assayed out of range.

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

The test should be used in conjunction with clinical observations and results of other laboratory tests. Elevated levels are found in patients with confirmed DVT, PE, DIC, and trauma¹⁻³. D-dimer levels rise during pregnancy and high levels are associated with complications⁷. The result may be reported either in D-dimer units or in fibrinogen equivalent units (FEU); 1 ng/mL of D-dimer is equivalent to approximately 2 ng/mL of FEU, however, a more accurate conversion factor, originating from the Fibrinogen/D-dimer weight ratio of 340 kDa/195 kDa, would be 1.74⁸.

LIMITATIONS

Presence of rheumatoid arthritis factor may result in false-positive results (influence not quantified). Results from patients with heterophilic antibody should be interpreted with caution since this test kit contains mouse antibodies and interference may occur resulting in falsely elevated or decreased values. Turbid or opalescent plasma may cause erratic results and should be interpreted with caution.

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. It is recommended that the D-dimer low control and D-dimer high control are assayed at regular intervals in order to ensure consistent assay results. If the D-Dimer Control H/L result deviates from the D-dimer concentration given in the lot-specific Instruction for Use, a new standard curve should be constructed.

REFERENCE VALUES

The concentration of D-dimer in any given specimen may differ from the concentration determined using D-dimer assays from different manufacturers. 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 a photo-optical coagulation instrument. The user should establish product performance characteristics for the specific instrumentation used.

Reproducibility					
		Intra-assay precision	Inter-assay precision		
Sample	n	D-dimer (ng/mL)	CV (%)	D-dimer (ng/mL)	CV (%)
High	42	1680	2.54	1622	1.21
Low	42	387	5.31	384.55	0.84

Auto Blue D-Dimer 400 is insensitive to the following substances: haemoglobin (up to 4 g/L), bilirubin (up to 0.1 g/L), triglycerides (up to 2.5 g/L), low molecular weight heparin (up to 100 U/mL), and non-fractionated heparin (up to 100 U/mL).

BIBLIOGRAPHY

- Declerck P *et al.* (1987) Fibrinolytic response and fibrin fragment D-dimer levels in patients with deep vein thrombosis, *Thrombosis and Haemostasis*, **58**:1024-1029
- Lindahl T *et al.* (1998) Clinical evaluation of a diagnostic strategy for deep venous thrombosis with exclusion by low plasma levels of fibrin degradation product D-dimer, *Scand. J. Clin. Lab. Invest*, **58**:307-316
- Hansson PO *et al.* (1994) Can laboratory testing improve screening strategies for deep vein thrombosis at an emergency unit? *J. Intern. Med*, **235**:143-151
- Holvoet P *et al.* (1989) Binding properties of monoclonal antibodies against human fragment D-dimer of cross-linked fibrin to human plasma clots in an in vivo model in rabbits, *Thrombosis and Haemostasis*, **61**:307-313
- 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
- Clinical and Laboratory Standards Institute (2011) Quantitative D-dimer for the Exclusion of Venous Thromboembolic Disease; Approved Guideline, CLSI: H59-A
- Ballegeer V *et al.* (1987) Fibrinolytic response to venous occlusion and fibrin fragment D-dimer levels in normal and complicated pregnancy, *Thrombosis and Haemostasis*, **58**:1030-1032
- Edlund B, Nilsson TK (2006) A proposed stoichiometrical calibration procedure to achieve transferability of D-dimer measurements and to characterize the performance of different methods, *Clin Biochem*, **39**(2):137-142

Auto Blue D-Dimer 400

UTILISATION

Le kit Auto Blue D-Dimer 400 est destiné à la réalisation des analyses de l'hémostase par immunoturbidimétrie.

Les fragments contenant des D-dimères résultent de la dégradation par la plasmine de la fibrine croisée avec le facteur XIIIa. On trouve des concentrations élevées de D-dimères dans le cadre de pathologies cliniques du type thrombose veineuse profonde (TVP), embolie pulmonaire (EP) et coagulation intravasculaire disséminée (CIVD)¹⁻³. Les mesures en laboratoire des produits de dégradation de la fibrine, y compris les D-dimères, sont importantes pour la première détermination de ce type de pathologies.

Auto Blue D-Dimer 400 est une méthode turbidimétrie utilisant des particules de latex chargées d'anticorps. En présence de D-dimères, les particules s'agrègent et la turbidité augmente. L'augmentation de la lumière diffusée est proportionnelle à la quantité de D-dimères dans un échantillon. Les particules de latex sont tapissées d'anticorps monoclonaux qui réagissent aux D-dimères de la fibrine ou au fragment D de la fibrine. L'anticorps n'a aucune réactivité croisée avec le fibrinogène⁴. Cela permet la détermination des D-dimères dans le plasma humain. Auto Blue D-Dimer 400 est une méthode immunoturbidimétrie utilisée pour la détermination quantitative des produits de dégradation de la fibrine contenant des D-dimères dans du plasma humain.

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 églements locaux.

Un dépistage des produits sanguins a été réalisé e 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

Important: Les réactifs sont spécifiques à chaque lot. Les lots ne sont donc pas interchangeables.

Composant	Contient	Description	Préparation
D-Dimer Blue Latex	1 x 3 mL (REF 5551) <p>2 x 3 mL (REF 5552)</p> <p>4 x 3 mL (REF 5554)</p>	Particules de latex chargées d'anticorps monoclonaux anti-D-dimères.	Prêt à l'emploi. Le latex peut former des sédiments lorsqu'il est stocké. Bien mélanger avant utilisation.
D-Dimer Blue Buffer	1 x 7 mL (REF 5551) <p>2 x 7 mL (REF 5552)</p> <p>4 x 7 mL (REF 5554)</p>	Contenant tampon et des conservateurs.	Prêt à l'emploi.
D-Dimer Diluent	1 x 7 mL (REF 5551) <p>1 x 7 mL (REF 5552)</p> <p>2 x 7 mL (REF 5554)</p>	Contenant tampon et des conservateurs.	Prêt à l'emploi.
D-Dimer Calibrator	1 x 1 mL (REF 5551) <p>1 x 1 mL (REF 5552)</p> <p>2 x 1 mL (REF 5554)</p>	Plasma humain lyophilisé enrichi en D-dimères.	Reconstituer chaque flacon du calibrateur approprié avec 1,0 mL D-Dimer Diluent. Agiter doucement. Attendre 15 minutes jusqu'à dissolution totale et bien mélanger avant d'utiliser.

Chaque kit contient une fiche technique.

Chaque kit contient valeurs de référence spécifiques du lot.

MATÉRIEL NÉCESSAIRE NON FOURNI

Analyséur de fonctionner à 350-600 nm.

Helena Biosciences Europe distribue les contrôles suivants à utiliser avec ce produit:

REF 5509 D-Dimer Control HL

Les réactifs du kit sont aussi disponibles séparément:

REF 32097SA D-Dimer Calibrator

REF 32096SA D-Dimer Diluent

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.

D-Dimer Blue Latex Une fois ouvert, le réactif est stable 4 semaines entre *2 –*8°C ou 2 semaines à *20°C.

D-Dimer Blue Buffer Une fois ouvert, le réactif est stable 4 semaines entre *2 –*8°C ou 2 semaines à *20°C.

D-Dimer Diluent A conserver entre *2 –*8°C et à utiliser dans les 4 semaines après ouverture.

D-Dimer Calibrator Une fois reconstitué, le réactif est stable 12 heures entre *4 –*25°C.

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 minutes⁵. Conserver le plasma entre *2 –*8°C ou *18 –*24°C. L'analyse doit être terminée dans les 24 heures suivant le prélèvement de l'échantillon; sinon, il est possible de congeler le plasma à -20°C ou -70°C à 24 mois⁶. Décongeler rapidement à *37°C avant de réaliser l'analyse. Ne pas laisser à *37°C plus de 5 minutes.

PROCÉDURE

Préparation de la courbe de calibration

Reportez-vous à la valeur spécifique de lot pour l'étalon D-dimère pour déterminer la concentration exacte des D-dimères dans chaque solution normale. Il est recommandé d'établir une nouvelle courbe chaque fois qu'un nouveau lot est utilisé ou tous les 6 mois, et si un plasma témoin (REF 5509) est dosé hors norme.

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

L'analyse doit être réalisée conjointement aux observations cliniques et aux résultats d'autres analyses de laboratoire. Des niveaux élevés sont relevés pour des patients avec diagnostic confirmé de TVP, EP, CIVD et traumatisme¹⁻³. Les concentrations de D-dimères augmentent lors de la grossesse et des concentrations particulièrement élevées sont relevées en cas de complications⁷. Les résultats peuvent être indiqués en unités de D-dimères ou en unités de fibrinogène équivalents (FEU) ; 1 ng/mL de D-dimères équivaut à environ 2 ng/mL de FEU, cependant, le rapport de poids Fibrinogène/D-dimère, soit 340 kDa/195 kDa, permet d'obtenir un facteur de conversion plus exact de 1,74⁸.

LIMITES

La présence d'un facteur de polyarthrite rhumatoïde peut entraîner de faux positifs (influence non quantifiée). Les résultats des patients ayant des anticorps hétérophiles doivent être interprétés avec précaution étant donné que le kit d'analyse contient des anticorps de souris et qu'il peut se produire des interférences entraînant des valeurs faussement élevées ou faussement faibles. Un plasma trouble ou opalescent peut entraîner des résultats irréguliers à interpréter avec précaution.

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. Il est recommandé de doser les D-dimères basse concentration et les D-dimères haute concentration du plasma témoin à intervalles réguliers afin de s'assurer de la cohérence des résultats. Si les résultats obtenus pour le plasma témoin diffèrent de la concentration de D-dimères indiquée dans les instructions d'utilisation du lot, il est impératif de réaliser une nouvelle courbe de calibration.

VALEURS DE RÉFÉRENCE

La concentration de D-dimères dans un échantillon peut différer de celle déterminée au moyen de systèmes de détection de D-dimères fournis par différents fabricants. 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 photo-optique. L'utilisateur doit établir des spécifications de performance de produit pour chaque appareil utilisé.

Reproductibilité					
		Précision intra-série	Précision inter-séries		
Échantillon	n	D-dimères (ng/mL)	CV (%)	D-dimères (ng/mL)	CV (%)
Haut	42	1680	2,54	1622	1,21
Faible	42	387	5,31	384,55	0,84

Auto Blue D-Dimer 400 n'est pas affecté par les substances suivantes : hémoglobine (jusqu'à 4 g/L), bilirubine (jusqu'à 0,1 g/L), triglycérides (jusqu'à 2,5 g/L), héparine de bas poids moléculaire (jusqu'à 100 U/mL) et héparine non fractionnée (jusqu'à 100 U/mL).

BIBLIOGRAPHIE

- Declerck P *et al.* (1987) Fibrinolytic response and fibrin fragment D-dimer levels in patients with deep vein thrombosis, *Thrombosis and Haemostasis*, **58**:1024-1029
- Lindahl T *et al.* (1998) Clinical evaluation of a diagnostic strategy for deep venous thrombosis with exclusion by low plasma levels of fibrin degradation product D-dimer, *Scand. J. Clin. Lab. Invest*, **58**:307-316
- Hansson PO *et al.* (1994) Can laboratory testing improve screening strategies for deep vein thrombosis at an emergency unit? *J. Intern. Med*, **235**:143-151
- Holvoet P *et al.* (1989) Binding properties of monoclonal antibodies against human fragment D-dimer of cross-linked fibrin to human plasma clots in an in vivo model in rabbits, *Thrombosis and Haemostasis*, **61**:307-313
- 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
- Clinical and Laboratory Standards Institute (2011) Quantitative D-dimer for the Exclusion of Venous Thromboembolic Disease; Approved Guideline, CLSI: H59-A
- Ballegeer V *et al.* (1987) Fibrinolytic response to venous occlusion and fibrin fragment D-dimer levels in normal and complicated pregnancy, *Thrombosis and Haemostasis*, **58**:1030-1032
- Edlund B, Nilsson TK (2006) A proposed stoichiometrical calibration procedure to achieve transferability of D-dimer measurements and to characterize the performance of different methods, *Clin Biochem*, **39**(2):137-142

Auto Blue D-Dimer 400

VERWENDUNGSZWECK

Das Auto Blue D-Dimer 400-Kit ist für immunturbidimetrische Gerinnungstests vorgesehen.

