Elecsys HCV Duo

cobas®

REF		Σ	SYSTEM
08110697190	08110697500	300	**cobas e** 402 **cobas e** 801

English

System information

Short name	ACN[a)]	Assay type	To be used for
HCVDUO	12028	**cobas e** flow	HCV Duo
HCVDUOR	12021	**cobas e** flow	HCV Duo duplicate repeat
HCVAG	11170	HCV Antigen (HCV Ag) embedded application	HCV Duo **cobas e** flow
AHCV	11171	Anti-HCV embedded application	HCV Duo **cobas e** flow

a) ACN = application code number

Intended use

Elecsys HCV Duo is an immunoassay for the in vitro qualitative detection of hepatitis C virus (HCV) core antigen (HCV Ag) and antibodies to HCV (anti-HCV) in human serum and plasma. The test, in conjunction with other laboratory results and clinical information, may be used to aid in the diagnosis of and the screening for HCV infection. The test can also be used as a screening test to prevent transmission of HCV to recipients of blood, blood components, cells, tissue, and organs. The subresults (HCV Ag and anti-HCV) are intended as an aid in the selection of the confirmatory testing algorithm for reactive samples.

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

Summary

The Elecsys HCV Duo assay is intended to be used by laboratory professionals as a tool in the diagnosis and screening of HCV infection. The HCV Ag and anti-HCV test module subresults of the assay can help to determine the presence or absence of an HCV infection, as well as the phase of the infection. This information can then be used to select an appropriate confirmatory testing algorithm. Additionally, the test is intended to be used as a first-line assay for screening of individual human donors of blood, blood components, cells, tissue, and organs, when donor samples are obtained while the donor's heart is still beating and of cadaveric blood specimens (specimens collected post-mortem, non-heart-beating). The use of cadaveric blood specimens has been established according to Paul-Ehrlich-Institut (PEI) recommendations.[1]

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 93 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]

HCV infection represents a major global health burden. Approximately 170-200 million people worldwide have been infected with HCV and an estimated 58 million live with chronic hepatitis C, with about 1.5 million new infections occurring per year. In 2019, approximately 290000 people died from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma.[8,9] Due to the often asymptomatic nature of the disease, hepatitis C infection remains heavily underdiagnosed.[10]

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.[5,9]

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, ethnicity and immune status.[2,3,4,5,8] 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.[2,3,4,5,8,11] 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). Advanced, highly efficacious pan-genotypic therapies based on combinations of direct acting antivirals (DAAs) 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.[5,13,14] 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.[3,15,16,17]

The Elecsys HCV Duo assay comprises 2 test modules (HCV Ag and anti-HCV) which use peptides and recombinant antigens representing the Core, NS3 and NS4 proteins for the detection of anti-HCV antibodies, and monoclonal antibodies for the detection of the HCV Core antigen, respectively. With the Elecsys HCV Duo assay, HCV Core antigen as well as antibodies to HCV can be detected simultaneously from a single specimen in 2 separate, but parallel reactions. The Elecsys HCV Duo main test result is automatically calculated by the analyzer, while the individual anti-HCV and HCV Ag results are also accessible.

Test principle

Sandwich principle. Total duration of assay: 27 minutes.

HCVAG:

- Pretreatment: 30 µL of sample are pretreated with 15 µL of pretreatment solution to release the HCV core antigen.
- 1st incubation: The pretreated sample from above reacts with biotinylated monoclonal anti-core antibodies and ruthenylated[b)] monoclonal anti-core antibodies, to form a sandwich complex.

AHCV:

- 1st incubation: 12 µL of sample reacts with biotinylated HCV-specific antigens and ruthenylated[b)] HCV-specific antigens, to form a sandwich complex.

HCVAG / AHCV:

- 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 II 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 sample with the cutoff value previously obtained by HCV-Antigen embedded (HCVAG) and anti-HCV embedded (AHCV) calibration. The incubations for HCVAG and AHCV are performed in parallel in separate vessels.

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

Reagents - working solutions

The **cobas e** pack 1 is labeled as PT.

The **cobas e** pack 2 (M, R1, R2) is labeled as HCVAG.

The **cobas e** pack 3 (M, R1, R2) is labeled as AHCV.

PT

PT Pretreatment reagent, 1 bottle, 9.1 mL:
Potassium hydroxide, pH 13.

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HCVAG

M Streptavidin-coated microparticles, 1 bottle, 16.0 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-HCV-Ab~biotin, 1 bottle, 11.1 mL:
Biotinylated anti-HCV core antibodies; TRIS buffer, pH 7.0; preservative.

