VITROS Products
Immunodiagnostic

INSTRUCTIONS FOR USE aHCV

VITROS Immunodiagnostic Products Anti-HCV Reagent Pack	REF	131 8450
VITROS Immunodiagnostic Products Anti-HCV Calibrator	REF	194 0667

Intended Use

For *in vitro* diagnostic use only.

VITROS Immunodiagnostic Products Anti-HCV Reagent Pack

For the qualitative detection of antibodies to hepatitis C virus (anti-HCV) in human serum and plasma (EDTA, heparin or citrate), using the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems.

VITROS Immunodiagnostic Products Anti-HCV Calibrator

For use in the calibration of the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems for the qualitative detection of antibodies to hepatitis C Virus (anti-HCV) in human serum and plasma (EDTA, heparin or citrate).

Summary and Explanation of the Test

The hepatitis C virus (HCV) is now known to be the causative agent for most, if not all, blood-borne non-A, non-B hepatitis (NANBH). Studies throughout the world indicate that HCV is transmitted through contaminated blood and blood products, through blood transfusions or through other close, personal contacts. The presence of anti-HCV indicates that an individual may have been infected with HCV and may be capable of transmitting HCV infection. [1]

Three recombinant hepatitis C virus encoded antigens are used in the VITROS Anti-HCV test. The three recombinant antigens are c22-3, c200 and NS-5. The recombinant protein c22-3 is encoded by the putative core region of the HCV genome. HCV recombinant protein c200 is encoded by the putative NS3 and NS4 regions of the HCV genome. The c200 protein contains the c33c protein sequence which is genetically linked to the c100-3 protein sequence. Studies have indicated that antibodies which develop after infection with HCV are often reactive with c22-3 and or c33c. [2] HCV recombinant protein NS5 is encoded by the putative NS5 region of the HCV genome. A significant proportion of persons infected with HCV develop antibodies to NS5. [3]

The host organism for all three HCV recombinant antigens is *S. cerevisiae* (yeast).

Principles of the Procedure

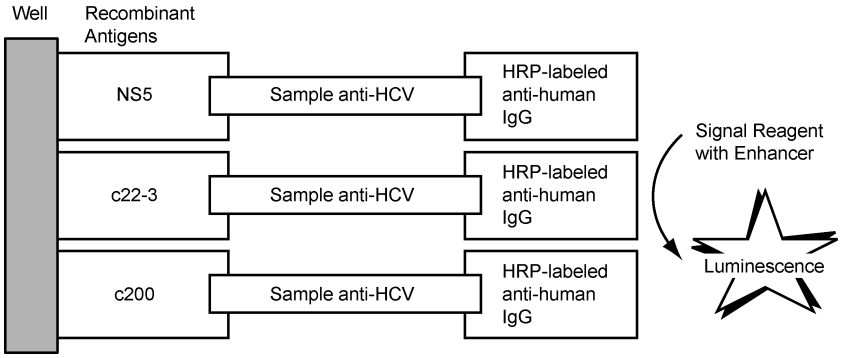
An immunometric technique is used, this involves a two stage reaction. In the first stage HCV antibody present in the sample binds with HCV recombinant antigens coated on the wells. Unbound sample is removed by washing. In the second stage horseradish peroxidase (HRP)-labeled antibody conjugate (mouse monoclonal anti-human IgG) binds to any human IgG captured on the well in the first stage. Unbound conjugate is removed by washing.

The bound HRP conjugate is measured by a luminescent reaction. [4] A reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent, is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminol derivative, producing light. The electron transfer agent (a substituted acetanilide) increases the level of light produced and prolongs its emission. The light signals are read by the system. The amount of HRP conjugate bound is or directly proportional to the concentration of anti-HCV present.

Test Type	System *	Incubation Time	Time to first result	Test Temperature	Reaction Sample Volume
Immunometric immunoassay	ECi/ECiQ, 3600, 5600, XT 7600	45 minutes	55 minutes	37 °C	20 µL

* Not all products and systems are available in all countries.