Beim Plasmin-Abbau von Fibrin, das durch den Faktor XIIIa quervernetzt ist, entstehen D-dimer enthaltende Spaltprodukte. Erhöhte Konzentrationen von D-dimer werden bei klinischen Zuständen wie tiefer Venenthrombose (TVT), Pulmonalemolie (PE) und disseminierter intravasärer Koagulation (DIC) beobachtet¹⁻³. Labormessungen von Fibrinospaltprodukten, einschließlich des D-dimers, spielen eine wichtige Rolle bei der Ersterkennung dieser Krankheitszustände. Auto Blue D-Dimer 400 ist ein turbidimetrischer Assay, bei dem mit Antikörpern beschichtete Latexpartikel eingesetzt werden. Bei Vorhandensein von D-dimer aggregieren die Partikel, und die Trübung erhöht sich. Diese Zunahme an Streulicht ist der in der Probe enthaltenen Menge an D-dimer proportional. Die Latexpartikel sind mit einem monoklonalen Antikörper beschichtet, der mit Fibrin D-dimer oder dem Fragment D von Fibrin reagiert. Der Antikörper weist keine Kreuzreaktivität mit Fibrinogen auf⁴. Dadurch wird die Bestimmung von D-dimer in Humanplasma ermöglicht. Auto Blue D-Dimer 400 ist ein immunoturbidimetrischer Assay für die quantitative Bestimmung der D-dimer enthaltenden Fibrinspaltprodukte in Humanplasma.

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 Vorbeugeklärungen 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

Wichtig: Die Reagenzien sind chargenspezifisch. Bestandteile verschiedener Chargen können nicht ausgetauscht werden.

Komponente	Inhalt	Beschreibung	Vorbereitung
D-Dimer Blue Latex	1 x 3 mL (REF 5551) <p>2 x 3 mL (REF 5552)</p> <p>4 x 3 mL (REF 5554)</p>	Latexpartikel, beschichtet mit monoklonalem Anti-D-dimer-Antikörper.	Gebrauchsfertig. Das Latex kann sich während der Lagerung absetzen. Vor dem Gebrauch gründlich mischen.
D-Dimer Blue Buffer	1 x 7 mL (REF 5551) <p>2 x 7 mL (REF 5552)</p> <p>4 x 7 mL (REF 5554)</p>	Enthält Puffer und Konservierungsstoffe.	Gebrauchsfertig.
D-Dimer Diluent	1 x 7 mL (REF 5551) <p>1 x 7 mL (REF 5552)</p> <p>2 x 7 mL (REF 5554)</p>	Enthält Puffer und Konservierungsstoffe.	Gebrauchsfertig.
D-Dimer Calibrator	1 x 1 mL (REF 5551) <p>1 x 1 mL (REF 5552)</p> <p>2 x 1 mL (REF 5554)</p>	Lyophilisiertes Humanplasma, angereichert mit D-dimer.	Jedes Fläschchen kalibrator mit 1,0 mL D-Dimer Diluent. Leicht schwenken. Zum vollständigen Auflösen 15 Minuten stehen lassen und vor Gebrauch gut mischen.

Jedes Kit enthält eine Gebrauchsanweisung.

Jedes Kit enthält chargenspezifischen Referenzwerten.

ERFORDERLICHE, ABER NICHT MITGELIEFERTE ARTIKEL

Analysér betreibbar bei 350-600 nm gemessen. In Verbindung mit diesem Produkt bietet Helena Biosciences Europe die folgenden Kontrollen an:

REF 5509 D-Dimer Control HL

Die Reagenzien dieses Kits sind auch einzeln erhältlich:

REF 32097SA D-Dimer Calibrator

REF 32096SA D-Dimer Diluent

LAGERUNG, HALTBARKEIT UND STABILITÄT

Ungeöffnete Reagenzien sind unter den auf Verpackung oder Fläschchen angegebenen Lagerbedingungen bis zum aufgedruckten Verfallsdatum stabil.

- ↑
Holvoet P *et al.* (1989) Binding properties of monoclonal antibodies against human fragment D-dimer of cross-linked fibrin to human plasma clots in an in vivo model in rabbits, *Thrombosis and Haemostasis*, 61:307-313
- ↑
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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Clinical and Laboratory Standards Institute (2011) Quantitative D-dimer for the Exclusion of Venous Thromboembolic Disease; Approved Guideline, CLSI: H59-A
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Ballegeer V *et al.* (1987) Fibrinolytic response to venous occlusion and fibrin fragment D-dimer levels in normal and complicated pregnancy, *Thrombosis and Haemostasis*, 58:1030-1032
- ↑
Eldund B, Nilsson TK (2006) A proposed stoichiometrical calibration procedure to achieve transferability of D-dimer measurements and to characterize the performance of different methods, *Clin Biochem*, 39(2):137-142

<p></p>
<div>Auto Blue D-Dimer 400</div> <div>Istruzioni per l'uso</div>

SCOPo PREVISTO
Il kit Auto Blue D-Dimer 400 è concepito per l'esecuzione di dosaggi di emostasi mediante test immunoturbidimetrico.

Le frazioni contenenti il D-dimero si formano in seguito alla degradazione, da parte della plasmina, della fibrina stabilizzata per il fattore XIIIa. Livelli elevati di D-dimero sono stati riscontrati in condizioni cliniche quali la trombosi venosa profonda (DVT), l'embolia polmonare (PE) e la coagulazione intravascolare disseminata (DIC)¹⁻³. La quantificazione in laboratorio dei prodotti di degradazione della fibrina, compreso il D-dimero, è quindi rilevante nella valutazione iniziale di queste condizioni.

Auto Blue D-Dimer 400 è un test turbidimetrico che utilizza particelle di lattice ricoperte di anticorpo. In presenza di D-dimero, le particelle si aggregano e la torbidità aumenta. L'aumento d'intensità della luce diffusa è proporzionale alla quantità di D-dimero presente nel campione. Le particelle di lattice sono ricoperte con un anticorpo monoclonale che reagisce con il D-dimero della fibrina o frammento D della fibrina. L'anticorpo non presenta cross-reattività con il fibrinogeno³. Ciò consente la determinazione del D-dimero nel plasma umano. Auto Blue D-Dimer 400 è un test immunoturbidimetrico utilizzato per la determinazione quantitativa dei prodotti di degradazione della fibrina che contengono il D-dimero nel plasma umano.

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 fiaala) 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

Importante: I reagenti sono specifici di ogni lotto. I lotti non sono intercambiabili.

Componente	Contiene	Descrizione	Preparazione
D-Dimer Blue Latex	1 x 3 mL (REF 5551) <p>2 x 3 mL (REF 5552)</p> 4 x 3 mL (REF 5554)	Particelle di lattice ricoperte con anticorpo monoclonale.	Pronto per l'uso. Il lattice può sedimentare durante la conservazione. Miscelare accuratamente prima dell'uso.
D-Dimer Blue Buffer	1 x 7 mL (REF 5551) <p>2 x 7 mL (REF 5552)</p> 4 x 7 mL (REF 5554)	Contiene tampone e conservanti.	Pronto per l'uso.
D-Dimer Diluent	1 x 7 mL (REF 5551) <p>1 x 7 mL (REF 5552)</p> 2 x 7 mL (REF 5554)	Contiene tampone e conservanti.	Pronto per l'uso.
D-Dimer Calibrator	1 x 1 mL (REF 5551) <p>1 x 1 mL (REF 5552)</p> 2 x 1 mL (REF 5554)	Plasma umano liofilizzato arricchito di D-dimero.	Ricostituire ogni flacone di calibratore appropriato con 1,0 mL di D-Dimer Diluent. Agitare delicatamente. Attendere 15 minuti per consentire al prodotto di sciogliersi completamente e miscelare bene prima dell'uso.

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

Analysér funzionante a 350-600 nm.

Helena Biosciences Europe mette a disposizione i seguenti controlli utilizzabili con questo prodotto:

REF 5509 D-Dimer Control H/L

Ireagenti contenuti in questo kit sono disponibili anche come materiale separato:

REF 32097SA D-Dimer Calibrator

REF 32096SA D-Dimer Diluent

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.

D-Dimer Blue Latex Dopo la apertura, il reagente è stabile per 4 settimane a *2 –*8°C o per 2 settimane a *20°C.

D-Dimer Blue Buffer Dopo la apertura, il reagente è stabile per 4 settimane a *2 –*8°C o per 2 settimane a *20°C.

D-Dimer Diluent Conservare a una temperatura compresa tra *2 –*8°C ed utilizzare entro 4 settimane dall'apertura.

D-Dimer Calibrator Dopo la ricostituzione, il reagente è stabile per 12 ore a *4 –*25°C.

RACCOLTA E PREPARAZIONE DEI CAMPIONI

Nel corso dell'intera procedura è necessario utilizzare plastica o vetro silicizzato. Il sangue (9 parti) deve essere raccolto in citrato sodico al 3,2% o al 3,8%, come anticoagulante (1 parte). Separare il plasma in seguito a centrifugazione a 1500 x g per 15 minuti⁴. Il plasma deve essere conservato a *2 –*8°C o *18 –*24°C. I test devono essere completati entro 24 ore dalla raccolta dei campioni; in alternativa, il plasma può essere conservato congelato a -20°C o a -70°C per 24 mese⁶. Decongelare rapidamente a *37°C prima di eseguire i test. Non conservare a *37°C per oltre 5 minuti.

PROCEDURA

Preparazione della curva standard

Per determinare l'esatta concentrazione di D-dimero in ogni diluizione calibratore, utilizzare il valore specifico di ogni lotto di D-dimero standard. È necessario creare una curva standard ogni volta che si utilizza un nuovo lotto di kit oppure ogni 6 mesi, nonché quando i valori del plasma di controllo (REF 5509) non sono compresi nell'intervallo.

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

Il test deve essere utilizzato in abbinamento alle osservazioni cliniche ed ai risultati di altri test di laboratorio. Livelli elevati vengono riscontrati in pazienti con DVT confermata, PE, DIC e trauma¹⁻³. I livelli di D-dimero aumentano durante la gravidanza e livelli elevati sono associati a complicazioni¹. I risultati possono essere espressi in unità di D-dimero oppure in unità di fibrinogeno-equivalenti (FEU); 1 ng/mL di D-dimero equivale a circa 2 ng/mL di FEU, anche se un fattore di conversione più accurato, ottenuto dal rapporto di peso Fibrinogeno/D-dimero di 340 kDa/195 kDa, sarebbe 1,74⁶.

LIMITAZIONI

La presenza del fattore dell'artrite reumatoide può dare luogo a falsi risultati positivi (influenza non quantificata). I risultati di pazienti con anticorpo eterofilo devono essere interpretati con cautela in quanto questo kit per test contiene anticorpi di topo e può verificarsi un'interferenza con conseguenti valori ridotti o falsamente elevati. Campioni di plasma torbido o opalescente possono generare risultati erratici e pertanto vanno interpretati con cautela.

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. Per garantire la correttezza e la coerenza dei risultati dei test, si raccomanda di testare ad intervalli regolari i plasma di controllo inferiore e superiore del D-dimero. Se la concentrazione di D-dimero presente nel plasma di controllo testato differisce da quella riportata nelle istruzioni per l'uso specifiche del lotto, è necessario creare una nuova curva standard.

VALORI DI RIFERIMENTO

La concentrazione di D-dimero di ogni singolo campione può variare quando si utilizzano kit per il test di diversi produttori. 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 foto-ottico. Le prestazioni del prodotto per lo strumento specifico vengono stabilite dall'utente.

Riproducibilità					
	Precisione intra-dosaggio	Precisione tra i dosaggi			
Campione	<i>n</i>	<i>D-dimero (ng/mL)</i>	<i>CV (%)</i>	<i>D-dimero (ng/mL)</i>	<i>CV (%)</i>
Superiore	42	1680	2,54	1622	1,21
Scasso	42	387	5,31	384,55	0,84

Il D-Dimero 400 Auto Blue è insensibile alle seguenti sostanze: emoglobina (fino a 4 g/L), bilirubina (fino a 0,1 g/L), trigliceridi (fino a 2,5 g/L), eparina a basso peso molecolare (fino a 100 U/mL) ed eparina non frazionata (fino a 100 U/mL).