R2 Anti-HCV-Ab~Ru(bpy)$_3^{2+}$, 1 bottle, 12.0 mL:
Anti-HCV core antibodies labeled with ruthenium complex; TRIS buffer, pH 7.0; preservative.

AHCV

M Streptavidin-coated microparticles, 1 bottle, 14.1 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 HCV-specific antigens~biotin, 1 bottle, 21.9 mL:
Biotinylated HCV-specific antigens; HEPES[c)] buffer, pH 7.4; preservative.

R2 HCV-specific antigens~Ru(bpy)$_3^{2+}$, 1 bottle, 18.8 mL:
HCV-specific antigens labeled with ruthenium complex; HEPES buffer, pH 7.4; preservative.

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

HCVDUO Cal1 Negative calibrator 1, 1 bottle of 1.0 mL:
Human serum, negative for HCV antigen; preservative.

HCVDUO Cal2 Positive calibrator 2, 1 bottle of 1.0 mL:
HEPES buffer, positive for HCV antigen; preservative.

HCVDUO Cal3 Negative calibrator 1, 1 bottle of 1.0 mL:
Human serum, negative for anti-HCV antibodies; preservative.

HCVDUO Cal4 Positive calibrator 2, 1 bottle of 1.0 mL:
Human serum, positive for anti-HCV antibodies (inactivated); preservative. Non-reactive for HBsAg, anti-HIV 1/2.

Precautions and warnings

For in vitro diagnostic use for laboratory professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

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:

Danger

H314 Causes severe skin burns and eye damage.

H317 May cause an allergic skin reaction.

Prevention:

P261 Avoid breathing mist or vapours.

P280 Wear protective gloves/ protective clothing/ eye protection/ face protection/ hearing protection.

Response:

P301 + P330 + P331 IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.

P303 + P361 + P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water.

P304 + P340 + P310 IF INHALED: Remove person to fresh air and keep comfortable for breathing.
Immediately call a POISON CENTER/ doctor.

P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor.

Hazardous components:

- 2-methyl-2H-isothiazol-3-one hydrochloride
- cetrimonium chloride
- potassium hydroxide

Product safety labeling follows EU GHS guidance.

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

All human material should be considered potentially infectious.

The negative calibrators (HCVDUO Cal1 and HCVDUO Cal3) have been prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV.

The testing methods use assays that have been approved or cleared by the FDA or that are in compliance with the legal rules of the European Union (IVDR 2017/746/EU, IVDD 98/79/EC, Annex II, List A).

The serum containing anti-HCV (HCVDUO Cal4) 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.[18,19]

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

The anti-HCV module of the Elecsys HCV Duo assay has a high dilution sensitivity. Avoid any sample cross-contamination during sample pre-analytics.

Reagent handling

The pouch of **cobas e** pack 3 (AHCV) should remain sealed until immediately prior to use.

The reagents (M, R1, R2, PT) in the kit are ready-for-use and are supplied in **cobas e** packs.

Calibrators:

The calibrators are supplied ready-for-use in bottles compatible with the system.

Unless the entire volume is necessary for calibration on the analyzer, 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.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the **cobas e** pack **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the **cobas e** pack:	
unopened at 2-8 °C	up to the stated expiration date
on the analyzers	31 days

Stability of the calibrators:	
unopened at 2-8 °C	up to the stated expiration date

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Stability of the calibrators:	
after opening at 2-8 °C	4 weeks
on the analyzers 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.[20] 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, CPD, CP2D, CPDA and Na-citrate plasma.

Plasma tubes containing separating gel can be used.

Criteria are listed in the following table.

Analyte range of serum reference*	Recovery of analyte relative to respective reference
COI[d] < 0.7**	COI ± 0.3
COI 0.7-1.5***	80-130 %
COI > 1.5-2.0***	70-130 %
COI > 2.0***	60-140 %

d) COI = cutoff index

* for separating gel tubes the respective tube without separating gel served as reference

** free of analyte

*** containing analyte

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 5 times.
For cadaveric specimens: Stable for 1 day at 20-25 °C, 7 days at 2-8 °C. The samples may be frozen 3 times.

Sampling devices containing liquid anticoagulants have a dilution effect resulting in lower COI values for individual patient specimens. In order to minimize dilution effects it is essential that respective sampling devices are filled completely according to manufacturer's instructions.

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.