Reaction Scheme



Warnings and Precautions

WARNING: Potentially Infectious Material

Treat as if capable of transmitting infection.

Use caution when handling material of human origin. Consider all samples potentially infectious. No test method can offer complete assurance that hepatitis B virus, hepatitis C virus (HCV), human immunodeficiency virus (HIV 1+2) or other infectious agents are absent. Handle, use, store and dispose of solid and liquid waste from samples and test components, in accordance with procedures defined by appropriate national biohazard safety guideline or regulation (e.g. CLSI document M29). [5]

The VITROS Anti-HCV Calibrator is the only component that contains human-derived material. The calibrator contains:

HCV antibody positive plasma obtained from donors who were tested individually and found to be negative for hepatitis B surface antigen, and for antibodies to the human immunodeficiency virus (HIV 1+2), using approved methods (enzyme immunoassays). The HCV antibody positive plasma has been treated in order to reduce the titer of potentially infectious virus. However, as no testing method can rule out the risk of potential infection, handle as if capable of transmitting infection.

HCV antibody negative plasma obtained from donors who were tested individually and found to be negative for hepatitis B surface antigen, and for antibodies to HCV and HIV 1+2, using approved methods (enzyme immunoassays).

WARNING: Contains ProClin 300 and Kathon or ProClin 200 (CAS 55965-84-9) [6]

The VITROS Anti-HCV Reagent Pack and VITROS Anti-HCV Calibrator contain 1% ProClin 300 and 2.0% Kathon or ProClin 200 respectively. H317: May cause an allergic skin reaction. P280: Wear protective gloves/protective clothing/eye protection/face protection. P302 + P352: IF ON SKIN: Wash with plenty of soap and water. P333 + P313: If skin irritation or rash occurs: Get medical advice/ attention. P363: Wash contaminated clothing before reuse.

WARNING

WARNING: Contains 2-Chloroacetamide (CAS 79-07-2) [6]

The VITROS Anti-HCV Reagent Pack contains 0.1% 2-Chloroacetamide. H317:May cause an allergic skin reaction. P280: Wear protective gloves/ protective clothing/eye protection/face protection. P302 + P352: IF ON SKIN: Wash with plenty of soap and water. P333 + P313: If skin irritation or rash

occurs: Get medical advice/attention. P363: Wash contaminated clothing before reuse. P308 + P313: IF exposed or concerned: Get medical advice/attention.

Refer to www.Orthoclinicaldiagnostics.com for the Safety Data Sheets and for Ortho contact information.

WARNING

Reagents

Reagent Pack Contents

1 reagent pack containing:

- 100 coated wells (hepatitis C Virus recombinant antigens derived from yeast; coated at 0.41 µg/well)
- 18.2 mL Assay Reagent - buffer with bovine serum albumin and anti-microbial agent
- 20.6 mL Conjugate Reagent (HRP-mouse monoclonal anti-human IgG, 1.04 ng/well) in buffer with bovine serum albumin and anti-microbial agent

Reagent Pack Handling

- The reagent pack is supplied ready for use.
- The reagent pack contains homogeneous liquid reagents that do not require shaking or mixing prior to loading onto the system.
- Handle the reagent pack with care. Avoid the following:
  - allowing condensation to form on the pack
  - causing reagents to foam
  - agitation of the pack

Reagent Pack Storage and Preparation

Reagent	Storage Condition		Stability
Unopened	Refrigerated	2–8 °C (36–46 °F)	expiration date
Opened	On system	System turned on	≤8 weeks
Opened	Refrigerated	2–8 °C (36–46 °F)	≤8 weeks

- The VITROS Anti-HCV Reagent Pack is suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- Do not freeze unopened reagent packs.
- Load reagent packs directly from refrigerated storage to minimize condensation.
- Store opened refrigerated reagent packs in a sealed reagent pack storage box that contains dry desiccant.