BIBLIOGRAFIA

- ↑ Declerck P *et al.* (1987) Fibrinolytic response and fibrin fragment D-dimer levels in patients with deep vein thrombosis, *Thrombosis and Haemostasis*, 58:1024-1029
- ↑ Lindahl T *et al.* (1998) Clinical evaluation of a diagnostic strategy for deep venous thrombosis with exclusion by low plasma levels of fibrin degradation product D-dimer, *Scand. J. Clin. Lab. Invest*, 58:307-316
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- ↑ Holvoet P *et al.* (1989) Binding properties of monoclonal antibodies against human fragment D-dimer of cross-linked fibrin to human plasma clots in an in vivo model in rabbits, *Thrombosis and Haemostasis*, 61:307-313
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- ↑ Eldund B, Nilsson TK (2006) A proposed stoichiometrical calibration procedure to achieve transferability of D-dimer measurements and to characterize the performance of different methods, *Clin Biochem*, 39(2):137-142

<p></p>
<div>Auto Blue D-Dimer 400</div> <div>Istrucciones de uso</div>

USO PREVISTO
El uso previsto del kit Auto Blue D-Dimer 400 es realizar ensayos de hemostasia basados en la immunoturbidimetria.

USO PREVISTO

El uso previsto del kit Auto Blue D-Dimer 400 es realizar ensayos de hemostasia basados en la immunoturbidimetria.

Los fragmentos que contienen dimero D se forman por la acción de la plasmina al degradar la fibrina estabilizada por el factor XIIIa. Niveles elevados de dimero D se observan en patologías clínicas tales como la trombosis venosa profunda (DVT), el embolismo pulmonar (PE) y la coagulación intravasclar diseminada (DIC)¹⁻³. Los análisis de laboratorio de los productos de degradación de la fibrina, incluido el dimero D, resultan significativos para la valoración inicial de estas patologías.

Auto Blue D-Dimer 400 es un ensayo turbidimétrico que utiliza partículas de látex tapizadas con anticuerpos. En la presencia del dimero D las partículas se agregan y aumenta la turbidez. El aumento de luz dispersa es proporcional a la cantidad de dimero D presente en la muestra. Las partículas de látex están tapizadas con un anticorpo monoclonal que reacciona con el dimero D o el fragmento D de la fibrina. El anticuerpo no presenta reactividad cruzada con el fibrinógeno³. Esto permite determinar el dimero D en el plasma humano. Auto Blue D-Dimer 400 es un ensayo immunoturbidimétrico para la determinación cuantitativa de los productos de degradación de la fibrina que contienen dimero D en plasma humano.

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. Desecha,r 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

Importante: Los reactivos son específicos de lote y los lotes no son intercambiables.

Componente	Contiene	Descripción	Preparación
D-Dimer Blue Latex	1 x 3 mL (REF 5551) <p>2 x 3 mL (REF 5552)</p> 4 x 3 mL (REF 5554)	Partículas de látex tapizadas con anticuerpo monoclonal antidimero D.	Listo para usar. El látex puede sedimentarse durante la conservación. Mezclar bien antes de su uso.
D-Dimer Blue Buffer	1 x 7 mL (REF 5551) <p>2 x 7 mL (REF 5552)</p> 4 x 7 mL (REF 5554)	Contiene tampón y conservantes.	Listo para usar.
D-Dimer Diluent	1 x 7 mL (REF 5551) <p>1 x 7 mL (REF 5552)</p> 2 x 7 mL (REF 5554)	Contiene tampón y conservantes.	Listo para usar.
D-Dimer Calibrator	1 x 1 mL (REF 5551) <p>1 x 1 mL (REF 5552)</p> 2 x 1 mL (REF 5554)	Plasma humano liofilizado enriquecido con dimero D.	Reconstituya cada vial del calibrador adecuado con 1,0 mL de D-Dimer Diluent. Agite suavemente. Deje que repose durante 10 minutos para que la disolución sea completa y mezcle bien antes de su uso.

Cada kit contiene instrucciones de uso.

Cada kit contiene valores de referencia específicos insertados del lote.

ARTÍCULOS NECESARIOS NO SUMINISTRADOS

Analizador operable a 350-600 nm. Helena Biosciences Europe suministra los siguientes controles disponibles para usar con este producto:

REF 5509 D-Dimer Control H/L

Los reactivos contenidos en este kit están también disponibles como artículos separados:

REF 32097SA D-Dimer Calibrator

REF 32096SA D-Dimer Diluent

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.

D-Dimer Blue Latex Una vez apertura, el reactivo es estable durante 4 semanas a *2 –*8°C o 2 semanas a *20°C.

D-Dimer Blue Buffer Una vez apertura, el reactivo es estable durante 4 semanas a *2 –*8°C o 2 semanas a *20°C.

D-Dimer Diluent Conservar a una temperatura entre *2 –*8°C y una vez abierto utilizar antes de 4 semanas.

D-Dimer Calibrator Una vez reconstituído, el reactivo es estable durante 12 horas a *4 –*25°C.

RECOGIDA Y PREPARACIÓN DE LAS MUESTRAS

Debe usarse siempre plástico o vidrio silicizado. 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 minutos⁴. El plasma debe conservarse a *2 –*8°C o *18 –*24°C. Las pruebas deberían terminarse en 24 horas desde la recogida de las muestras o el plasma puede conservarse congelado a -20°C o -70°C durante 24 mes⁶. Decongelar rápidamente a *37°C antes de realizar la prueba. No conservar a *37°C durante más de 5 minutos.

PROCEDIMIENTO

Preparación de la curva patrón

Para determinar la concentración exacta de dimero D en cada dilución calibrador deberá utilizarse el valor específico de lote para el patrón dimero D. El usuario deberá construirse una curva patrón cada vez que utilice un nuevo lote de kit o cada 6 meses, y si el plasma de control (REF 5509) se determina fuera de rango.

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

El ensayo debe utilizarse conjuntamente con las observaciones clínicas y con los resultados de otros ensayos de laboratorio.Los niveles elevados se observan en pacientes con confirmación de DVT, PE, DIC o traumatiso¹⁻³. Normalmente los niveles de dimero D aumentan durante el embarazo, aunque los niveles elevados están asociados a complicaciones¹. Los resultados pueden expresarse en unidades de dimero D o en unidades de fibrinógeno equivalente (FEU); 1 ng/mL de dimero D es equivalente a aproximadamente 2 ng/mL de FEU; no obstante, un factor de conversión más preciso, derivado de una relación de peso del fibrinógeno/dimero D de 340 kDa/195 kDa, sería 1,74⁶.

LIMITACIONES

La presencia del factor de artritis reumatoide puede dar lugar a resultados falsos positivos (influenca no cuantificada). Los resultados de pacientes con anticuerpos heterofílos deben interpretarse con cuidado porque este kit de pruebas contiene anticuerpos de ratón y puede producirse interferencia dando lugar a valores falsamente elevados o disminuidos. El plasma turbio u opalescente puede provocar resultados erráticos y debe interpretarse con precaución.

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. Para garantizar unos resultados coherentes se recomienda determinar los plasmas de control bajo en dimero D y control alto en dimero D a intervalos regulares. Si el resultado del plasma de control se desvía de la concentración de dimero D indicada en las Instrucciones de uso específicas del lote, deberá construirse una nueva curva patrón.

VALORES DE REFERENCIA

La concentración determinada de dimero D de una muestra puede diferir cuando se utilizan ensayos de dimero D de diferentes fabricantes. 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 foto-óptico. El usuario deberá determinar las características de rendimiento del producto para cada instrumento utilizado.

Reproductibilidad					
	Precision intra-ensayo	Precision inter-ensayo			
Muestra	<i>n</i>	<i>Dimero D (ng/mL)</i>	<i>CV (%)</i>	<i>Dimero D (ng/mL)</i>	<i>CV (%)</i>
Elevado	42	1680	2,54	1622	1,21
Escaso	42	387	5,31	384,55	0,84

Auto Blue D-Dimer 400 es insensibLe a las siguientes sustancias: hemoglobina (hasta 4 g/L), bilirrubina (hasta 0,1 g/L), triglicéridos (hasta 2,5 g/L), heparina de bajo peso molecular (hasta 100 U/mL) y heparina no fraccionada (hasta 100 U/mL).

BIBLIOGRAFÍA

- ↑ Declerck P *et al.* (1987) Fibrinolytic response and fibrin fragment D-dimer levels in patients with deep vein thrombosis, *Thrombosis and Haemostasis*, 58:1024-1029
- ↑ Lindahl T *et al.* (1998) Clinical evaluation of a diagnostic strategy for deep venous thrombosis with exclusion by low plasma levels of fibrin degradation product D-dimer, *Scand. J. Clin. Lab. Invest*, 58:307-316
- ↑ Hansson PO *et al.* (1994) Can laboratory testing improve screening strategies for deep vein thrombosis at an emergency unit? *J. Intern. Med*, 235:143-151
- ↑ Holvoet P *et al.* (1989) Binding properties of monoclonal antibodies against human fragment D-dimer of cross-linked fibrin to human plasma clots in an in vivo model in rabbits, *Thrombosis and Haemostasis*, 61:307-313
- ↑ 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
- ↑ Clinical and Laboratory Standards Institute (2011) Quantitative D-dimer for the Exclusion of Venous Thromboembolic Disease; Approved Guideline, CLSI: H59-A
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- ↑ Eldund B, Nilsson TK (2006) A proposed stoichiometrical calibration procedure to achieve transferability of D-dimer measurements and to characterize the performance of different methods, *Clin Biochem*, 39(2):137-142

<p></p>
<div>Test-sistema "Авто Синий Д-димер 400"</div> <div>инструкция</div>

НАЗНАЧЕНИЕ
Комплект "Авто Синий Д-димер 400" предназначен для выполнения анализов гемостаза на иммунотурбидиметрической основе.

Частицы, содержащие Д-димеры, образуются путем распада плазмина фибрина, перекрестно связанного фактором XIIIa. Повышенные уровни содержания Д-димеров встречаются в таких

клинических состояниях, как тромбоз глубоких вен (ТГВ), легочная эмболия (ЛО) и синдром диссеминированной внутрисосудистой коагуляции (СДКВ)¹⁻³. Лабораторные измерения продуктов распада фибрина, в том числе Д-димеров, имеют значение при начальной оценке этих состояний.

Тест-система "Авто Синий Д-димер 400" – это турбидиметрический анализ, который задействует частицы латекса, покрытые антителами. В присутствии Д-димера частицы соединяются, и усиливается мутность. Повышение светорассеяния пропорционально количеству Д-димера в пробе. Частицы латекса покрыты моноклональными антителами, которые вступают в реакцию с Д-димером фибрина или фрагментом D фибрина. Эти антитела не обладают перекрестной реактивностью с фибриногеном³. Это позволяет выявить Д-димер в плазме крови человека. Тест-система "Авто Синий Д-димер 400" – это иммунофелометрический анализ, используемый для количественного определения продуктов распада фибрина, содержащих Д-димер, в плазме крови человека.

ПРЕДУПРЕЖДЕНИЯ И МЕРЫ ПРЕДОСТОРОЖНОСТИ

Содержащиеся в данном наборе реагенты предназначены только для *in vitro* диагностики– НЕ ПРИНИМАТЬ ВНИТУРЬ! При работе со всеми компонентами набора использовать соответствующие средства индивидуальной защиты. В случае необходимости см. свидетельства 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 B (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

Важный:</

SAFETY DECLARATION

Product Description	D-Dimer Control H/L
Product Code	5509

The product as received is an IVD kit containing the following materials:

Product Code	Product Description
HL-3-2069SA	D-Dimer Control - H 1 mL
HL-3-2068SA	D-Dimer Control - L 1 mL

Each material has been assessed for the chemicals used in its manufacture and has been found to contain **either** no hazardous substances **or** contain them at concentrations or quantities less than those requiring classification under EU regulation 2015/830 or EU regulation 1272/2008.

