08836981500V2.0

Elecsys Anti-HCV II

cobas®

REF		Σ	SYSTEM
08836981190	08836981500	100	**cobas e** 411 **cobas e** 601 **cobas e** 602

English

System information

For **cobas e** 411 analyzer: test number 2150
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 503

Intended use

The Elecsys Anti-HCV II assay is an in vitro diagnostic test for the qualitative detection of antibodies to hepatitis C virus (HCV) in human serum and plasma.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

Regulatory approval

This assay has been CE marked according to Directive 98/79/EC. Test performance has been established and certified by a Notified Body according to the Common Technical Specifications (CTS) for diagnostic use and for screening of blood donations and, according to Paul-Ehrlich-Institut (PEI) recommendation,[1] for use of cadaveric blood specimens (specimens collected post-mortem, non-heart-beating).

Summary

The hepatitis C virus (HCV), first identified in 1989, is a member of the Flaviviridae family and has a single-stranded, positive-sense RNA genome encoding 3 structural (Core, Envelope 1 and 2) and 7 non-structural (p7, NS2, NS3, NS4A, NS4B, NS5A, NS5B) proteins.[2,3,4,5] Currently 90 subtypes have been identified, which have been classified into 8 genotypes.[6] Globally, genotype 1 is the most common, accounting for 46 % of all infections, followed by genotype 3 (22 %), and genotypes 2 and 4 (13 % each).[7]

The total global seroprevalence of antibodies against HCV (indicating past exposure to HCV) was estimated to be 1.6 %, corresponding to approximately 115 million past infections.[7] The prevalence of HCV RNA positivity indicating active HCV infection was determined to be 1 %, corresponding to 71.1 million viremic infections.[8] 1.7 million new infections occur annually.[9] Prevalence of HCV infection shows considerable variation across the globe. The most affected regions are Eastern Europe, Northern Africa, and Central Asia, with the highest infection rate found in countries with a past or present history of infections due to the activity of a physician or medical therapy.

Transmission of HCV occurs by percutaneous exposure to blood, blood products, or organs from an infected person. In developed regions where blood donor screening programs have operated for many years the major mode of HCV transmission is through intravenous drug use. In less developed regions, the major routes of transmission are through medical treatment with unsterilized equipment or unscreened blood.[5,8,9]

Infection with HCV can lead to acute and chronic liver inflammation (hepatitis). Approximately 70-85 % of HCV infections progress to chronic disease, although this varies according to patient gender, age, ethnic group and immune status.[2,3,4,5,9] In acute infection, the average incubation period is 6-7 weeks and 70-85 % of patients exhibit no symptoms; in the remainder, non-specific symptoms and jaundice are observed around this time. Symptoms last for several weeks before spontaneous resolution, which occurs in 15-30 % of patients.[2,3,4,5,9,10] Patients who develop chronic HCV infection are much less likely to exhibit symptoms, but can develop long-term complications. If untreated, 20 % of patients develop liver cirrhosis, and a fraction of these progress to hepatocellular carcinoma (HCC). Annually, 400000 patients die globally due to HCV infection.[5,11,12] Advanced, highly efficacious direct-acting antivirals (DAAs) combination therapies cure more than 95 % of treated patients.[12]

HCV infection can be detected by measuring alanine aminotransferase (ALT), HCV-specific immunoglobulins (anti-HCV), HCV RNA and/or viral antigens in patient serum or plasma samples. This can also indicate if the infection is acute or chronic.[5,11,13] International guidelines recommend initial screening by anti-HCV testing. A positive result is recommended to be followed up by measuring HCV RNA or HCV antigen as markers of active infection.[3,14,15,16]

The Elecsys Anti-HCV II assay is a third-generation test.[17,18] The Elecsys Anti-HCV II assay uses peptides and recombinant proteins representing HCV core, NS3 and NS4 antigens for the determination of anti-HCV antibodies.

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 50 µL of sample, 55 µL of a reagent containing biotinylated HCV-specific antigens and 55 µL of a reagent containing HCV-specific antigens labeled with a ruthenium complex[a)] react to form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined automatically by the software by comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by calibration.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The reagent rackpack (M, R1, R2) is labeled as A-HCV II.