Calibrator Contents

- 1 VITROS Anti-HCV Calibrator (anti-HCV positive human plasma in anti-HCV negative human plasma with antimicrobial agent, 2mL)
- Lot calibration card
- Protocol card
- 8 calibrator bar code labels

Calibrator Handling

- Use only with reagent packs of the same lot number. Mix thoroughly by inversion and bring to 15–30 °C (59–86 °F) before use. Each pack contains sufficient for a minimum of 6 determinations of each calibrator.
- Handle calibrators in stoppered containers to avoid contamination and evaporation. To avoid evaporation, limit the amount of time calibrators are on the system. Refer to the operating instructions for your system. Return to 2–8 °C (36–46 °F) as soon as possible after use, or load only sufficient for a single determination.

Calibrator Storage and Preparation

Calibrator	Storage Condition		Stability
Unopened	Refrigerated	2–8 °C (36–46 °F)	expiration date
Opened	Refrigerated	2–8 °C (36–46 °F)	≤13 weeks
Opened	Frozen	≤-20 °C (≤-4 °F)	≤13 weeks

- VITROS Anti-HCV Calibrator is supplied ready for use.
- The VITROS Anti-HCV Calibrator is suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- Opened calibrators may be stored frozen (with no more than 1 freeze-thaw cycle).
- The VITROS Anti-HCV test uses 20 µL of calibrator for each determination. The VITROS Anti-HCV Calibrator may be used directly on the VITROS Immunodiagnostic and VITROS Integrated Systems. Alternatively, transfer an aliquot of each calibrator into a sample container (taking account of the minimum fill volume of the container), which may be bar coded with the labels provided. For details on minimum fill volume of sample cups or containers, refer to the operating instructions for your system.
- The VITROS Anti-HCV Calibrator is automatically processed in duplicate.

Specimen Collection, Preparation and Storage

Patient Preparation

No special patient preparation is necessary.

Specimens Recommended

- Serum
- Heparin plasma
- EDTA plasma
- Citrate plasma

Note: Results from citrate plasma samples will be proportionally lower due to dilution by the liquid anti-coagulant.

Specimens Not Recommended

Do not use turbid specimens. Turbidity in specimens may affect test results.

Special Precautions

IMPORTANT: Certain collection devices have been reported to affect other analytes and tests.[7] Owing to the variety of specimen collection devices available, Ortho Clinical Diagnostics is unable to provide a definitive statement on the performance of its products with these devices. Confirm that your collection devices are compatible with this test.

Specimen Collection and Preparation

- Collect specimens using standard procedures.[8-9]
- Samples should be thoroughly separated from all cellular material. Failure to do so may lead to an erroneous result.
- Thoroughly mix samples by inversion and bring to 15–30 °C (59–86 °F) before use.
- The VITROS Anti-HCV test uses 20 µL of sample for each determination. This does not take account of the minimum fill volume of the chosen sample container. For details on minimum fill volume of sample cups or containers, refer to the operating instructions for your system.

Handling and Storage Conditions

- Handle samples in stoppered containers to avoid contamination and evaporation.
- The amount of time samples are on the system prior to analysis should be limited to avoid evaporation. Refer to the operating instructions for your system.
- Return to 2–8 °C (36–46 °F) as soon as possible after use, or load sufficient volume for a single determination.
- Serum and plasma samples may be stored for up to 7 days at 2-8 °C (36–46 °F). Serum and plasma samples tested initially and after 4 weeks storage at -20 °C (36–46 °F) showed no differences in clinical performance.
- Avoid repeated freeze-thaw cycles.

Testing Procedure

Materials Provided

- VITROS Immunodiagnostic Products Anti-HCV Reagent Pack
- VITROS Immunodiagnostic Products Anti-HCV Calibrator

Materials Required but Not Provided

- VITROS Immunodiagnostic Products Signal Reagent
- VITROS Immunodiagnostic Products Universal Wash Reagent
- Quality control materials such as VITROS Immunodiagnostic Products Anti-HCV Controls
- VITROS Immunodiagnostic Products Reagent Pack Storage Box (optional) with desiccant

Operating Instructions

Check the inventory regularly to aid the management of reagents and ensure that sufficient VITROS Signal Reagent, VITROS Universal Wash Reagent and calibrated reagent lots are available for the work planned. When performing panels of tests on a single sample, ensure that the sample volume is sufficient for the tests ordered.