Tel +44 (0)191 482 8440
Fax +44 (0)191 482 8442
info@helena-biosciences.com
www.helena-biosciences.com

Helena Biosciences Europe
Queensway South, Team Valley Trading Estate,
Gateshead, Tyne and Wear, NE11 0SD,
United Kingdom

D-Dimer Control



REF 5509 D-Dimer Control H/L



Helena Biosciences Europe, Queensway South, Team Valley Trading Estate, Gateshead, Tyne and Wear, NE11 0SD, United Kingdom

Tel: +44 (0)191 482 8440

Fax: +44 (0)191 482 8442

Email: info@helena-biosciences.com

Web: www.helena-biosciences.com

HL-2-1188P 2015/10 (10)

D-Dimer Control Instructions for use

en

INTENDED PURPOSE

The D-Dimer Control H/L kit is intended for use as a quality control material.

D-dimer containing moieties are formed by plasmin degradation of Factor XIIIa cross-linked fibrin. Elevated levels of D-dimer are found in clinical conditions such as deep vein thrombosis (DVT), pulmonary embolism (PE) and disseminated intravascular coagulation (DIC).^{1,2} D-dimer levels rise during pregnancy and high levels are associated with complications.³ The negative predictive value of D-dimer for thrombosis is high,⁴ although a negative D-dimer does not completely rule out thrombosis. The Helena Biosciences Europe D-Dimer Control H/L kit contains plasmas with low and high levels of D-dimer. These plasmas are for use with the Helena Biosciences Europe latex-enhanced immunoassay methods for D-dimer and should be tested before patient samples to ensure the satisfactory performance of the assay system.

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
D-Dimer Control - L	5 x 1 mL (REF 5509)	Each vial contains lyophilised D-dimer enriched human plasma.	Reconstitute each vial with 1 mL of saline solution. Allow to stand for 5 minutes and mix well before use. Do not shake.
D-Dimer Control - H	5 x 1 mL (REF 5509)	Each vial contains lyophilised D-dimer enriched human plasma.	Reconstitute each vial with 1 mL of saline solution. Allow to stand for 5 minutes and mix well before use. Do not shake.

Each kit contains instructions for use.

Each kit contains lot specific reference values insert.

ITEMS REQUIRED BUT NOT PROVIDED

REF 5551 / 5552 / 5554	Auto Blue D-Dimer 400
REF 5501 / 5601	Auto Red D-Dimer 700

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. Reconstituted vials are stable for 5 days at 2 – 8 °C, or 3 months at -20°C. Do not freeze / thaw more than once.

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 (REF 5551, 5552, 5554, 5501, 5601).

INTERPRETATION OF RESULTS

Lot specific expected values are provided with each pack of controls. Recalibration may be required if results fall outside quoted ranges.

LIMITATIONS

The values listed are for use with Helena Biosciences Europe D-dimer procedures only. The use of other D-dimer procedures and products may lead to erroneous results.

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

Sample	n	Intra-assay precision		Inter-assay precision	
		CV (%)	CV (%)	CV (%)	CV (%)
D-Dimer Control - L	35	3,3	2,5	3,3	2,5
D-Dimer Control - H	35	6,4	0,9	6,4	0,9

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3. Ballegaer V *et al* (1987) Fibrinolytic Response to Venous Occlusion and Fibrin Fragment D-dimer Levels in Normal and Complicated Pregnancy, *Thromb. Haemost.* **58**: 1030-2.
4. Hansson PO *et al* (1994) Can Laboratory Testing Improve Screening Strategies for Deep Vein Thrombosis at an Emergency Unit?, *J. Intern. Med.* **235**: 143-51.

D-Dimer Control Fiche technique

fr

UTILISATION

Le kit D-Dimer Control H/L est destiné à être utilisé comme produit de contrôle qualité.

Les fragments contenant des D-dimères résultent de la dégradation par la plasmine de la fibrine croisée avec le facteur XIIIa. On trouve des concentrations élevées de D-dimères dans le cadre de pathologies cliniques du type thrombose veineuse profonde (TVP), embolie pulmonaire (EP) et coagulation intravasculaire disséminée (CIVD).² Les taux de D-dimères augmentent pendant la grossesse et des taux élevés sont également observés en cas de complications.³ La valeur prédictive négative du D-dimère pour une thrombose est élevée⁴, bien qu'un résultat négatif n'en écarte pas totalement la possibilité. Le kit de D-Dimer Control H/L Helena Biosciences Europe contient des plasmas avec des taux faible et élevé de D-dimère. Ces plasmas sont destinés à être utilisés avec les méthodes de dosage immunologique optimisé avec des particules de latex pour le D-dimère et doivent être testés avant les échantillons patients afin de vérifier que les performances du système de dosage sont satisfaisantes.

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 réglementations 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 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
D-Dimer Control - L	5 x 1 mL (REF 5509)	Chaque flacon contient du plasma humain lyophilisé enrichi en D-dimères.	Reconstituer chaque flacon avec 1 mL de solution physiologique. Laisser reposer 5 minutes et bien mélanger avant utilisation. Ne pas agiter.
D-Dimer Control - H	5 x 1 mL (REF 5509)	Chaque flacon contient du plasma humain lyophilisé enrichi en D-dimères.	Reconstituer chaque flacon avec 1 mL de solution physiologique. Laisser reposer 5 minutes et bien mélanger avant utilisation. Ne pas agiter.

Chaque kit contient une fiche technique.

Chaque kit contient valeurs de référence spécifiques du lot.

MATÉRIEL NÉCESSAIRE NON FOURNI

REF 5551 / 5552 / 5554	Auto Blue D-Dimer 400
REF 5501 / 5601	Auto Red D-Dimer 700

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 flacons de plasma reconstitués sont stables 5 jours entre 2 – 8°C ou 3 mois à -20°C. Ne pas congeler / décongeler plus d'une fois.

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 (REF 5551, 5552, 5554, 5501, 5601).

INTERPRÉTATION DES RÉSULTATS

Les valeurs prévues spécifiques du lot sont fournies avec chaque kit de contrôles. Il est nécessaire de réaliser un nouvel étalonnage si les résultats se situent hors des plages indiquées.

LIMITES

Les valeurs indiquées ne sont valables que pour les méthodes de dosage du D-dimère Helena Biosciences Europe. L'utilisation d'autres protocoles et produits peut conduire à des résultats erronés.

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		Précision inter-série	
	n	CV (%)	n	CV (%)
D-Dimer Control - L	35	3,3	35	2,5
D-Dimer Control - H	35	6,4	35	0,9

BIBLIOGRAPHIE

1. Elms MJ *et al* (1986) Rapid Detection of Cross-Linked Fibrin Degradation Products in Plasma Using Monoclonal Antibody-Coated Latex Particles, *J. Clin. Pathol.* **35**: 360-64.
2. Declercq PV *et al* (1987) Fibrinolytic Response and Fibrin Fragment D-dimer in Patients With Deep Vein Thrombosis, *Thromb. Haemost.* **58**: 1025-9.
3. Ballegaer V *et al* (1987) Fibrinolytic Response to Venous Occlusion and Fibrin Fragment D-dimer Levels in Normal and Complicated Pregnancy, *Thromb. Haemost.* **58**: 1030-2.
4. Hansson PO *et al* (1994) Can Laboratory Testing Improve Screening Strategies for Deep Vein Thrombosis at an Emergency Unit?, *J. Intern. Med.* **235**: 143-51.

D-Dimer Control Anleitung

de

VERWENDUNGSSZWECK

Das D-Dimer Control H/L-Kit ist für die Qualitätskontrolle vorgesehen.

Beim Plasmin-Abbau von Fibrin, das durch den Faktor XIIIa quervernetzt ist, entstehen D-dimer enthaltende Spaltprodukte. Erhöhte Konzentrationen von D-dimer werden bei klinischen Zuständen wie tiefer Venenthrombose (TVT), Pulmonalembolie (PE) und disseminierter intravasculärer Koagulation (DIC)^{1,2} beobachtet. D-dimer Werte steigen während der Schwangerschaft an, hohe Werte weisen auf Komplikationen hin.³ Der negative Prognosewert des D-dimers für Thrombose ist hoch,⁴ obwohl ein negatives D-dimer eine Thrombose nicht vollständig ausschließen kann. Das Helena Biosciences Europe D-Dimer Control H/L Kit enthält Plasmen mit niedrigen und hohen D-dimer Werten. Diese Plasmen sind zum Gebrauch mit den Helena Biosciences Europe Latex verstärkten Immunoassay-Methoden für D-dimer bestimmt und sollen vor den Patientenproben getestet werden, um eine zufrieden stellende Leistung des Test-Systems zu gewährleisten.

WARNHINWEISE UND VORSICHTSMASSNAHMEN

Die in diesem Kit enthaltenen Reagenzien sind ausschließlich für die Verwendung von *in-vitro*-Diagnosen vorgesehen. NICHT VERSCHLÜCKEN. Tragen Sie beim Umgang mit sämtlichen Komponenten des Kits geeignete Schutzausrüstung. Beachten Sie gegebenenfalls die Verweise auf entsprechende Gefahren- und Vorbeugeerklärungen in der Produktsicherheitsklärung. 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
D-Dimer Control - L	5 x 1 mL (REF 5509)	Jedes Fläschchen enthält lyophilisiertes, D-dimer angereichertes Humanplasma.	Jedes Fläschchen mit 1 mL Kochsalzlösung rekonstituieren. 5 Minuten stehen lassen und vor Gebrauch gut mischen. Nicht schütteln.
D-Dimer Control - H	5 x 1 mL (REF 5509)	Jedes Fläschchen enthält lyophilisiertes, D-dimer angereichertes Humanplasma.	Jedes Fläschchen mit 1 mL Kochsalzlösung rekonstituieren. 5 Minuten stehen lassen und vor Gebrauch gut mischen. Nicht schütteln.

Jedes Kit enthält eine Gebrauchsanweisung.

Jedes Kit enthält chargenspezifischen Referenzwerten.

ERFORDERLICHE, ABER NICHT MITGELIEFERTER ARTIKEL

REF 5551 / 5552 / 5554	Auto Blue D-Dimer 400
REF 5501 / 5601	Auto Red D-Dimer 700

LAGERUNG, HALTBARKEIT UND STABILITÄT

Ungelöfnete Fläschchen sind unter den auf Verpackung oder Fläschchen angegebenen Lagerbedingungen bis zum aufgedruckten Verfallsdatum stabil. Rekonstituierte Fläschchen sind bei 2 – 8°C 5 Tage oder bei -20°C 3 Monate stabil. Nicht wiederholt einfrieren / auftauen.

PROBENTNAHME UND VORBEREITUNG

Entfällt.

VORGEHENSWEISE

Jede Kontrolle sollte gemäß den Anleitungen der einzelnen Testprotokolle wie unbekannte Probe behandelt werden (REF 5551, 5552, 5554, 5501, 5601).

INTERPRETATION DER ERGEBNISSE

Chargenspezifische Normalwerte sind in jeder Packung mit Kontrollen enthalten. Liegen die Ergebnisse außerhalb des angegebenen Bereichs, kann eine erneute Kalibrierung erforderlich sein.

EINSCHRÄNKUNGEN

Die aufgelisteten Werte gelten nur mit den Helena Biosciences Europe D-dimer Verfahren. Andere D-dimer Verfahren und Produkte können falsche Ergebnisse liefern.

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 seinen eigenen Referenzwertbereiche erstellen.

LEISTUNGSMERKMALE

Die folgenden Leistungseigenschaften wurden von Helena Biosciences Europe oder in ihrem Auftrag mit einem optomechanischen Gerinnselgerät ermittelt. Jede Labor muss seine eigenen Werte ermitteln.

Reproduzierbarkeit

Probe	n	Intra-assay-Präzision		Inter-assay-Präzision	
		CV (%)	CV (%)	CV (%)	CV (%)
D-Dimer Control - L	35	3,3	2,5	3,3	2,5
D-Dimer Control - H	35	6,4	0,9	6,4	0,9

LITERATURVERZEICHNIS

1. Elms MJ *et al* (1986) Rapid Detection of Cross-Linked Fibrin Degradation Products in Plasma Using Monoclonal Antibody-Coated Latex Particles, *J. Clin. Pathol.* **35**: 360-64.
2. Declercq PV *et al* (1987) Fibrinolytic Response and Fibrin Fragment D-dimer in Patients With Deep Vein Thrombosis, *Thromb. Haemost.* **58**: 1025-9.
3. Ballegaer V *et al* (1987) Fibrinolytic Response to Venous Occlusion and Fibrin Fragment D-dimer Levels in Normal and Complicated Pregnancy, *Thromb. Haemost.* **58**: 1030-2.
4. Hansson PO *et al* (1994) Can Laboratory Testing Improve Screening Strategies for Deep Vein Thrombosis at an Emergency Unit?, *J. Intern. Med.* **235**: 143-51.

