Order information

Product	Material configuration	Material Number
Elecsys® HCV Duo*	300 tests	08 110 697 190
PreciControl HCV Duo	10 × 1.0 mL, 5 × 2.0 mL	08 335 923 190

* for use on the **cobas®** e 402 and **cobas®** e 801 analytical units

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21 Internal data on file. Roche Diagnostics GmbH, Penzberg, Germany.

Published by
Roche Diagnostics International Ltd
CH-6343 Rotkreuz
Switzerland

diagnostics.roche.com

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Elecsys® HCV Duo

Immunoassay for the qualitative dual detection of HCV core antigen and antibodies to HCV

Summary

Hepatitis C is an inflammatory liver disease caused by infection with the hepatitis C virus (HCV), which can cause both acute and chronic hepatitis.[1] HCV is a member of the Flaviviridae family and has a single-stranded, positive-sense RNA genome, which encodes 3 structural and 7 non-structural proteins.[2,3] HCV is classified into 8 genotypes with a total of currently 90 subtypes.[4]

Hepatitis C represents a major global health burden: the total global prevalence of antibodies against HCV, indicating past exposure to HCV, was estimated to be 1.6 %, corresponding to approx. 115 million people with a past infection.[5] The prevalence of HCV RNA positivity indicating active HCV infection or viremia was determined to be 0.75 %, corresponding to 58 million people. In 2019, 1.5 million new infections occurred and 290,000 people died of HCV.[1,6]

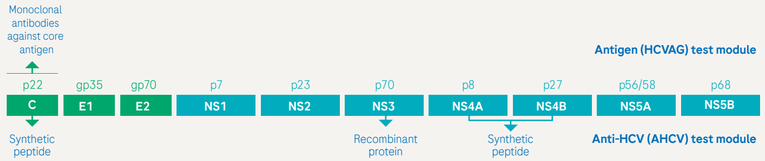
Most acute HCV infections (70 – 85 %) are asymptomatic and approximately 15 – 45 % of patients will clear acute infection. In case of symptomatic acute hepatitis C, symptoms usually appear within 7 – 8 weeks after exposure and consist of jaundice, malaise, and nausea (similar to hepatitis A and B).[2,7-9] Chronic HCV infection is characterized by persistence of HCV RNA in the blood for longer than 6 months. Most chronic infections will lead to hepatitis and to some degree of fibrosis, which may be accompanied by relatively nonspecific symptoms such as fatigue. 20 % of people with chronic hepatitis C will eventually develop cirrhosis.[2,7-9] Once cirrhosis is established, the risk of developing hepatocellular carcinoma (HCC) is 1 – 4 % per year.[10] Highly efficacious direct-acting antiviral (DAA) combination therapies are now available which can cure more than 95 % of treated patients.[11]

Infection with HCV and the state of infection (acute or chronic) can be diagnosed by measuring HCV-specific antibodies (anti-HCV), and HCV RNA or viral antigens in patient serum or plasma samples. Measurement of the alanine aminotransferase (ALT) level is an associated indicator of liver inflammation or damage due to infection.[2,7,12] International guidelines recommend initial screening by anti-HCV testing. A positive anti-HCV result is recommended to be followed up by measuring HCV RNA or HCV antigen (HCV Ag) as markers of active infection.[8,13-15]

Anti-HCV antibodies are detected on average 6 – 12 weeks after infection, while HCV RNA and core antigen appear much earlier already in the incubation and acute phases of infection (2 - 14 days and 10 - 30 days after infection, respectively). Detection of HCV core antigen, as a surrogate marker of HCV RNA, is thus a means to shorten the diagnostic window period and confirm active infection.[2,9,13,15-18]

The Elecsys® HCV Duo assay comprises two test modules, one for the detection of HCV Ag (HCVAG) and one for the detection of anti-HCV (AHCV). HCVAG uses monoclonal antibodies for the detection of the HCV core antigen. AHCV uses synthetic peptides and a recombinant protein representing the core, NS3 and NS4 antigens for the detection of anti-HCV antibodies. With the Elecsys® HCV Duo assay, HCV core antigen as well as antibodies to HCV can be detected simultaneously from a single specimen in two separate, but parallel reactions. The Elecsys® HCV Duo main test result is automatically calculated by the analyzer, while the individual HCV Ag and anti-HCV results are also accessible.[19]