M	Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
R1	HCV-specific antigens~biotin (gray cap), 1 bottle, 18 mL: Biotinylated HCV-specific antigens, HEPES[b)] buffer, pH 7.4; preservative.
R2	HCV-specific antigens~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 18 mL: HCV-specific antigens labeled with ruthenium complex ≥ 0.3 mg/L, HEPES buffer, pH 7.4; preservative.

b) HEPES = [4-(2-hydroxyethyl)-piperazine]-ethane sulfonic acid

A-HCV II Cal1	Negative calibrator 1 (white cap), 2 bottles of 1.3 mL each: Human serum, preservative.
A-HCV II Cal2	Positive calibrator 2 (black cap), 2 bottles of 1.3 mL each: Human serum positive for anti-HCV Ab; preservative. Non-reactive for HBsAg, anti-HIV 1/2.

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317	May cause an allergic skin reaction.
H319	Causes serious eye irritation.

Elecsys Anti-HCV II

cobas®

Prevention:

P261	Avoid breathing mist or vapours.
P280	Wear protective gloves/ eye protection/ face protection.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P337 + P313	If eye irritation persists: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

All human material should be considered potentially infectious.

All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV (A-HCV II Cal1 only) and HIV.

The testing methods used assays approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

The serum containing anti-HCV (A-HCV II Cal2) was inactivated using β-propiolactone and UV-radiation.

However, as no inactivation or testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[19,20]

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

The Elecsys Anti-HCV II assay has a high dilution sensitivity. Avoid any sample cross-contamination during sample pre-analytics.

Reagent handling

The reagents in the kit are ready-for-use and are supplied in bottles compatible with the system.

cobas e 411 analyzer: The calibrators should only be left on the analyzer during calibration at 20-25 °C. After use, close the bottles as soon as possible and store upright at 2-8 °C.

Due to possible evaporation effects, not more than 5 calibration procedures per bottle set should be performed.

cobas e 601 and **cobas e** 602 analyzers: Unless the entire volume is necessary for calibration on the analyzers, transfer aliquots of the ready-for-use calibrators into empty snap-cap bottles (CalSet Vials). Attach the supplied labels to these additional bottles. Store the aliquots at 2-8 °C for later use.

Perform **only one** calibration procedure per aliquot.

All information required for correct operation is read in from the respective reagent barcodes.

Please note for **cobas e** 602 analyzers: Both the vial labels, and the additional labels (if available) contain 2 different barcodes. Please turn the vial cap 180° into the correct position so that the barcode between the yellow markers can be read by the system. Place the vial on the analyzer as usual.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the Elecsys reagent kit **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the reagent rackpack	
unopened at 2-8 °C	up to the stated expiration date
after first opening at 2-8 °C	8 weeks

Stability of the reagent rackpack	
on the analyzers	31 days if continuously stored onboard (20-25 °C) or 7 weeks and up to 80 hours in total onboard (20-25 °C) if stored alternately in the refrigerator and on the analyzer

Stability of the calibrators	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	8 weeks
on **cobas e** 411 at 20-25 °C	up to 5 hours
on **cobas e** 601 and **cobas e** 602 at 20-25 °C	use only once

Store calibrators **upright** in order to prevent the calibrator solution from adhering to the snap-cap.

Specimen collection and preparation

Specimen collected from living patients, blood donors, or individual organ, tissue or cell donors may be used, including donor samples obtained while the donor's heart is still beating.
Performance for the use of cadaveric blood specimens (specimens collected post-mortem, non-heart-beating) was established according to Paul-Ehrlich-Institut recommendation[1] with samples obtained within 24 hours after death.[21] Qualitative differences of neat (non-reactive) or spiked (reactive) specimens from cadaveric compared to living donors were not observed.

Criterion: Mean value of cadaveric specimens compared to specimens from living donors within a recovery of 75-125 %.

Only the specimens listed below were tested and found acceptable.

Serum collected using standard sampling tubes or tubes containing separating gel.

Li-heparin, Na-heparin, K_2-EDTA, K_3-EDTA, ACD, CPDA, CPD, CP2D and Na-citrate plasma as well as plasma tubes containing separating gel.
Criterion: Correct assignment of positive and negative samples within a recovery of 80-120 % of serum value for positive samples and within ± 0.2 COI for negative samples.

Stability:
For living patients and donor specimens obtained while the donor's heart is still beating: Stable for 7 days at 20-25 °C, 14 days at 2-8 °C, 3 months at -20 °C (± 5 °C). The samples may be frozen 6 times.
For cadaveric specimens: Stable for 3 days at 20-25 °C, 7 days at 2-8 °C. The samples may be frozen 3 times.