D-Dimer Control

Istruzioni per l'uso

SOPO PREVISTO

Il kit D-Dimer Control HL è concepito per l'uso come materiale di controllo qualità.

Le frazioni contenenti il D-dimero si formano in seguito alla degradazione, da parte della plasmina, della fibrina stabilizzata dal fattore XIIIa. Livelli elevati di D-dimero sono stati riscontrati in condizioni cliniche quali la trombosi venosa profonda (DVT), l'embolia polmonare (PE) e la coagulazione intravascolare disseminata (DIC) ^[1]. I livelli di D-dimero aumentano durante la gravidanza e livelli molto elevati sono associati a complicazioni^[2]. Il valore predittivo negativo del D-dimero relativo alla trombosì è elevato^[3], sebene un D-dimero negativo non escluda completamente la trombosi.

Il kit di D-Dimer Control HL di Helena Biosciences Europe contiene plasmi con livelli ridotti ed elevati di D-dimero. Questi plasmi sono destinati ad essere utilizzati con i metodi di immunodosaggio al lattice di Helena Biosciences Europe per il D-dimero e devono essere testati prima dei campioni dei pazienti, per garantirne le prestazioni soddisfacenti del sistema di dosaggio.

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 presente, 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
D-Dimer Control - L	5 x 1 mL (REF 5509)	Ogni fialone contiene plasma umano arricchito con d-dimero liofilizzato	Ricostituire ogni fialcone con 1 mL di soluzione fisiologica. Lasciare riposare per 5 minuti e miscelare bene prima dell'uso. Non scuotere.
D-Dimer Control - H	5 x 1 mL (REF 5509)	Ogni fialcone contiene plasma umano arricchito con D-dimero liofilizzato.	Ricostituire ogni fialcone con 1 mL di soluzione fisiologica. Lasciare riposare per 5 minuti e miscelare bene prima dell'uso. Non scuotere.

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

REF 5551 / 5552 / 5554	Auto Blue D-Dimer 400
REF 5501 / 5601	Auto Red D-Dimer 700

CONSERVAZIONE, VITA UTILE E STABILITÀ

I fialconi non aperti sono stabili fino alla data di scadenza indicata se conservati nelle condizioni riportate sul fialcone o sull'etichetta del kit. I fialconi ricostituiti sono stabili per 5 giorni a 2 – 8°C o 3 mesi a -20°C. Non congelare / scongelare più di una volta.

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 (REF 5551, 5552, 5554, 5501, 5601).

INTERPRETAZIONE DEI RISULTATI

I valori previsti specifici per il lotto vengono forniti con ciascuna confezione di controlli. Può essere necessario eseguire una ricalibrazione qualora i risultati fuoriscano dai range indicati.

LIMITAZIONI

I valori elencati sono destinati ad essere utilizzati esclusivamente con le procedure per D-dimero di Helena Biosciences Europe. L'utilizzo di altri prodotti e procedure per il D-dimero può portare a risultati errati.

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	Precisione tra i dosaggi	
<i>Campione</i>	<i>n</i>	<i>CV (%)</i>	<i>CV (%)</i>
D-Dimer Control - L	35	3,3	2,5
D-Dimer Control - H	35	6,4	0,9

BIBLIOGRAFIA

- Elms MJ *et al* (1986) Rapid Detection of Cross-Linked Fibrin Degradation Products in Plasma Using Monoclonal Antibody-Coated Latex Particles, *J. Clin. Pathol.*, **35**: 360-64.
- Declercq PV *et al* (1987) Fibrinolytic Response and Fibrin Fragment D-dimer in Patients With Deep Vein Thrombosis, *Thromb. Haemost.* **58**: 1025-9.
- Ballegeer V *et al* (1987) Fibrinolytic Response to Venous Occlusion and Fibrin Fragment D-dimer Levels in Normal and Complicated Pregnancy, *Thromb. Haemost.* **58**: 1030-2.
- Hansson PO *et al* (1994) Can Laboratory Testing Improve Screening Strategies for Deep Vein Thrombosis at an Emergency Unit?, *J. Intern. Med.* **235**: 143-51.

D-Dimer Control

Instrucciones de uso

USO PREVISTO

El uso previsto del kit D-Dimer Control HL es como material de control de calidad.

Los fragmentos que contienen dimero D se forman por la acción de la plasmina al degradar la fibrina estabilizada por el factor XIIIa. Niveles elevados de dimero D pueden observarse en patologías clínicas tales como la trombosis venosa profunda (DVT), el embolismo pulmonar (PE) y la coagulación intravascular diseminada (DIC) ^[1]. Los niveles de dimero D aumentan durante el embarazo, estando asociados los niveles altos a complicaciones^[2]. El valor de pronóstico negativo de dimero-D para trombosis es alto^[3], aunque un dimero-D negativo no descarta completamente la trombosis.

El kit de D-Dimer Control HL de Helena Biosciences Europe contiene plasmas con niveles altos y bajos de dimero-D. Estos plasmas sirven para utilizarse con los métodos de inmunoanálisis mejorados con látex de Helena Biosciences Europe para dimero-D y deben probarse ante muestras de paciente para garantizar un rendimiento satisfactorio del sistema de análisis.

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. Desectar 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
D-Dimer Control - L	5 x 1 mL (REF 5509)	Cada vial contiene plasma humano enriquecido con dimero-D liofilizado.	Reconstituir cada vial con 1 mL de solución salina. Dejar reposar durante 5 minutos y mezclar bien antes de usar. No agitar.
D-Dimer Control - H	5 x 1 mL (REF 5509)	Cada vial contiene plasma humano enriquecido con dimero-D liofilizado.	Reconstituir cada vial con 1 mL de solución salina. Dejar reposar durante 5 minutos y mezclar bien antes de usar. No agitar.

Cada kit contiene instrucciones de uso.

Cada kit contiene valores de referencia específicos insertados del lote.

ARTÍCULOS NECESARIOS NO SUMINISTRADOS

REF 5551 / 5552 / 5554	Auto Blue D-Dimer 400
REF 5501 / 5601	Auto Red D-Dimer 700

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 viales reconstituidos permanecen estables durante 5 días a 2 – 8°C, o 3 meses a -20°C. No congelar / descongelar más de una vez.

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 (REF 5551, 5552, 5554, 5501, 5601).

INTERPRETACIÓN DE LOS RESULTADOS

Se facilitan los valores esperados específicos de lote con cada paquete de controles. Puede ser necesaria una nueva calibración si los resultados no están dentro de los intervalos mencionados.

LIMITACIONES

Los valores mencionados se aplican únicamente a los procedimientos de dimero-D de Helena Biosciences Europe. El uso de otros procedimientos y productos de dimero-D puede conllevar resultados erróneos.

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.

Reproducibilidad			
	Precisión intra-ensayo	Precisión inter-ensayo	
<i>Muestra</i>	<i>n</i>	<i>CV (%)</i>	<i>CV (%)</i>
D-Dimer Control - L	35	3,3	2,5
D-Dimer Control - H	35	6,4	0,9

BIBLIOGRAFÍA

- Elms MJ *et al* (1986) Rapid Detection of Cross-Linked Fibrin Degradation Products in Plasma Using Monoclonal Antibody-Coated Latex Particles, *J. Clin. Pathol.*, **35**: 360-64.
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- Hansson PO *et al* (1994) Can Laboratory Testing Improve Screening Strategies for Deep Vein Thrombosis at an Emergency Unit?, *J. Intern. Med.* **235**: 143-51.

Контроль качества высокий и низкий для тест-систем "Д-димер" ИНСТРУКЦИЯ

НАЗНАЧЕНИЕ

Комплект D-Dimer Control H/L предназначен для использования в качестве материала для контроля качества.

Частицы, содержащие Д-димер, образуются путем распада плазмина фибрина, перекрестно связанного фактором XIIIa. Повышенные уровни содержания Д-димера встречаются в таких клинических состояниях, как тромбоз глубоких вен (ТГВ), легочная эмболия (ЛЭ) и синдром диссеминированной внутрисосудистой коагуляции (СДВК)^[2]. Уровни содержания Д-димера повышаются во время беременности; высокие уровни содержания сопутствуют осложнениям^[3]. Прогностичность отрицательного результата Д-димера для тромбоза высока^[4], хотя отрицательный показатель Д-димера не полностью исключает тромбоз.

Набор Контроля качества высокий и низкий для тест-систем "Д-димер" содержит плазмы с низким и высоким уровнем Д-димера. Эти плазмы предназначены для использования с методиками иммуноанализа с латексным усилением Helena Biosciences Europe для Д-димера и должны подвергаться анализу перед образцами пациентов, чтобы обеспечить удовлетворительную работу тест-систем.

ПРЕДУПРЕЖДЕНИЯ И МЕРЫ ПРЕДОСТОРОЖНОСТИ

Содержащиеся в данном наборе реагенты предназначены только для *in vitro* диагностики— НЕ ПРИНИМАТЬ ВНУТРИ! 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 указан комплект или на пробирке не указано иное) на: Антиген к гепатиту В (HbsAg) Антигена к ВИЧ 1 Антигена 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

Компонент	Содержание	Описание	Приготовление
Контроль низкий «Д-Димер»	5 x 1 мл (Кат. № 5509)	В каждой ампуле содержится лиофилизированная плазма крови человека, обогащенная Д-димером.	Восстановите каждую ампулу с помощью 1 мл физиологического раствора. Оставьте на 5 минут и хорошо перемешайте перед использованием. Не встряхивайте.
Контроль высокий «Д-Димер»	5 x 1 мл (Кат. № 5509)	В каждой ампуле содержится лиофилизированная плазма крови человека, обогащенная Д-димером.	Восстановите каждую ампулу с помощью 1 мл физиологического раствора. Оставьте на 5 минут и хорошо перемешайте перед использованием. Не встряхивайте.

В каждом наборе содержится инструкция по применению.

В каждом наборе содержится вкладыш с эталонными значениями, определенными для данной партии продукта.

НЕОБХОДИМЫЕ КОМПОНЕНТЫ, НЕ ВКЛЮЧЕННЫЕ В КОМПЛЕКТ ПОСТАВКИ

Кат. № 5551 / 5552 / 5554	Тест-система "Авто Синий Д-димер 400"
Кат. № 5501 / 5601	Тест-система "Авто Красный Д-димер 700"

ХРАНЕНИЕ, СРОК ГОДНОСТИ И УСТОЙЧИВОСТЬ

Невыскртые ампулы сохраняют стабильность до истечения указанного срока годности при соблюдении условий хранения, указанных на этикетке ампулы или набора. Восстановленные ампулы сохраняют стабильность в течение 5 дней при температуре 2° – 8°С, или 3 месяца – при температуре -20°С. Не замораживайте / растапливайте более одного раза.

ОТБОР И ПОДГОТОВКА ОБРАЗЦОВ

Не применимо.

ПРОЦЕДУРА

С каждым контролем следует обращаться так же, как с неизвестным образцом в соответствии с инструкциями, указанными в каждом отдельном протоколе анализа (REF 5551, 5552, 5554, 5501, 5601).

С каждой упаковки контролей предоставляются ожидаемые результаты, определенные для данной партии. Если результаты выходят за указанные пределы, может потребоваться повторная калибровка.

ОГРАНИЧЕНИЯ

Указанные значения предназначены для использования только в процедурах с Д-димером компании Helena Biosciences Europe. Использование других процедур с Д-димером и продуктов может привести к ошибочным результатам.

КОНТРОЛЬ КАЧЕСТВА

В каждой лаборатории должна быть установлена программа контроля качества. Перед каждой партией проб пациентов следует проанализировать нормальную плазму и контрольный патологий, чтобы обеспечить удовлетворительную работу инструмента и оператора. Если контроли действуют не так, как ожидалось, результаты анализов проб пациентов следует считать неверными.