For detailed information refer to the operating instructions for your system.

Note:	Do not use visibly damaged product.

Default Test Name

The default test name which will appear on patient reports is Anti-HCV. The default short name that will appear on the test selection menus and laboratory reports is aHCV. These defaults may be reconfigured, if required. For detailed information refer to the operating instructions for your system.

Calibration

Calibration Procedure

- Calibration is lot specific; reagent packs and calibrators are linked by lot number. Reagent packs from the same lot may use the same calibration.
- A Master Calibration is established for each new reagent lot by performing multiple tests. This is the process by which a lot-specific parameter [a] which links the signal at the cutoff (cutoff value) to the calibrator signal is determined.

Cutoff value = (a x Signal of Cal 1)

- Ensure that the Master Calibration for each new reagent lot is available on your system.
- Process the calibrator in the same manner as samples. Load sufficient for the automatic duplicate determination. Calibration need not be programmed if bar code labels are used; Calibration will be initiated automatically.
- When the calibrator is processed the validity of the calibration is assessed against quality parameters which compares the actual signal of the calibrator with the expected signal. If the calibration is acceptable the cutoff value is calculated and stored for use with any reagent pack of that lot.
- The quality of calibration cannot be completely described by a single parameter. The calibration report should be used in conjunction with acceptable control values to determine the validity of the calibration.
- Recalibration is required after a pre-determined calibration interval, or when a different reagent lot is loaded.
- Calibration results are assessed against a range of quality parameters. Failure to meet any of the defined quality parameter ranges will be coded in the calibration report. For actions to be taken following a failed calibration, refer to the operating instructions for your system.

Refer to the operating instructions for your system for detailed instructions on the calibration process.

When to Calibrate

- Calibrate when the reagent pack and calibrator lot changes.
- Calibrate every 28 days.
- After specified service procedures have been performed.
- If quality control results are consistently outside of your acceptable range.

For additional information on when to calibrate, refer to the operating instructions for your system.

Traceability of Calibration

The calibration of the VITROS Anti-HCV test is traceable to an in-house reference calibrator which has been value assigned to optimize the clinical sensitivity and specificity performance.

Calibration Model

Results are calculated as a normalized signal, relative to a cutoff value. During the calibration process a lot-specific parameter, is used to determine a valid stored cutoff value for the VITROS Immunodiagnostic and VITROS Integrated System.

Quality Control

Quality Control Material Selection

VITROS Anti-HCV Controls are recommended for use with the VITROS Immunodiagnostic and VITROS Integrated System. There are 2 VITROS Anti-HCV Controls (Anti-HCV negative and Anti-HCV positive). The performance of other commercial control fluids should be evaluated for compatibility with this test before they are used for quality control.

Control materials may show a difference when compared with other anti-HCV methods if they contain high concentrations of preservatives, stabilizers, or other nonphysiological additives, or otherwise depart from a true human sample matrix.

Appropriate quality control value ranges must be established for all quality control materials used with the VITROS Anti-HCV test.

Quality Control Procedure Recommendations

- Good laboratory practice requires that controls be processed to verify the performance of the test.
- Choose control levels that check the clinically relevant concentrations.
- To verify system performance, analyze control materials:
  - After calibration
  - According to local regulations or at least once each day that the test is being performed
  - After specified service procedures are performed

If quality control procedures within your laboratory require more frequent use of controls, follow those procedures.

- Analyze quality control materials in the same manner as patient specimens.
- If control results fall outside your acceptable range, investigate the cause before deciding whether to report patient results.
- Refer to the published guidelines for general quality control recommendations. [10]

For more detailed information, refer to the operating instructions for your system.

Quality Control Material Preparation and Storage

Refer to the manufacturer's product literature for preparation, storage, and stability information.