The sample types listed were tested with a selection of sample collection tubes or systems that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube/collection system manufacturer.

Centrifuge samples containing precipitates before performing the assay.

Ensure the samples, calibrators and controls are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples, calibrators and controls on the analyzers should be analyzed/measured within 2 hours.

The performance of the Elecsys Anti-HCV II assay has not been established with body fluids other than serum and plasma.

Materials provided

See "Reagents – working solutions" section for reagents.

- 2 x 6 bottle labels

Materials required (but not provided)

- REF 03290379190, PreciControl Anti-HCV, for 16 x 1.3 mL
- General laboratory equipment
- **cobas e** analyzer

Elecsys Anti-HCV II

cobas®

Additional materials for the **cobas e** 411 analyzer:

- REF 11662988122, ProCell, 6 x 380 mL system buffer
- REF 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution
- REF 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive
- REF 11933159001, Adapter for SysClean
- REF 11706802001, AssayCup, 60 x 60 reaction cups
- REF 11706799001, AssayTip, 30 x 120 pipette tips
- REF 11800507001, Clean-Liner

Additional materials for **cobas e** 601 and **cobas e** 602 analyzers:

- REF 04880340190, ProCell M, 2 x 2 L system buffer
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- REF 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- REF 03004899190, PreClean M, 5 x 600 mL detection cleaning solution
- REF 12102137001, AssayTip/AssayCup, 48 magazines x 84 reaction cups or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M

Additional materials for all analyzers:

- REF 11298500316, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

cobas e 601 and **cobas e** 602 analyzers: PreClean M solution is necessary.

Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Calibrators:

Place the calibrators in the sample zone.

All the information necessary for calibrating the assay is automatically read into the analyzer.

After calibration has been performed, store the calibrators at 2-8 °C or discard (**cobas e** 601 and **cobas e** 602 analyzers).

Calibration

No internationally accepted standard for anti-HCV exists.

Every Elecsys Anti-HCV II reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using the A-HCV II Cal1 and A-HCV II Cal2.

Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Renewed calibration is recommended as follows:

- after 1 month (28 days) when using the same reagent lot
- after 7 days (when using the same reagent kit on the analyzer)
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl Anti-HCV.

In addition, other suitable control material can be used.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local guidelines for quality control.

Note:
For technical reasons re-assigned target values valid only for a specific reagent and control lot combination must be entered manually on all analyzers (except for the **cobas e** 602 analyzer). Therefore always refer to the value sheet included in the reagent kit or PreciControl kit to make sure that the correct target values are used.
When a new reagent or control lot is used, the analyzer will use the original values encoded in the control barcodes.

Calculation

The analyzer automatically calculates the cutoff based on the measurement of A-HCV II Cal1 and A-HCV II Cal2.

The result of a sample is given either as reactive or non-reactive as well as in the form of a cutoff index (COI; signal sample/cutoff).

Interpretation of the results

Numeric result	Result message	Interpretation/ further steps
COI[c] < 0.9	Non-reactive	Negative for anti-HCV, no further testing needed.
COI ≥ 0.9 to < 1.0	Borderline	All initially reactive or borderline samples should be retested in duplicate using the Elecsys Anti-HCV II assay.
COI ≥ 1.0	Reactive	

c) COI = cutoff index

Retest result	Final result/ interpretation	Further steps
One or both of the duplicate retests have a COI ≥ 0.9.	Repeatedly reactive	Confirmation via supplemental methods (e.g. immunoblot or detection of HCV RNA). If one or both measurements remain borderline the analysis of a follow-up sample is recommended.
Both of the duplicate retests have a COI < 0.9.	Negative for anti-HCV	No further testing needed.

Limitations - interference

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 1129 µmol/L or ≤ 66 mg/dL
Hemoglobin	≤ 0.621 mmol/L or ≤ 1000 mg/dL
Intralipid	≤ 2000 mg/dL

Elecsys Anti-HCV II

cobas®

Compound	Concentration tested
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Rheumatoid factors	≤ 1200 IU/mL

Criterion: Recovery of positive samples within ± 20 % of initial value, cutoff-index for negative samples ± 0.2 of initial value.

Pharmaceutical substances
In vitro tests were performed on 18 commonly used pharmaceuticals and 3 drugs used in HCV therapy. No interference with the assay was found.