НОРМАЛЬНЫЕ ПОКАЗАТЕЛИ

Эталонные значения могут различаться в различных лабораториях в зависимости от используемых методов и систем. В связи с этим каждая лаборатория должна установить свой собственный диапазон нормальных значений.

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):

Изучение повторяемости			
	Внутрианалитическая сходимость	Внутрианалитическая CV (%)	Внутрианалитическая CV (%)
<i>Образец</i>	<i>Число образцов</i>	<i>CV (%)</i>	<i>CV (%)</i>
Контроль низкий «Д-Димер»	35	3,3	2,5
Контроль высокий «Д-Димер»	35	6,4	0,9

ЛИТЕРАТУРА

- Elms MJ *et al* (1986) Rapid Detection of Cross-Linked Fibrin Degradation Products in Plasma Using Monoclonal Antibody-Coated Latex Particles, *J. Clin. Pathol.*, **35**: 360-64.
- Declercq PV *et al* (1987) Fibrinolytic Response and Fibrin Fragment D-dimer in Patients With Deep Vein Thrombosis, *Thromb. Haemost.* **58**: 1025-9.
- Ballegeer V *et al* (1987) Fibrinolytic Response to Venous Occlusion and Fibrin Fragment D-dimer Levels in Normal and Complicated Pregnancy, *Thromb. Haemost.* **58**: 1030-2.
- Hansson PO *et al* (1994) Can Laboratory Testing Improve Screening Strategies for Deep Vein Thrombosis at an Emergency Unit?, *J. Intern. Med.* **235**: 143-51.

CERTIFICADO CE DE SISTEMA DE GARANTÍA DE CALIDAD TOTAL
de acuerdo con el Anexo IV (excepto punto 4) de la Directiva 98/79/CE
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Certificado nº/Certificate no 2003 12 0388 CT	Fecha de validez/Date of validity Desde/From 20-05-2022 Hasta/To 26-05-2025	ON nº/NB no 0318
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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: Idem

Para el producto/For the product:

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 el Anexo de este Certificado/ *Specified in Annex to this Certificate*

Elaborado en/In the facilities:

Via G. Carducci, 27. 20099 Sesto San Giovanni. Milano (Italy).

Fecha inicial/ Initial date: 11/12/2003

Fecha de prórroga anterior/ Previous extension date: 26/11/2018

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 0240, and guarantees that the described products fulfils the requirements of the Directive.*

Madrid, 19 de mayo de 2022

DIRECTORA DE LA AGENCIA ESPAÑOLA DE MEDICAMENTOS Y PRODUCTOS SANITARIOS



agencia española de medicamentos y productos sanitarios

Fdo. Mª Jesús Lamas Díaz

Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)
 Fecha de la firma: 19/05/2022
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 28022 MADRID
 Tel.: (+34) 91 822.57.87 / (+34) 91.822.59.97
 Fax: (+34) 91.822.52.89

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2003 12 0388 CT	Desde/From 20-05-2022 Hasta/To 26-05-2025	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: Idem

Tipo de producto/ Devices type: Reactivos y productos reactivos, calibradores y materiales de control para el diagnóstico de enfermedades infecciosas humanas./ Reagents, and reagent products, calibrators and control materials for diagnostic of human infectious diseases.

Clasificación/ Classification: Lista A del Anexo II / List A of 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 Ab

- SAB.CE (96 tests) Descrito en el certificado/ Described in the certificate 2003 12 0390 ED

1.2. HBc Ab

- BCAB.CE (96 tests) Descrito en el certificado/ Described in the certificate 2003 12 0391 ED

1.3. HBc IgM

- BCM.CE (96 tests) Descrito en el certificado/ Described in the certificate 2004 03 0424 ED

1.4. HBe Ag & Ab

- HBE.CE (96 tests) Descrito en el certificado/ Described in the certificate 2004 03 0425 ED

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1.5. HBs Ag Confirmation

- SCONF.CE (20 tests) Descrito en el certificado/ *Described in the certificate* 2006 11 0511 ED
- SCONF.CE.40 (40 tests)

1.6. HBs Ag one Version ULTRA

- SAGIULTRA.CE (192 tests) Descrito en el certificado/ *Described in the certificate* 2008 12 0588 ED
- SAGIULTRA.CE.96 (96 tests)
- SAGIULTRA.CE.480 (480 tests)
- SAGIULTRA.CE.960 (960 tests)
- SAGIULTRA.CE.DB (192 tests)

1.7. HCV Ab

- CVAB.CE (192 tests) Descrito en el certificado/ *Described in the certificate* 2003 12 0392 ED
- CVAB.CE.96 (96 tests)
- CVAB.CE.480 (480 tests)
- CVAB.CE.960 (960 tests)
- CVAB.CE.DB (192 tests)

1.8. HCV Ab Confirmation

- CCONF.CE (12 tests) Descrito en el certificado/ *Described in the certificate* 2005 09 0485 ED

1.9. HCV IgM

- CVM.CE (96 tests) Descrito en el certificado/ *Described in the certificate* 2007 09 0532 ED

MODELO -I ANEXO IV CT Cert. 98/79/I-Rev. -18/05/2020

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ANEXO N°/ANNEX NO: I

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2003 12 0388 CT	Desde/From 20-05-2022 Hasta/To 26-05-2025	0318

1.10. 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 certificate* 2015 10 0842 ED

1.11. HDV Ab

- DAB.CE (96 tests)

Descrito en el certificado/ *Described in the certificate* 2003 12 0393 ED

1.12. HDV Ag

- DAG.CE (96 tests)

Descrito en el certificado/ *Described in the certificate* 2003 12 0394 ED

1.13. HDV IgM

- DIM.CE (96 tests)

Descrito en el certificado/ *Described in the certificate* 2003 12 0395 ED

1.14. 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 certificate* 2011 11 0775 ED

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1.15. HIV Ab & Ag

- IVCOMB.CE (192 tests) Descrito en el certificado/ *Described in the certificate* 2008 02 0539 ED
- IVCOMB.CE.96 (96 tests)
- IVCOMB.CE.480 (480 tests)
- IVCOMB.CE.960 (960 tests)
- IVCOMB.CE.DB (192 tests)

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) Descrito en el certificado/ *Described in the certificate* 2012 09 0790 ED
- HBVDNAQT.CE.25 (25 tests)
- HBVDNAQT.CE.100 (100 tests)
- HBVDNAQT.CE.150 (150 tests)

2.2 HDV RNA Quantitation (QT)

- DRNA.CE (50 tests) Descrito en el certificado/ *Described in the certificate* 2009 11 0660 ED
- DRNA.CE.25 (25 tests)
- DRNA.CE.100 (100 tests)
- DRNA.CE.150 (150 tests)

MODELO -1 ANEXO IV CT Cert. 98/79/I-Rev. -18/05/2020

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2.3 HDV ONESTEP Quantitation (QT)

- HDVONEQT.CE (50 tests) Descrito en el certificado/ *Described in the certificate* 2022 04 0973 ED
- HDVONEQT.CE.25 (25 tests)
- HDVONEQT.CE.100 (100 tests)

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 certificate* 2015 01 0834 ED

3.2 DIA.CHEMILUX HBs Ag

- RASAG.CE (100 tests) Descrito en el certificado/ *Described in the certificate* 2015 10 0841 ED

3.3 DIA.CHEMILUX HIV Ab & Ag

- RAIVCOMB.CE (100 tests) Descrito en el certificado/ *Described in the certificate* 2016 02 0844 ED

3.4 DIA.CHEMILUX HBc Ab

- RABCAB.CE (100 tests) Descrito en el certificado/ *Described in the certificate* 2017 07 0863 ED

Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)

Fecha de la firma: 19/05/2022

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3.5 DIA.CHEMILUX HTLV I & II Ab

- RAHTLVAB.CE (100 tests)

Descrito en el certificado/ *Described in the certificate* 2018 11 0878 ED

3.6 DIA.CHEMILUX HDV Ab

- RADAB.CE (100 tests)

Descrito en el certificado/ *Described in the certificate* 2020 07 0932 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, 19 de mayo de 2022

DIRECTORA DE LA AGENCIA ESPAÑOLA DE MEDICAMENTOS Y PRODUCTOS SANITARIOS

 **agencia española de
medicamentos y
productos sanitarios**

Fdo. M^a Jesús Lamas Díaz

Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)

Fecha de la firma: 19/05/2022

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ORGANISMO NOTIFICADO 0318



MEDICAL
DEVICES
ISO 13485:2016
NSAI Certified

DECLARATION OF CONFORMITY

Product Family TOTAL AND FREE PROSTATE SPECIFIC ANTIGEN (PSA and FPSA)

Specific Product Details						
Product Description	Item # ELISA	Item # CLIA	EDMS Code	GMDN ELISA Code	GMDN CLIA Code	Risk Class
Total PSA Test System	2125-300A 2125-300B	2175-300A 2175-300B	12.03.01.32.00	54664	54665	High/ List B
Total PSA Extra Sensitive Test System	8725-300A 8725-300B	8775-300A 8775-300B	12.03.01.32.00	54664	54665	High/ List B
Free PSA Test System	2325-300A 2325-300B	2375-300A 2375-300B	12.03.01.33.00	54668	54669	High/ List B
Cancer VAST Test System	8425-300B 8425-300D 8425-300E	8475-300B 8475-300D 8475-300E	12.03.01.32.00	54664	54665	High/ List B
Multi Ligand Control	ML-300B	ML-300B	12.03.01.32.00	38207	38207	High/ List B

Manufacturer

Name Monobind Inc.
Address 100 North Pointe, Lake Forest, CA 92630
Country United States

Representative

Name CEpartner4U BV,
Address Esdoornlaan 13, 3951DB Maarn
Country The Netherlands
Telephone +31 (0)6 – 516.536.26

Notified Body

Name NSAI
Body ID Number 0050
CE Cert # 304.1006
Registration # NL-CA002-2011-23306

Means of Conformity

Monobind Inc. declares that the product listed is in conformity with the Annex IV, IVD Type List B essential requirements and provisions of Council Directive: 98/79/EC

And is in conformance with the following standards:

EN 13612:2002	EN 15223-1:2016	EN ISO 14971:2019
EN ISO 18113:2011	EN 13641:2002	EN ISO 23640:2015
Under the principles of	EN ISO 13485:2016	

Signature

Place and effective date Monobind Inc. January 30, 2021 revision 04

Signature

Ashatola

Name

Tony Shatola

Title

QA Director

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 44386771

e-mail: info@diapro.it

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 0.045% ProClin 300 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 0.045% ProClin 300 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 0.045% 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 Diluent CONJ DIL

2x16ml/vial. Ready to use and pink/red color coded reagent. It contains 10 mM Tris buffer pH 6.8+/-0.1, 1% normal mouse serum, 5% BSA, 0.045% ProClin 300 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, 0.045% ProClin 300 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 H₂SO₄ 0.3 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:

	N°1	N°5	N°10
Microplates			
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-borne 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. 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. 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.

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G. SPECIMEN: PREPARATION AND WARNINGS

- 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.
- 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.
- 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.
- 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.
- 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 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 0.2-0.8µ 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

- 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%.
- 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.
- 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.
- 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

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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.

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 of 620-630nm, mandatory 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 ; (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 $2..8^{\circ}\text{C}$, 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 $+37^{\circ}\text{C}$ 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.
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 150ul 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 $+37^{\circ}\text{C}$** .

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.*

- When the first incubation is over, wash the microwells as previously described (section I.4)
- 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.

- 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.
- 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.
- 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, mandatory), blanking the instrument on A1.

Important general notes:

- Ensure that no fingerprints or dust are present on the external bottom of the microwell before reading. They could generate false positive results on reading.
- 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.
- 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 ±150 as follows:
 - dispense 100 µl of controls, calibrator and samples
 - incubate 60 min at +37°C on shaking
 - wash according to instructions (section I.4)
 - dispense 100 µl diluted enzyme tracer
 - incubate 30 min at +37°C on shaking
 - wash
 - dispense 100 µl 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.
- 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	150 µl
Diluted Enzyme Conjugate	100 µl
1st incubation	120 min
Temperature	+37°C
Washing steps	n° 5 cycles with 20" of soaking OR n° 6 cycles without soaking
Chromogen/Substrate	200µl
2nd incubation	30 min
Temperature	room
Sulphuric Acid	100 µl
Reading OD	450nm / 620-630nm

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 > 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	<ol style="list-style-type: none"> 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	<ol style="list-style-type: none"> 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.