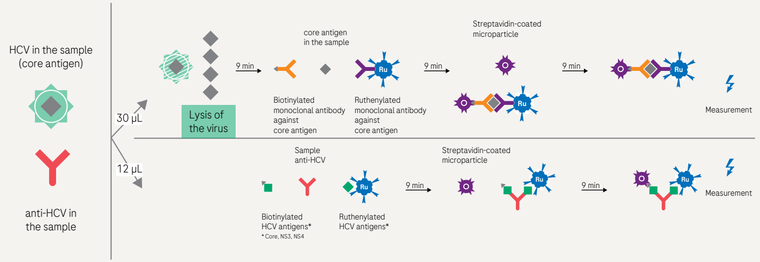
Targets used by the Elecsys® HCV Duo assay for the detection of HCV antigen and antibodies



Elecsys® HCV Duo is an electrochemiluminescence immunoassay ("ECLIA") for the in vitro qualitative detection of 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 sub-results (HCV Ag and anti-HCV) are intended as an aid in the selection of the confirmatory testing algorithm for reactive samples.

Electro-chemiluminescence immunoassay (ECLIA)[20]

HCVAG test principle: double-antibody sandwich assay



AHCV test principle: double-antigen sandwich assay

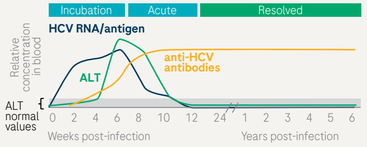
Step 1 (9 minutes):
HCVAG only:
30 µL of sample are pretreated with 15 µL of pretreatment solution to release the HCV core antigen.

Step 2 (9 minutes):
HCVAG:
The pretreated sample reacts with biotinylated and ruthenylated monoclonal anti-core antigen antibodies to form a sandwich complex.
AHCV:
12 µL of sample react with biotinylated and ruthenylated HCV-specific antigens, to form a sandwich complex.

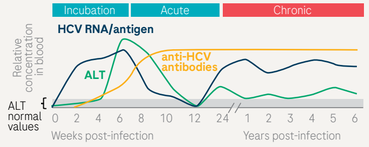
Step 3 (9 minutes):
After addition of streptavidin-coated microparticles, the sandwich complexes bind to the solid phase via interaction of biotin and streptavidin.

Step 4 (measurement):
The reagent mixture is transferred to the measuring cell, where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are subsequently removed. Electrochemiluminescence is then induced by applying a voltage and measured with a photomultiplier. The signal yield increases with the antibody or antigen titer.

Illustrative representation of the marker profile after HCV infection[2,9,16-18]



~15 – 45% of infected people spontaneously clear the virus within 6 months of infection without any treatment.



Chronic HCV infection is characterized by persistence of HCV RNA for longer than 6 months.

Elecsys® HCV Duo assay characteristics[20]

Systems	**cobas**® e 402 / **cobas**® e 801 analytical modules
Testing time	27 minutes
Calibration	Individual 2-point calibration for HCV antigen and anti-HCV antibodies
cobas e flow	Duplicate repeat testing of initially reactive samples (HCVDUOR)
Traceability	**HCVAG:** 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
Interpretation	**HCVAG** sub-result: COI <1.0 = non-reactive for HCV antigen / COI ≥1.0 = reactive for HCV antigen **AHCV** sub-result: COI <1.0 = non-reactive for anti-HCV / COI ≥1.0 = reactive for anti-HCV **HCV Duo** main result: calculated automatically based on the HCVAG and AHCV sub-results: HCVDUO COI <1.0 = non-reactive / HCVDUO COI ≥1.0 = reactive.
Specimen types	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. 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, and cadaveric blood specimens (specimens collected post-mortem, non-heart-beating).
Sample volume	42 µL (**HCVAG:** 30 µL; **AHCV:** 12 µL)
Onboard stability	31 days
Intermediate precision in positive samples	**HCVAG:** CV* 3.0 – 4.8 % ; **AHCV:** CV 3.3 – 4.3 %