In rare cases, interference due to extremely high titers of antibodies to streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

Studies have been performed to assess the high-dose hook effect. Out of 765 positive samples no false negative result was found. Occurrence of high-dose hook effect cannot be completely excluded.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Due to a long time period from infection to seroconversion, negative anti-HCV test results may occur during early infection. If acute hepatitis C infection is suspected, measuring of HCV RNA by reverse transcriptase polymerase chain reaction (RT-PCR e.g. by the **cobas** HCV Test for use on the **cobas** 6800/8800 Systems) may give evidence of HCV infection.

The detection of anti-HCV antibodies indicates a present or past infection with HCV, but does not differentiate between acute, chronic or resolved infection. It is recognized within the scientific community that presently available methods for anti-HCV detection are not sensitive enough to detect all potentially infectious units of blood or possible cases of HCV infection. The antibody concentration may be beneath the detection limit of this assay or the patient´s antibodies do not react with the antigens used in this test. In addition, non-specific results cannot be ruled out with the Elecsys Anti-HCV II assay.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). The following results were obtained:

cobas e 411 analyzer					
		Repeatability[d]		**Intermediate precision**[e]	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS[f], negative	0.060	0.002	3.1	0.002	4.0
HS, negative	0.662	0.024	3.7	0.034	5.2
HS, negative	0.933	0.022	2.4	0.045	4.8
HS, weakly positive	1.13	0.042	3.7	0.057	5.1
HS, positive	6.68	0.263	3.9	0.435	6.5
PC[g] Anti-HCV1	0.074	0.007	10.0	0.008	10.8
PC Anti-HCV2	3.03	0.102	3.4	0.164	5.4

d) Repeatability = within-run precision

e) Intermediate precision = within-laboratory precision

f) HS = Human serum

g) PC = PreciControl

cobas e 601 and **cobas e** 602 analyzers					
		Repeatability		**Intermediate precision**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS, negative	0.032	0.0004	1.4	0.0006	2.0
HS, negative	0.804	0.011	1.4	0.025	3.1
HS, weakly positive	1.09	0.017	1.6	0.022	2.0
HS, weakly positive	1.26	0.017	1.4	0.025	2.0
HS, positive	7.35	0.061	0.8	0.234	3.2
PC[g] Anti-HCV1	0.042	0.0005	1.1	0.0009	2.1
PC Anti-HCV2	3.26	0.091	2.8	0.250	7.7

Analytical specificity

1037 samples containing potentially interfering substances or derived from high-risk groups were tested with the Elecsys Anti-HCV II assay comprising specimens:

- containing antibodies against HBV, HAV, HEV, EBV, CMV, HSV, HIV, VZV, Parvovirus, Mumps, Dengue, tick-borne encephalitis virus (TBEV), Rubella, Toxoplasma gondii, Treponema pallidum
- containing autoantibodies and elevated titers of rheumatoid factor, IgG, IgM or IgA antibodies
- positive for HBsAg and E. coli
- after vaccination against HBV and Influenza
- non-viral liver diseases
- alcoholic liver disease
- high-risk groups: hemophiliacs, homosexuals and intravenous drug abusers

	N	Elecsys Anti-HCV II reactive	Positive or indeterminate by immunoblot	Negative by immunoblot
Specimens containing potentially interfering substances	1037	59	58 positive	1[h]

h) EBV IgM positive patients: 1 out of 69 samples

Clinical sensitivity

Of 765 samples from HCV infected patients with different stages of disease and infected with different HCV genotypes (type 1, 2, 3, 4, 5 and 6), all samples were found to be reactive with the Elecsys Anti-HCV II assay.

Group	N	Reactive
HCV infected persons with different stages of disease	224	224
HCV genotypes (type 1, 2, 3, 4, 5, 6)	541	541

In the above study the diagnostic sensitivity was 100 %. The 95 % lower confidence limit was 99.61 %.

Seroconversion sensitivity

Seroconversion sensitivity of the Elecsys Anti-HCV II assay has been shown by testing 60 commercial seroconversion panels. The Elecsys Anti-HCV II assay detected more positive bleedings than all other registered anti-HCV assays tested and was more sensitive in the recognition of early HCV infection than the Elecsys Anti-HCV assay and the other registered anti-HCV screening assays.

Clinical specificity

In a group of randomly selected European blood donors the specificity of the Elecsys Anti-HCV II assay was 99.85 % (RR[i]). The 95 % confidence interval (2-sided) was 99.73-99.93 %.