Important note:

The analysis must be done proceeding as the reading step described in the section M, point 11.

P. CALCULATION OF THE CUT-OFF

The test results are calculated by means of a cut-off value determined on the mean OD450nm/620-630nm value of the negative control (NC) with the following formula:

$$NC + 0.050 = \text{Cut-Off (Co)}$$

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/620-630nm (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 (data obtained proceeding as the the reading step described in the section M, point 11):

The following data must not be used instead of 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	1 st 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.

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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:

Dia.Pro Diagnostic Bioprobes S.r.l.
Via G. Carducci n° 27 – Sesto San Giovanni (MI) – Italy



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 -



DIA.PRO

**Diagnostic Bioprobes Srl
Via G. Carducci n° 27
20099 Sesto San Giovanni
(Milano) - Italy**

Phone +39 02 27007161

Fax +39 02 44386771

e-mail: info@diapro.it

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: 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 0.045% ProClin 300 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 0.045% ProClin 300.

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 0.045% ProClin 300 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% tetramethyl-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 H₂SO₄ 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 0.045% ProClin 300 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. 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 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 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.

5. If particles are present, centrifuge at 2.000 rpm for 20 min or filter using 0.2-0.8µ 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 µl of each specimen with 450 µl of Cal 0 (1:10). Then 50 µl of the 1:10 dilution are diluted with 450 µl 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 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 350µl/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 ≥ 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.

- 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.
- 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

- Check the expiration date of the kit printed on the external label of the kit box. Do not use if expired.
- 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.
- Dilute all the content of the 20x concentrated Wash Solution as described above.
- Dissolve the Control Serum as described above.
- Allow all the other components to reach room temperature (about 1 hr) and then mix as described.
- 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.
- Check that the ELISA reader has been turned on at least 20 minutes before reading.
- If using an automated workstation, turn it on, check settings and be sure to use the right assay protocol.
- Check that the micropipettes are set to the required volume.
- 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

- 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.

- 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.

- Wash the microplate as reported in section I.3.
- 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 notes:

- Be careful not to touch the inner surface of the well with the pipette tip when dispensing the Enzyme Conjugate. Contamination might occur.*
- Mix thoroughly the Enzyme Conjugate on vortex before use.*

- Wash the microplate as described.
- Pipette 100µl TMB/H₂O₂ 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.

- 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, mandatory), blanking the instrument on A1 and B1 wells.

M.2 Qualitative analysis

- 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.
- 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**.
- Wash the microplate as reported in section I.3.
- 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 notes:

- Be careful not to touch the inner surface of the well with the pipette tip when dispensing the Enzyme Conjugate. Contamination might occur.*
- Mix thoroughly the Enzyme Conjugate on vortex before use.*

- Wash the microplate as described.
- Pipette 100µl TMB/H₂O₂ 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 (blinking, mandatory), blanking the instrument on A1 and B1 wells.

Important general 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 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	50 ul
Calibrators	100 ul
Control Serum	100 ul
Samples	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

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

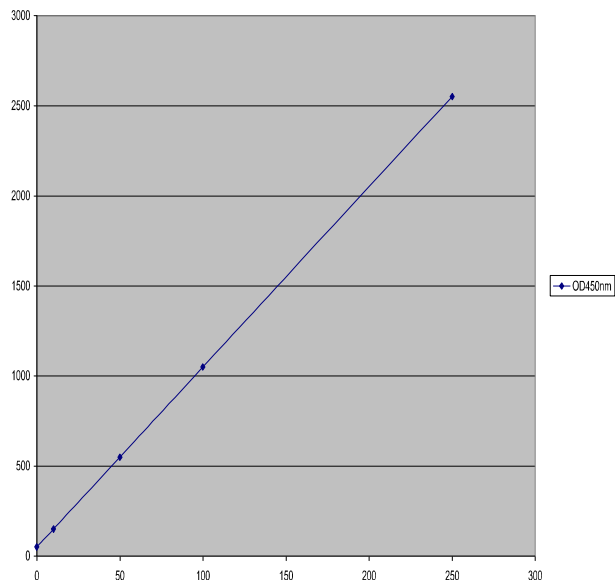
If the results of the test match the requirements stated above, proceed to the next section.

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	1. that the washing procedure and the washer settings are as validated in the pre qualification study;
coefficient of variation > 30%	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 (e.g.: 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 (e.g.: 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.

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/620-630nm values for the Calibrators 0 and 10 mIU/ml and then check that the assay is valid.

Example of calculation (data obtained proceeding as the reading step described in the section M, point 7).

The following data must not be used instead of 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

Important note:

The analysis must be done proceeding as the reading step described in the section M, point 7.

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.

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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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.

Important note:

The performance data have been obtained proceeding as the reading step described in the section M, point 7.

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 S.r.l.
Via G. Carducci n° 27 – Sesto San Giovanni (MI) - Italy



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
Via G. Carducci n° 27
20099 Sesto San Giovanni
(Milano) - Italy**

Phone +39 02 27007161

Fax +39 02 44386771

e-mail: info@diapro.it

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°C.

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 0.045% ProClin 300 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 0.045% ProClin 300 as preservatives. The positive control is green color coded.

4. Calibrator **CAL ...**

n° 1 vial. Lyophilised. To be dissolved with EIA grade 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 0.045% ProClin 300 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 0.045% 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 mouse monoclonal antibody to HBcAg in presence of 0.3 mg/ml gentamicine sulphate and 0.045% ProClin 300. 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 (H₂O₂) 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 0.045% ProClin 300 for the pre-treatment of samples and controls in the plate, blocking interference. The component is blue colour coded.

Note: Use all the content of one vial before opening a second one. The reagent is sensitive to oxidation.

9. Sulphuric Acid **H₂SO₄ 0.3 M**

1x15ml/vial. Contains 0.3 M H₂SO₄ solution. Attention: Irritant (H315; H319; P280; P302+P352; P332+P313; P305+P351+P338; P337+P313; P362+P363)

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°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-borne 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.
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 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°C 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 RECOMMENDATIONS

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 0.2-0.8µ 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 (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 $\pm 5\%$.
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 ≥ 2.0 ; (c) linearity to ≥ 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 $+37^{\circ}\text{C}$ and prepare the ELISA washer by priming with the diluted washing solution, according to the manufacturer's 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 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 μl Specimen Diluent into all the control and sample wells.
4. Pipette 50 μl of the Negative Control in triplicate, 50 μl of the Calibrator in duplicate and then 50 μl of the Positive Control in single. Then dispense 50 μl of each of the samples.
5. Incubate the microplate for **60 min at $+37^{\circ}\text{C}$** .
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 $+37^{\circ}\text{C}$** .

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 ($18-24^{\circ}\text{C}$) 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, 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 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

Specimen Diluent	50 ul
Controls&calibrator and samples	50 ul
1st incubation	60 min
Temperature	+37°C
Wash	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	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

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 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 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.

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/620-630nm 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:

Important note:

The analysis must be done proceeding as the reading step described in the section M, point 12.

P. RESULTS

The results are calculated by means of a cut-off value determined with the following formula:

$$\text{Cut-Off} = (\text{NC} + \text{PC}) / 5$$

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 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 (data obtained proceeding as the the reading step described in the section M, point 12):

The following data must not be used instead of 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. In addition to the first study, where a total of 5179 unselected donors, including 1st time donors, 206 samples from hospitalized patients and 164 potentially interfering specimen were examined, the diagnostic specificity was recently assessed by testing a total of 1498 negative samples on seven different lots. A value of specificity of 100% was observed. In addition to the above population, 189 potentially interfering samples (other liver diseases, pregnant women, hemolized, lipemic, RF positives) have been tested and found negative, confirming a 100% of specificity of the device. 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. In addition to the first Performance Evaluation Study, in order to further evaluate the diagnostic sensitivity of the device, a total of 262 positive samples were recently evaluated. The respective results, collected from seven different lots of the device show a diagnostic sensitivity of 100%.

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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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.

Important note:

The performance data have been obtained proceeding as the reading step described in the section M, point 12.

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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Manufacturer:
Dia.Pro Diagnostic Bioprobes S.r.l.
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 -



DIA.PRO

**Diagnostic Bioprobes Srl
Via G. Carducci n° 27
20099 Sesto San Giovanni
(Milano) - Italy**

Phone +39 02 27007161

Fax +39 02 44386771

e-mail: info@diapro.it

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 hepatocytes, 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 reHBeAg, 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 H₂O₂.

Note: To be stored protected from light as sensitive to strong illumination.

11. Sulphuric Acid: H₂SO₄ 0.3 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 (blinking) 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-borne 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 RECOMMENDATIONS

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 $\pm 2\%$.
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 $\pm 5\%$.
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+H₂O₂) 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.

- Dilute all the content of the 20x concentrated Wash Solution as described above.
- Dissolve the Calibrator as described above and gently mix.
- Allow all the other components to reach room temperature (about 1 hr) and then mix gently on vortex all liquid reagents.
- 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.
- Check that the ELISA reader is turned on or ensure it will be turned on at least 20 minutes before reading.
- If using an automated work station, turn on, check settings and be sure to use the right assay protocol.
- Check that the micropipettes are set to the required volume.
- 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:

- Place the required number of strips in the plastic holder and carefully identify the wells for controls, calibrator and samples.
- Leave the A1 well empty for blanking purposes.
- 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.
- Then dispense 100 µl of samples in the proper wells.
- 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).
- 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.

- When the first incubation is finished, wash the microwells as previously described (section I.3)
- 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.

- Check that the reagent has been dispensed properly and then incubate the microplate for **60 min at +37°C**.
- When the second incubation is finished, wash the microwells as previously described (section I.3)
- 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.

- 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.

- 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.
- 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:

- Place the required number of strips in the plastic holder and carefully identify the wells for controls, calibrator and samples.
- Leave the A1 well empty for blanking purposes.
- 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.
- Then dispense 50 µl of samples in the proper wells.
- 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).
- Dispense then 50 µl of HBe Antigen in all the wells, except for A1.
- 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.

- When the first incubation is finished, wash the microwells as previously described (section I.3)
- Finally proceed as described for the HBeAg assay from point 8 to the last one.

Important notes:

- Ensure that no finger prints are present on the bottom of the microwell before reading. Finger prints could generate false positive results on reading.
- 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.
- 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	100 ul
Samples	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	50 ul
Samples	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:

$$NC + 0.100 = \text{Cut-Off (Co)}$$

The value found for the test is used for the interpretation of results as described in the next paragraph.

HBeAb:

$$(NC + PC) / 3 = \text{Cut-Off (Co)}$$

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:

$$S = OD450nm/620-630nm \text{ of the sample}$$

$$Co = \text{cut-off value}$$

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 of 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 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) / 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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 -



DIA.PRO

**Diagnostic Bioprobes Srl
Via G. Carducci n° 27
20099 Sesto San Giovanni
(Milano) - Italy**

Phone +39 02 27007161

Fax +39 02 44386771

e-mail: info@diapro.it

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 asymptomatic. 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 **H2SO4 0.3 M**

1x32ml/bottle. It contains 0.3 M H2SO4 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 (blinking) 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 RECOMMENDATIONS

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.

baths are suitable for the incubations, provided that the instrument is validated for the incubation of ELISA tests.

- 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.
- Incubation times have a tolerance of $\pm 5\%$.
- 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 ≥ 2.0 ; (c) linearity to ≥ 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.
- 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.
- 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.
- 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.