Results

Results are automatically calculated by the VITROS Immunodiagnostic and VITROS Integrated System.

Result Calculation

Results are calculated as a normalised signal, relative to a cutoff value. During the calibration process a lot-specific parameter is used to determine a valid stored cutoff value for the VITROS Immunodiagnostic and VITROS Integrated System.

$$\text{Result} = \frac{\text{Signal for test sample}}{\text{Cutoff value}}$$

A result of ≥1.00 indicates a reactive sample and the possible presence of Anti-HCV.

A result <0.90 indicates a non-reactive sample, negative for Anti-HCV.

A result of ≥0.90 and <1.00 indicates a borderline sample.

Interpretation of Results

A sample found borderline or reactive must be retested in duplicate to verify its status. Before retesting, the sample should be centrifuged to ensure freedom from cells, cellular debris or fibrin. If results on repeat testing are <0.90 for both replicates, the sample should be considered negative. If either duplicate retest result is ≥0.90, the sample should be tested by supplemental tests to confirm the result. A repeatedly reactive sample, confirmed by supplemental tests should be considered positive for anti-HCV. In the case of repeatedly borderline results, analysis of follow-up samples is recommended.

Limitations of the Procedure

Known Interferences

The VITROS Anti-HCV test was evaluated for interference consistent with CLSI document EP7. [11] Commonly encountered substances were tested on 2 lots of reagents. Of the compounds tested, none was found to interfere with the clinical interpretation of the test. Refer to “Substances that do not Interfere” for a list of compounds tested that did not show interference.

Other Limitations

- The results from this or any other diagnostic test should be used and interpreted only in the context of the overall clinical picture.
- A negative test result does not exclude the possibility of exposure to or infection with HCV. HCV antibodies may be undetectable in some stages of the infection and in some clinical conditions. [12]
- Heterophilic antibodies in serum or plasma samples may cause interference in immunoassays. [13] These antibodies may be present in blood samples from individuals regularly exposed to animals or who have been treated with animal serum products. Results which are inconsistent with clinical observations indicate the need for additional testing.

Performance Characteristics

Sensitivity

435 patient samples previously determined as positive by an anti-HCV immunoblot test were tested in the VITROS Anti-HCV test. The sensitivity for this population of samples in the VITROS Anti-HCV test was calculated as 100% (435/435).

In addition, 29 commercially available seroconversion panels were tested. The VITROS Anti-HCV test showed equivalent or greater seroconversion sensitivity for 29/29 panels, when compared to the published results from another commercially available test.

25 positive fresh serum and plasma samples, (≤1 day after sampling), were tested in direct comparison with a commercially available CE-marked test. Both tests gave comparable results.

Specificity

Samples from 5374 presumed healthy blood donors, and 393 clinical specimens were tested in the VITROS Anti-HCV test and another commercially available test.

Samples	Number of test samples	Initially Reactive	Repeatedly Reactive	Confirmed Positive
Donor	5374	14	13	0
Clinical	393	1	1	0

The specificity for the VITROS Anti-HCV test for the donor population was calculated as 99.76% (5 361/5 374) based on repeat reactives. The specificity for the VITROS Anti-HCV test for the clinical population was calculated as 99.75% (392/393) based on repeat reactives.

Potentially Cross-Reacting Subgroups

Additionally 161 samples from the following potentially cross-reacting sub-groups were tested in the VITROS Anti-HCV test: CMV positive, EBV positive, HIV positive, non-viral liver disease patients, other viral liver diseases (e.g. HBV, HAV), SLE, rheumatoid factor positive, recent vaccinees (e.g. flu), yeast reactive samples. Of these categories none were found to result in false reactives in the VITROS Anti-HCV test.

Precision

VITROS ECi/ECiQ Immunodiagnostic System

Precision was evaluated consistent with NCCLS Protocol EP5. [14] Two replicates each of 4 samples were tested once per day on at least 20 different days. The experiment was performed using 2 reagent lots on 2 different systems. The data presented are a representation of the product performance.