Specimens should not be subsequently altered with additives (e.g. biocides, anti-oxidants or substances that could possibly change the pH or ionic strength of the sample) in order to avoid erroneous findings.

Centrifuge samples containing precipitates and thawed samples before performing the assay.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

Do not use post-mortem samples collected later than 24 hours after last heart beat.

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

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

The performance of the Elecsys HCV Duo 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 08335923190, PreciControl HCV Duo, 10 x 1.0 mL, 5 x 2.0 mL
- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles
- General laboratory equipment
- **cobas e** analyzer

Additional materials for **cobas e** 402 and **cobas e** 801 analyzers:

- REF 06908799190, ProCell II M, 2 x 2 L system solution
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 07485409001, Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
- REF 06908853190, PreClean II M, 2 x 2 L wash solution
- REF 05694302001, Assay Tip/Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
- REF 07485425001, Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning Detection Unit
- REF 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
- 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.

Place the cooled (stored at 2-8 °C) **cobas e** pack on the reagent manager. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the **cobas e** pack.

Calibrators:

Place the calibrators in the sample zone.

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

Calibration

Traceability:

HCVAG:
This method has been standardized against the WHO International Standard for Hepatitis C virus (HCV) core antigen, PEI code 129096/12.

AHCV:
No internationally accepted standard for anti-HCV exists.

Calibration frequency: Calibration must be performed once per reagent lot using HCVDUO Cal1, HCVDUO Cal2, HCVDUO Cal3, HCVDUO Cal4 and fresh reagent (i.e. not more than 24 hours since the **cobas e** pack 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 12 weeks when using the same reagent lot
- After 28 days when using the same **cobas e** pack on the analyzer
- As required: e.g. quality control findings outside the defined limits

Quality control

Use Elecsys PreciControl HCV Duo or other suitable controls for routine quality control procedures.

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Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per **cobas e** pack, 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.

Calculation

The analyzer automatically calculates the cutoffs based on the measurement of HCVDUO Cal1 and HCVDUO Cal2, HCVDUO Cal3 and HCVDUO Cal4.
The result of a sample is given both as positive or negative and in the form of a cutoff index (signal sample/cutoff).

Interpretation of the results

HCVDUO (initial result)

Numeric result	Initial result	Interpretation/ further steps
COI < 1.0	Antigen test negative, antibody test negative	Non-reactive in the Elecsys HCV Duo assay: non-reactive for HCV core antigen and anti-HCV antibodies. No further testing needed.
COI ≥ 1.0	Antigen test positive, antibody test positive or antigen test positive, antibody test negative or antigen test negative, antibody test positive	Reactive in the Elecsys HCV Duo assay. Redetermine initially reactive samples in duplicate with the Elecsys HCV Duo assay.*

* Optional, or if required by specific local testing guidelines; redetermination of samples with an initial COI ≥ 1.0 can be performed automatically (see section **cobas e** flows).

HCVDUO R (result after duplicate repeat)

Retest result	Final result	Interpretation/ further steps
One or both of the duplicate repeats have a COI ≥ 1.0.	Antigen test positive, antibody test positive or antigen test positive, antibody test negative or antigen test negative, antibody test positive	Repeatedly reactive samples must be confirmed according to recommended confirmatory algorithms. Confirmatory tests include immunoblot and HCV RNA tests. For the right choice of method the HCVAG and AHCV module-specific subresults can be used.
Both of the duplicate retests have a COI < 1.0.	Antigen test negative, antibody test negative	Non-reactive for HCV Ag and non-reactive for anti-HCV antibodies. No further testing needed.

Subresult HCVAG

Numeric result	Interpretation
COI < 1.0	Non-reactive for HCV core antigen.
COI ≥ 1.0	Reactive for HCV core antigen.

Subresult AHCV

Numeric result	Interpretation
COI < 1.0	Non-reactive for antibodies to HCV.
COI ≥ 1.0	Reactive for antibodies to HCV.

cobas e flows
cobas e flows are procedures programmed into the system to enable a fully automated sequence of measurements and the calculation of assay combinations to perform decision algorithms.
The HCVDUO **cobas e** flow is required to enable simultaneous separate measurement of HCVAG and AHCV with subsequent determination of the main result.
The HCVDUO R **cobas e** flow is available to perform automated repetition of measurements in duplicate for samples with an initial COI ≥ 1.0. Subresults and the overall result message will be reported.