I. INSTRUMENTS AND TOOLS USED IN COMBINATION WITH THE KIT

- 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 $\pm 2\%$. Decontamination of spills or residues of kit components should also be carried out regularly.
- The ELISA incubator has to be set at $+37^{\circ}\text{C}$ (tolerance of $\pm 0.5^{\circ}\text{C}$) and regularly checked to ensure the correct temperature is maintained. Both dry incubators and water

L. PRE ASSAY CONTROLS AND OPERATIONS

- Check the expiration date of the kit printed on the external label of the kit box. Do not use if expired.
- 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.
- Dilute all the content of the 20x concentrated Wash Solution as described above.
 - Dissolve the Calibrator as described above.
 - Allow all the other components to reach room temperature (about 1 hr) and then mix as described.
 - 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.
 - Check that the ELISA reader has been turned on at least 20 minutes before reading.
 - If using an automated workstation, turn it on, check settings and be sure to use the right assay protocol.
 - Check that the micropipettes are set to the required volume.
 - 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 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:

- Place the required number of Microwells in the microwell holder. Leave the 1st well empty for the operation of blanking.
- 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 !
- 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.*

- 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.
- 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.*

- Wash the microplate with an automatic washer by delivering and aspirating 350ul/well of diluted washing solution as reported previously (section I.3).
- Pipette 100ul 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.*

- Incubate the microplate for **45 min at +37°C**.
- Wash microwells as in step 6.
- Pipette 100ul 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.*

- Pipette 100ul 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.
- 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:

- Ensure that no finger prints are present on the bottom of the microwell before reading. Finger prints could generate false positive results on reading.
- 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.
- Shaking at 350 ±150 rpm during incubation has been proved to increase the sensitivity of the assay of about 20%.
- 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	200 ul 200ul dil.+10ul
Assay Diluent (DILAS)	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

	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.

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/Substrate 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

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):

$$NC + 0.350 = \text{Cut-Off (Co)}$$

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 of 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	Lot # 2	Lot # 2	Results expected
	S/Co	S/Co	S/Co	
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.

REFERENCES

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Manufacturer:
Dia.Pro Diagnostic Bioprobes Srl.
Via G. Carducci n° 27 – Sesto San Giovanni (MI) - Italy

CE
0318



Total Prostate Specific Antigen (tPSA) Test System

Product Code: 2125-300

1.0 INTRODUCTION

Intended Use: The Quantitative Determination of Total Prostate Specific Antigen (tPSA) Concentration in Human Serum by a Microplate Immunoassay

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 prostate but is not found in any other normal or malignant tissue.

PSA is found in benign, malignant and metastatic prostate 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 to be 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.

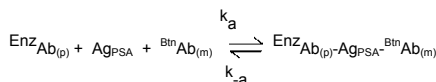
3.0 PRINCIPLE

Immunoassay (TYPE 3):

The essential reagents required for an immunoassay 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:



$\text{B}^{\text{tn}}\text{Ab}_{(m)}$ = Biotinylated Antibody (Excess Quantity)

Ag_{PSA} = Native Antigen (Variable Quantity)

$\text{EnzAb}_{(p)}$ = Enzyme labeled Antibody (Excess Quantity)

$\text{EnzAb}_{(p)}\text{-Ag}_{\text{PSA}}\text{-B}^{\text{tn}}\text{Ab}_{(m)}$ = 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:



$\text{Streptavidin}_{\text{C.W.}}$ = 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:

- Prostate Specific antigen (PSA) 1ml/vial – Icon 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.
- 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.
- Streptavidin Coated Plate – 96 wells - Icon J**
One 96-well microplate coated with streptavidin and packaged in an aluminum bag with a drying agent. Store at 2-8°C.
- Wash Solution Concentrate – 20 ml - Icon K**
One (1) vial containing a surfactant in buffered saline. A preservative has been added. Store at 2-30°C.
- Substrate A – 7ml/vial - Icon S^A**
One (1) bottle containing tetramethylbenzidine (TMB) in buffer. Store at 2-8°C.
- Substrate B – 7ml/vial - Icon S^B**
One (1) bottle containing hydrogen peroxide (H₂O₂) in buffer. Store at 2-8°C.
- Stop Solution – 8ml/vial - Icon STOP**
One (1) bottle containing a strong acid (1N HCl). Store at 2-30°C.
- 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:

- Pipette(s) capable of delivering 25 & 50µl volumes with a precision of better than 1.5%.
- Dispenser(s) for repetitive deliveries of 0.100ml and 0.350ml volumes with a precision of better than 1.5%.
- Microplate washers or a squeeze bottle (optional).
- Microplate Reader with 450nm and 620nm wavelength absorbance capability.
- Absorbent Paper for blotting the microplate wells.
- Plastic wrap or microplate cover for incubation steps.
- Vacuum aspirator (optional) for wash steps.
- Timer.
- 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:

- 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.
- 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.
Note 1: 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****

- 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.**
- Pipette 0.025 ml (25µl) of the appropriate serum reference, control or specimen into the assigned well.
- 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.**
- Swirl the microplate gently for 20-30 seconds to mix and cover.
- Incubate 30 minutes at room temperature.
- Discard the contents of the microplate by decantation or aspiration. If decanting, tap and blot the plate dry with absorbent paper.
- 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.**
- 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
- Incubate at room temperature for fifteen (15) minutes.
- 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.**
- 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.

- Record the absorbance obtained from the printout of the microplate reader as outlined in Example 1.
- 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).
- Draw the best-fit curve through the plotted points.
- 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).

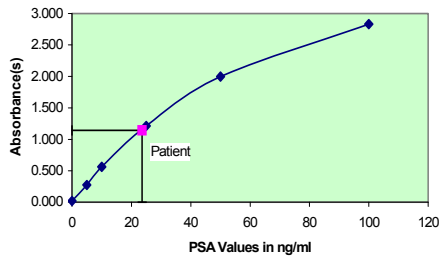
Note: Computer data reduction software designed for ELISA assays may also be used for the data reduction. If such software is utilized, the validation of the software should be ascertained.

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 ≥ 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 cancer** 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 1
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
Least Square Regression Analysis

Method	Mean	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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Revision: 3 Date: 081511 DCO: 0524

Cat #: 2125-300

Size	96(A)	192(B)
Reagent (fill)	A)	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)

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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 -



DIA.PRO

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Via G. Carducci n° 27
20099 Sesto San Giovanni
(Milano) - Italy**

Phone +39 02 27007161

Fax +39 02 44386771

e-mail: info@diapro.it

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 H₂O₂.

Note: To be stored protected from light as sensitive to strong illumination.

8. Sulphuric Acid: H₂SO₄ 0.3 M

1x15ml/vial. Contains 0.3 M H₂SO₄ 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-borne microbial agents, when opening kit vials and microplates and when performing the test. Protect the Chromogen/Substrate (TMB/H₂O₂) 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 0.2-0.8µ 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 $\pm 2\%$.
2. The ELISA incubator has to be set at $+37^{\circ}\text{C}$ (tolerance of $\pm 0.5^{\circ}\text{C}$) 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 $\pm 5\%$.
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 $\geq 1\%$. 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/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 $+37^{\circ}\text{C}$ 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 $+2..8^{\circ}\text{C}$, 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 **$+37^{\circ}\text{C}$ 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 **$+37^{\circ}\text{C}$ 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/H₂O₂ 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	100 ul
Samples	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/H ₂ O ₂ 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 ≤ 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	<ol style="list-style-type: none"> 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	<ol style="list-style-type: none"> 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:

$$\text{Cut-Off} = (\text{NC} + \text{PC}) / 5$$

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 #	DAB.CE	Lot #	DAB.CE	Lot #
	1102	0103	0403	0103	0403	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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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	3 rd 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.

Manufacturer:
Dia.Pro Diagnostic Bioprobes Srl
Via G. Carducci n° 27 – Sesto San Giovanni (MI) – Italy

CE
0318

Certificate



Quality Management System EN ISO 13485:2016

Registration No.: SX 1006099-1

Organization: 77 Elektronika Műszeripari Kft.
Fehérvári út 98.
1116 Budapest
Hungary

Scope: Design and development, production, distribution, installation and servicing of blood glucose measuring systems, urine analyzers and rapid test readers, including related consumables.

The Certification Body of TÜV Rheinland LGA Products GmbH certifies that the organization has established and applies a quality management system for medical devices. Proof has been furnished that the requirements specified in the abovementioned standard are fulfilled. The quality management system is subject to yearly surveillance.

Report No.: 93389457-30
Effective date: 2022-11-18
Expiry date: 2025-11-17
Issue date: 2022-11-09

A handwritten signature in blue ink is written over a circular seal. The seal contains the TÜV Rheinland logo and the text "TÜV Rheinland LGA Products GmbH" and "Zertifizierungsstelle".

Rafał Byczkowski
TÜV Rheinland LGA Products GmbH
Tillystraße 2 · 90431 Nürnberg · Germany



Certificate



Quality Management System EN ISO 13485:2016

Registration No.: SX 1006099-1

Organization: 77 Elektronika Műszeripari Kft.
Fehérvári út 98.
1116 Budapest
Hungary

The scope of certification includes the following additional sites:

No.	Facility	Scope
/01	77 Elektronika Műszeripari Kft. Fehérvári út 98. 1116 Budapest Hungary	Design and development, production, distribution, installation and servicing.
/02	77 Elektronika Műszeripari Kft. Telephey Sztregova utca 1 1116 Budapest Hungary	Manufacture and warehouse of blood glucose measuring systems, urine analyzers, related consumables and parts. Manufacturing of SMT technology.

Report No.: 93389457-30
Effective date: 2022-11-18
Expiry date: 2025-11-17
Issue date: 2022-11-09



Rafał Byczkowski
TÜV Rheinland LGA Products GmbH
Tillystraße 2 · 90431 Nürnberg · Germany

Certificate

Quality Management System
EN ISO 13485:2016
EN ISO 13485:2016/AC:2018
EN ISO 13485:2016/A11:2021

Registration No.: SX 1614112-1
Certificate Holder: KABE-Labortechnik GmbH
Jägerhofstr. 17
51588 Nümbrecht
Germany

Scope: Design and development, production and distribution of in vitro diagnostic devices and consumption materials for sample withdrawal, preparation and storage as well as single-use medical devices:
- cannulas for blood collection,
- winged cannulas for blood collection and
- capillaries for micro blood collection (KABE MBU capillaries).

The Certification Body of TÜV Rheinland LGA Products GmbH certifies that the organization has established and applies a quality management system for medical devices.
Proof has been furnished that the requirements specified in the abovementioned standard are fulfilled. The quality management system is subject to yearly surveillance.

Report No.: 1160508-40
Effective date: 2024-10-16
Expiry date: 2027-10-15
Issue date: 2024-09-24
Replaces certificate SX 1614112-1 issued 2021-10-25.

This certificate can be validated on <https://www.certipedia.com>

Daniele Wiedemuth
Dipl.-Ing. (FH) Daniele Wiedemuth
TÜV Rheinland LGA Products GmbH
Tillystraße 2 · 90431 Nürnberg · Germany

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Certificate

Quality Management System
EN ISO 13485:2016
EN ISO 13485:2016/AC:2018
EN ISO 13485:2016/A11:2021

Registration No.: SX 1614112-1
Certificate Holder: KABE-Labortechnik GmbH
Jägerhofstr. 17
51588 Nümbrecht
Germany

The scope of certification also covers the following sites:

No.	Facility	Scope
/01	c/o KABE-Labortechnik GmbH Jägerhofstr. 17 51588 Nümbrecht Germany	Design and development, production and distribution of in vitro diagnostic devices and consumption materials for sample withdrawal, preparation and storage as well as single-use medical devices
/02	c/o KABE-Labortechnik GmbH Werner-von-Siemens-Str. 1 51674 Wiehl Germany	Warehouse and shipping

This certificate can be validated on <https://www.certipedia.com>

CERTIFICATO N° 505SGQ06

CERTIFICATE N° 505SGQ06

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 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 e dispositivi medici di classe I non sterile. Commercializzazione di dispositivi medici invasivi e non di classe IIa, Is, I 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 and non-sterile class I medical devices.
Marketing of invasive and non-invasive medical devices of class IIa, Is, I and in vitro diagnostics. Marketing of laboratory items.*

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

1998-07-23

Data di Prima Emissione ITALCERT
First Issue Date ITALCERT

2011-10-30

Data di Rinnovo
Renewal Date

2023-10-24

Data di Scadenza
Expiration Date

2026-10-29

Settore IAF 14 - 29



SGQ N° 023A

Membro degli Accordi di Mutuo Riconoscimento EA, IAF e ILAC
Signatory of EA, IAF and ILAC Mutual Recognition Agreements