VITROS 3600 Immunodiagnostic System and VITROS 5600 Integrated System

Precision was evaluated consistent with NCCLS document EP5. [15] Two replicates each of 2 control samples and 4 patient sample pools were tested on 2 separate occasions per day on at least 20 different days. The experiment was performed using 1 reagent lot on each system. The data presented are a representation of the product performance.

System	Units = Result (S/C)							No. Observ.	No. Days
	Mean aHCV Result	Within-run*		Within-calibration**		Within-lab***			
		SD	CV (%)	SD	CV (%)	SD	CV (%)		
ECi/ECiQ system 1	0.14	0.00320	2.3	0.00940	6.7	0.0110	7.9	40	20
	2.04	0.0542	2.7	0.147	7.2	0.148	7.3	40	20
	5.76	0.0998	1.7	0.368	6.4	0.341	5.9	40	20
	14.8	0.147	1.0	0.449	3.0	0.493	3.3	40	20
ECi/ECiQ system 2	0.14	0.00350	2.5	0.00720	5.1	0.00770	5.5	42	21
	2.02	0.0314	1.6	0.116	5.7	0.120	5.9	42	21
	5.65	0.157	2.8	0.309	5.5	0.366	6.5	42	21
	14.8	0.219	1.5	0.459	3.1	0.645	4.4	42	21
3600	0.19	0.00794	4.2	0.0143	7.5	0.0159	8.4	96	24
	6.20	0.128	2.1	0.216	3.5	0.318	5.0	96	24
	0.09	0.00214	2.4	0.00476	5.3	0.00594	6.7	96	24
	0.87	0.0187	2.1	0.0600	6.9	0.0695	8.0	96	24
	1.35	0.0388	2.9	0.0757	5.6	0.098	7.1	96	24
	2.51	0.0393	1.6	0.119	4.7	0.166	6.5	96	24
5600****	0.16	0.00405	2.5	0.00979	6.1	0.0110	6.5	96	24
	5.79	0.111	1.9	0.239	4.1	0.318	5.1	96	24
	0.08	0.00169	2.1	0.00332	4.2	0.00464	5.6	96	24
	0.80	0.0184	2.3	0.0628	7.9	0.0573	6.7	96	24
	1.24	0.0321	2.6	0.0644	5.2	0.0684	5.1	96	24
	2.36	0.0398	1.7	0.0799	3.4	0.115	4.5	96	24

* Within-run (repeatability). Between Duplicate precision averaged over all runs

** Within-calibration. Total precision with weighted components of within-run, between–run and between-day variation

*** Within-lab. A measure of the effect of recalibration on total precision, calculated within reagent lot, using data from at least 4 calibrations

**** Performance characteristics for the VITROS 5600 System are applicable to the VITROS XT 7600 System.

Substances that do not Interfere

The effect of Bilirubin, Hemoglobin and Triolein were tested in an anti-HCV negative and an anti-HCV positive sample. For each substance, the highest concentration, which was considered not to impact the clinical interpretation of results, are shown in the table below.

Compound	Concentration	
Bilirubin	0.342 mmol/L	20 mg/dL
Hemoglobin	0.310 mmol/L	500 mg/dL
Triolein	33.9 mmol/L	3000 mg/dL

ADM working group: Summary of Evaluation

The VITROS Anti-HCV test was evaluated by the ADM working group. 450 samples from 246 patients infected with different genotypes of hepatitis C virus and 50 samples from the HCV SFTS panel, including 27 RNA reactive samples, were tested. The VITROS Anti-HCV test showed good sensitivity for the detection of early seroconversion and for the screening of other categories of reactive samples, including those showing an isolated reactivity and those from chronic carriers.

A population of 2018 blood donor samples were tested with the VITROS Anti-HCV test. Eight samples gave repeatably reactive results, of which 1 was confirmed as reactive and 6 were found negative by other tests. The result of the remaining sample could not be interpreted (indeterminate NS3, PCR negative). The specificity for the VITROS Anti-HCV test was approximately 99.70%.