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	≤ 616 µmol/L or ≤ 36 mg/dL
Hemoglobin	≤ 0.341 mmol/L or ≤ 550 mg/dL
Intralipid	≤ 2000 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Rheumatoid factors	≤ 1200 IU/mL
Albumin	≤ 7 g/dL; reference range (adults) 3.5-5.2 g/dL
IgG	≤ 5.6 g/dL; reference range (adults) 0.7-1.6 g/dL
IgA	≤ 1.2 g/dL; reference range (adults) 0.07-0.4 g/dL
IgM	≤ 0.4 g/dL; reference range (adults) 0.04-0.23 g/dL

No false negative result due to high-dose hook effect was found with the Elecsys HCV Duo assay.
Occurrence of high-dose hook effect cannot be excluded.

Pharmaceutical substances
In vitro tests were performed on 12 commonly used pharmaceuticals. No interference with the assay was found.

For further 5 commonly used drugs no interferences were found up to the following concentration.

Compound	Concentration tested mg/L
Acetylcystein	≤ 150
Itraconazol	≤ 20
Phenylbutazon	≤ 133
Doxycyclin	≤ 17
Acetylsalicyl acid	≤ 330

In addition, the following special drugs used in hepatitis B, hepatitis C and HIV therapy were tested. No interference with the assay was found.

Compound	Concentration tested mg/L
PEGylated Interferon-alpha-2a	≤ 0.18
Dolutegravir	≤ 30
Abacavir	≤ 600
Elvitegravir	≤ 150
Raltegravir	≤ 800
Fumarate/Emitricitabine	≤ 240
Entecavir	≤ 0.33

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Compound	Concentration tested mg/L
Tenofovir	≤ 300
Lamivudine	≤ 300

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.

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

In addition, non-specific results cannot be ruled out with the Elecsys HCV Duo assay.
A negative test result does not completely rule out the possibility of an infection with HCV. Serum or plasma samples from the very early (pre-seroconversion) phase of HCV infection can occasionally yield negative findings. Yet unknown HCV variants can also lead to a negative HCV finding.

Due to the possible interactions between the Elecsys HCV Duo assay and the Elecsys Anti-HCV II assay, both assays should not be run simultaneously on the same **cobas e** 402 or **cobas e** 801 analytical unit.

Limits and ranges

Antigen detection (HCVAG/HCVDUO)
≤ 50 IU/mL
Antigen sensitivity was determined based on serial dilutions of the WHO International Standard for Hepatitis C virus (HCV) core antigen, PEI code 129096/12 in human HCV negative serum.

Antibody detection (AHCV/HCVDUO)
No internationally accepted standard for HCV-specific antibody detection exists.

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:

HCVAG

cobas e 402 and **cobas e** 801 analyzers					
		Repeatability[e]		**Intermediate precision**[f]	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS 1[g]	0.536	0.0453	8.4	0.0457	8.5
HS 2	0.926	0.0387	4.2	0.0542	5.9
HS 3	0.871	0.0422	4.8	0.0514	5.9
HS 4	1.23	0.0319	2.6	0.0556	4.5
HS 5	1.44	0.0535	3.7	0.0694	4.8
HS 6	3.83	0.0783	2.0	0.152	4.0
PC[h] HCVDUO 1	0.569	0.0390	6.8	0.0476	8.4
PC HCVDUO 2	4.23	0.0796	1.9	0.129	3.0

e) Repeatability = within-run precision

f) Intermediate precision = within-laboratory precision

g) HS = Human sample (serum/plasma)

h) PC = PreciControl

AHCV

cobas e 402 and **cobas e** 801 analyzers					
		Repeatability		**Intermediate precision**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS 1	0.0290	0.00148	5.1	0.00159	5.5
HS 2	0.821	0.00842	1.0	0.0144	1.7
HS 3	0.902	0.0133	1.5	0.0318	3.5
HS 4	1.22	0.0245	2.0	0.0414	3.4
HS 5	1.34	0.0564	4.2	0.0580	4.3
HS 6	1.66	0.0241	1.5	0.0557	3.3
PC HCVDUO 1	0.0337	0.000477	1.4	0.000623	1.8
PC HCVDUO 3	3.89	0.0779	2.0	0.130	3.3

Analytical specificity

204 samples containing potentially interfering substances or derived from high-risk groups were tested with the Elecsys HCV Duo assay.