Elecsys Anti-HCV II

cobas®

The diagnostic specificity of the Elecsys Anti-HCV II assay in a group of hospitalized patients was 99.66 %. The 95 % confidence interval (2-sided) was 99.41-99.82 %.

	N	Elecsys Anti-HCV II IR[i] COI ≥ 1	Elecsys Anti-HCV II RR COI ≥ 1	Positive or indeterminate by immunoblot and/or HCV RNA
European blood donors	6850	15	15	2 confirmed positive, 3 indeterminate
Hospitalized patients	3922	153[j]	152[k]	128 confirmed positive, 8 indeterminate
Dialysis patients	731	19	18	12 confirmed positive
Pregnant women	629	3	3	2 confirmed positive

i) IR = Initially Reactive

j) 4 (positive) samples had to be excluded from calculation due to "qns" for immunoblot analysis; qns = quantity not sufficient

k) 4 (positive) samples had to be excluded from calculation due to "qns" for immunoblot analysis

l) RR = Repeatedly Reactive

References

1 Proposal for the Validation of Anti-HIV-1/2 or HIV Ag/Ab Combination Assays, anti-HCV-Assays, HBsAg and Anti-HBc assays for Use with Cadaveric Samples; PEI 08/05/2014.

2 Knipe D and Howley P (2013). Fields Virology, Wolters Kluwe.

3 Manns MP, Buti M, Gane E, et al. Hepatitis C virus infection. Nat Rev Dis Prim 2017;3:17006.

4 Ahmad J. Hepatitis C. BMJ 358:j2861.

5 Mauss S, Berg T, Rockstroh J, et al. (2018). Hepatology. A Clinical Textbook. Ninth Edition. Available at: https://www.hepatologytextbook.com Last accessed: Jan 2020.

6 Smith D, Bukh J, Kuiken C, et al. (2019). A web resource to manage the classification and genotype and subtype assignments of hepatitis C virus. https://talk.ictvonline.org/ictv_wikis/flaviviridae/w/sg_flavi/56/hcv-classification

7 Gower E, Estes C, Blach S, et al. Gobal epidemiology and genotype distribution of the hepatitis C virus infection. Hepatology 2014;61:S45-S57.

8 Razzawi H. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol 2017;2:161-176

9 World Health Organization (2020). Hepatitis C factsheet. Available from: http://www.who.int/mediacentre/factsheets/fs164/en/ Last accessed Feb 2021.

10 Kamal SM. Acute Hepatitis C: A Systematic Review. Am J Gastroenterol 2008;103:1283-1297.

11 Hoofnagle J H. Course and outcome of hepatitis C. Hepatology 2002;36:S21-29.

12 Pietschmann T and Brown RJP. Hepatitis C Virus. Trends in Microbiology 2020;27(4):379-380.

13 Dufour DR. Diagnosis and Monitoring of Hepatic Injury. II. Recommendations for Use of Laboratory Tests in Screening, Diagnosis, and Monitoring. Clin Chem 2000;46:2050-2068.

14 European Association for the Study of the Liver (2020). EASL recommendations on treatment of hepatitis C: Final update of the series. J Hepatol. https://doi.org/10.1016/j.jhep.2020.08.018.

15 Centers for Disease Control and Prevention. Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians. MMWR 2013;62(18):362-365.

16 AASLD-IDSA. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. Available: http://hcvguidelines.org

17 Couroucé A-M. Development of Screening and Confirmation Tests for Antibodies to Hepatitis C Virus. In: Reesink HW (ed.): Hepatitis C Virus. Curr Stud Hematol Blood Transf 1998;62:64-75.

18 Vernelen K, Claeys H, Verhaert H, et al. Significance of NS3 and NS5 antigens in screening for HCV antibody. The Lancet 1994;343(8901):853.

19 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

20 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.

21 Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells.

For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets and the Method Sheets of all necessary components (if available in your country).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume for reconstitution
GTIN	Global Trade Item Number

COBAS, COBAS E, ELECSYS and PRECICONTROL are trademarks of Roche. INTRALIPID is a trademark of Fresenius Kabi AB.

All other product names and trademarks are the property of their respective owners.

Additions, deletions or changes are indicated by a change bar in the margin.

© 2022, Roche Diagnostics

CE 0123

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

Roche