License Statement

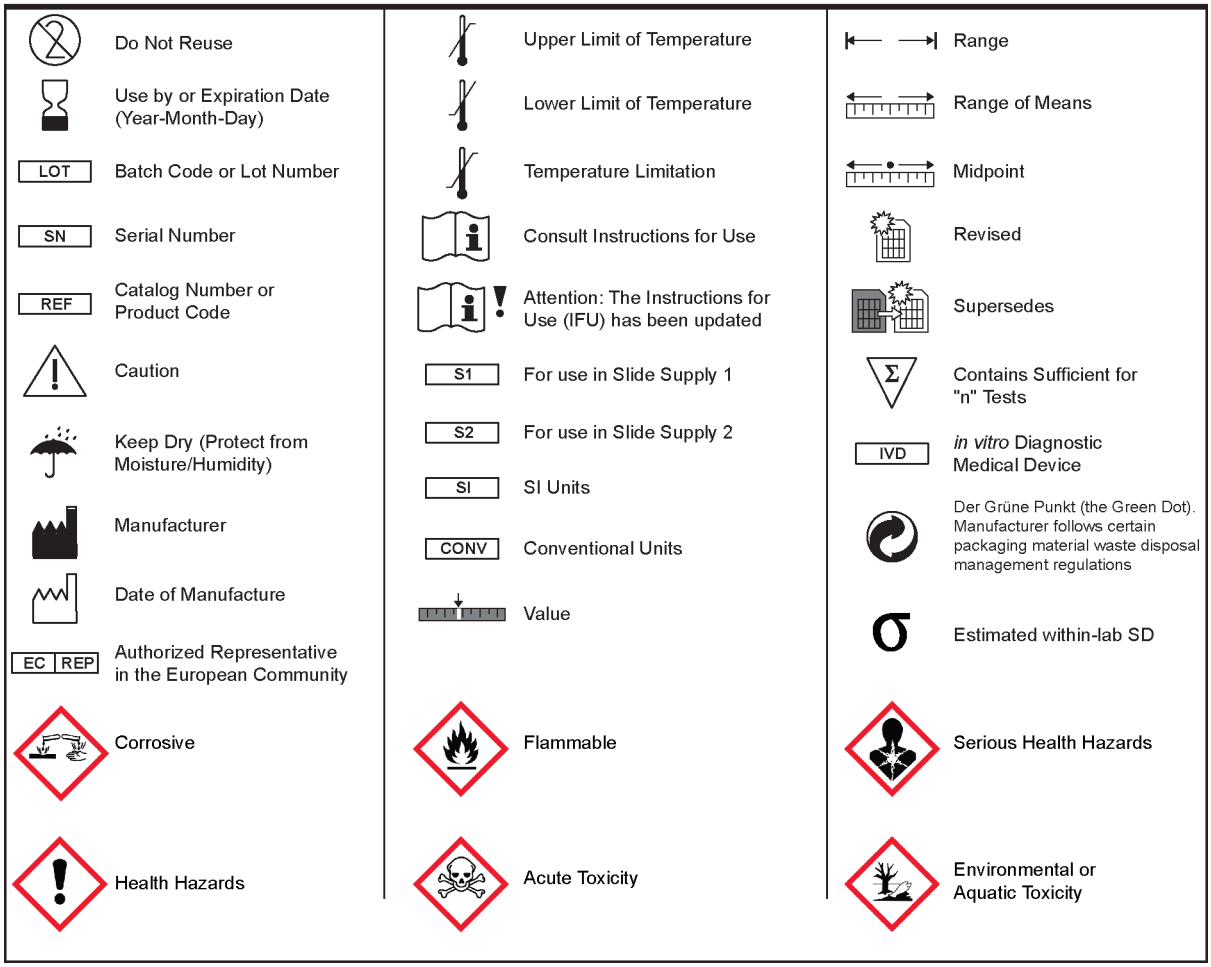
HCV recombinant antigens used in the VITROS Anti-HCV test are prepared under U.S. license by Grifols Diagnostic Solutions Inc. under a shared manufacturing agreement.