Potentially interfering substances / disease states	N	Reactive	Positive or indeterminate by immunoblot	Negative by immunoblot
Antibodies against HIV, HAV, HBV, HEV, CMV, HSV, EBV, Toxoplasma gondii, Treponema pallidum	204	11	10	1[i]
Autoantibodies				
HBsAg and E. coli				
Vaccination for HBV and Influenza				
Non-viral liver disease				
Alcoholic liver disease				
Multipara Pregnancy and RF				

i) One sample of 10 samples from the cohort of chronic HBV infection. Also negative in a second commercially available anti-HCV assay. Testing of additional 22 samples of chronic HBV infection did not show any further (false) positive result

Seroconversion sensitivity

Seroconversion sensitivity of the Elecsys HCV Duo assay was shown by testing a total of 85 commercial seroconversion panels in comparison to other registered HCV Ag/anti-HCV combination assays, anti-HCV assays, HCV Ag assays, and HCV RNA tests.

The Elecsys HCV Duo assay detected an additional 136 panel members compared with the Elecsys Anti-HCV II assay (40 panels, 8 panels were undetected by the comparator assay), and an additional 107 and 65 panel members, respectively, compared with 2 comparator HCV Ag/anti-HCV combination assays (58 and 19 panels, respectively; in each case 11 panels were undetected by the comparator assay). On average, the time for the Elecsys HCV Duo assay to turn positive was 17.9 days before the Elecsys Anti-HCV II assay, and 8.6 or 2.2 days, respectively, before the comparator HCV Ag/anti-HCV combination assays.

In another subset of 48 seroconversion panels the Elecsys HCV Duo assay was compared to a registered HCV RNA test. These panels had subsequent samples where the HCV RNA test turned from negative to positive. As a reference, the first HCV RNA negative sample of a panel was taken as day zero. The number of days between day zero and the first positive sample of a panel was calculated for the Elecsys HCV Duo assay. On average, the time for the Elecsys HCV Duo assay to turn positive was calculated as 1.8 days after HCV RNA.

Clinical sensitivity

257 samples from a reference center with a characterized antibody and RNA status were analyzed. All samples except 1 antibody-negative/RNA-positive specimen were found reactive with the Elecsys HCV Duo assay. The non-reactive sample corresponded to an early phase of infection with a low viral load measured by PCR. The comparator, a registered HCV

Ag/anti-HCV combination assay, detected 11 samples in the antibody-negative/RNA-positive and 88 in the antibody-positive/RNA-negative cohort.

Anti-HCV status	HCV RNA status	N	Elecsys HCV Duo Reactive
Positive	Positive	148	148
Negative	Positive	19	18
Positive	Negative	90	90

Further 486 samples from HCV infected patients with different stages of HCV infection and infected with HCV genotypes 1, 2, 3, 4, 5 and 6 were tested. All 486 samples were found to be reactive with the Elecsys HCV Duo assay.

Group	N	Reactive
HCV infected persons with different stages of disease	386	386
HCV genotypes 1-6	100	100

In the above study the diagnostic sensitivity was 100 %. The 95 % lower confidence limit was 99.2 %.

Clinical specificity

In a group of randomly selected blood donors (n = 20634) from Europe and South Africa the specificity of the Elecsys HCV Duo assay was 99.94 %.

The specificity in the European cohort (n = 15591) was 99.96 %. In the South African cohort (n = 5043) the specificity was 99.88 %.

All 13 false reactive results in the overall blood donor cohort occurred in the HCVAG module of the Elecsys HCV Duo assay. No false reactive result was observed in this cohort in the AHCV module.

In a group of 2531 samples from unselected daily routine, dialysis patients, and pregnant women the specificity of the Elecsys HCV Duo assay was 99.92 %. The 95 % confidence interval (2-sided) was 99.71-99.99 %.

	N	Elecsys HCV Duo RR[j] COI ≥ 1	Positive or indeterminate by immunoblot and/or HCV RNA	Specificity (95 % CI[k]) %
Blood donors overall	20634	16	3	99.94 (99.89-99.97)
European blood donors	15591	9	2	99.96 (99.91-99.98)
South African blood donors	5043	7	1	99.88 (99.74-99.96)
Samples from unselected daily routine	1251	32	31	99.92 (99.54-100.00)
Dialysis patients	223	2	1	99.55 (97.52-99.99)
Pregnant women	1057	2	2	100.00 (99.65-100.00)

j) repeatedly reactive

k) confidence interval

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For further information, please refer to the appropriate user guide or 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.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

Symbols

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

CONTENT Contents of kit

Elecsys HCV Duo

cobas®

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

Rx only — For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

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