References

1. Choo Q-L, Weiner AJ, Overby LR, Kuo G, Houghton M. Hepatitis C virus : the major causitive agent of viral non-A, non-B hepatitis. Br Med Bull 46: 423-41 (1990).
2. van der Poel CL, Cuypers HTM, Reesink HW et al. Confirmation of hepatitis C virus infection by new four antigen recombinant immunoblot assay. Lancet 337: 317-319 (1991).
3. Chien D, Choo Q-L et al. Diagnosis of hepatitis C virus (HCV) infection using an immunodominant chimeric polyprotein to capture circulating antibodies: reevaluation of the role of HCV in liver disease. Proc Natl Acad Sci 89: 10,011-10,015 (1992).
4. Summers M et al. Luminogenic Reagent Using 3-Chloro 4-Hydroxy Acetanilide to Enhance Peroxidase/Luminol Chemiluminescence. *Clin Chem*. 41:S73; 1995.
5. CLSI. *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline - Fourth Edition*. CLSI document M29-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
6. Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.
7. Calam RR. Specimen Processing Separator Gels: An Update. *J Clin Immunoassay*. 11:86–90; 1988.
8. CLSI. *Collection of Diagnostic Venous Blood Specimens. 7th ed.*CLSI standard GP41. Wayne, PA: Clinical and Laboratory Standards Institute; 2017.
9. NCCLS. *Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens; Approved Standard – Fifth Edition*. NCCLS document H4-A5 [ISBN 1-56238-538-0]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2004.
10. CLSI. *Statistical Quality Control for Quantitative Measurements: Principles and Definitions; Approved Guideline - Third Edition*. CLSI document C24-A3 [ISBN 1-56238-613-1]. CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2006.
11. CLSI. *Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition*. CLSI document EP7-A2 (ISBN 1-56238-584-4). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2005.
12. Lee Dong-Soon et al. Significance of Anti-E2 in the Diagnosis of HCV Infection in Patients on Maintenance Hemodialysis. J American Society of Nephrology V7, No.11, 2409-2413 (1996).
13. Levinson SS. The Nature of Heterophilic Antibodies and Their Role in Immunoassay Interference , J Clin Immunoassay 15: 108-115 (1992).
14. Evaluation of Precision Performance of Clinical Chemistry Devices - Second Edition. National Committee for Clinical Laboratory Standards. Order Code EP5-T2; 1992.
15. NCCLS. *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition*. NCCLS document EP5-A2 [ISBN 1-56238-542-9]. CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2004.

Glossary of Symbols

The following symbols may have been used in the labeling of this product.



Revision History

Date of Revision	Version	Description of Technical Changes*
2019-09-06	11.2	• Glossary of Symbols: updated • Added EC Representative address
2019-05-16	11.1	Removed statement “Not Intended for Use in Canada” from the header
2017-09-29	11.0	• Added information for the VITROS XT 7600 Integrated System • Minor formatting and wording updates • References: updated • Glossary of Symbols: updated

* The change bars indicate the position of a technical amendment to the text with respect to the previous version of the document.

When this Instructions For Use is replaced, sign and date below and retain as specified by local regulations or laboratory policies, as appropriate.

Signature

Obsolete Date

Conditions of supply: all supplies are made subject to the standard terms and conditions of Ortho Clinical Diagnostics or its distributors. Copies of these are available on request.

CE
0459

EC REP
Ortho-Clinical Diagnostics
1500 Boulevard Sébastien Brant
B.P. 30335
67411 Illkirch
CEDEX, France

Ortho-Clinical Diagnostics
Felindre Meadows
Pencoed
Bridgend
CF35 5PZ
United Kingdom

Digitally signed by Maftei Tatiana
Date: 2022.10.13 12:27:40 EEST
Reason: MoldSign Signature
Location: Moldova

Ortho Clinical Diagnostics

Co-developed with

GRIFOLS