* coefficient of variation

Analytical specificity[20]

Analytical specificity was evaluated using 204 samples containing potentially interfering substances (antibodies against HIV, HAV, HBV, HEV, CMV, HSV, EBV, Toxoplasma gondii, Treponema pallidum; autoantibodies; HBsAg and E. coli; vaccination for HBV and influenza) or derived from high-risk groups (non-viral liver disease; alcoholic liver disease). 10 of 11 initially reactive samples were confirmed to be positive or indeterminate by immunoblot. The analytical specificity of the Elecsys® HCV Duo assay was **99.48 % (95 % CI* 97.16 – 99.99 %)**.

Clinical specificity[20,21]

Clinical specificity of the Elecsys® HCV Duo assay was determined in a multi-center evaluation study in groups of randomly selected European and South African blood donors as well as samples from unselected daily routine patients, dialysis patients, and pregnant women. The overall (N = 23,165) clinical specificity of the Elecsys® HCV Duo assay was **99.94 % (95 % CI 99.89 – 99.96 %)**.
A subset of this sample cohort was also tested with the Monolisa HCV Ag-Ab ULTRA V2 assay as comparator.

Cohort	Samples total	Reactive	Elecsys® HCV Duo Specificity (95% CI)	Reactive	Monolisa HCV Ag-Ab ULTRA V2 Specificity (95% CI)
Blood donors	20634[a] 10574[b]	13**	99.94 % (99.89 – 99.97 %)	11	99.94 % (99.89 – 99.97 %)
Unselected daily	1251	1	99.92 % (99.54 – 100 %)	3	99.94 % (99.89 – 99.97 %)
Pregnant women	1057	0	100 % (99.65 – 100 %)	0	99.94 % (99.89 – 99.97 %)
Dialysis patients	223	1	99.55 % (97.52 – 99.99 %)	1	99.94 % (99.89 – 99.97 %)
Overall	**23165[a] 13105[b]**	**15**	**99.94 % (99.89 – 99.96 %)**	15	99.94 % (99.89 – 99.97 %)

* confidence interval; **All 13 false reactive results in the overall blood donor cohort occurred in the HCVAG module of the Elecsys® HCV Duo assay.
[a] Elecsys® HCV Duo; [b] Monolisa HCV Ag-Ab ULTRA V2

Seroconversion sensitivity[20,21]

Seroconversion sensitivity of the Elecsys® HCV Duo assay was shown by testing 85 commercial seroconversion panels comprising 777 panel members. The Elecsys® HCV Duo assay detected 485 (62.4 %) of all panel members. Subsets of these seroconversion panels were used to compare the Elecsys® HCV Duo seroconversion sensitivity to other registered HCV assays: two antigen/antibody combination assays (Murex HCV Ag/Ab Combination; Monolisa HCV Ag-Ab Ultra V2); and two antibody-only assays (Elecsys® Anti-HCV II; Architect Anti-HCV); The number and rate of panel members detected by each assay, as well as the time difference between the Elecsys® HCV Duo assay and the comparator assay for detecting the first positive panel member, are shown in the table below.

	Elecsys® HCV Duo	Murex HCV Ag/Ab Combination	Elecsys® HCV Duo	Monolisa HCV Ag-Ab Ultra V2	Elecsys® HCV Duo	Elecsys® Anti-HCV II	Elecsys® HCV Duo	Architect Anti-HCV
Panels tested	58		19		40		46	
Detected panel members / total panel members	325/577	218/577	92/167	27/167	264/349	128/349	288/392	127/392
Detection rate	56.3 %	37.8 %	55.1 %	16.2 %	75.6 %	36.7 %	73.5 %	32.4 %
Time difference	–	+ 2.2 days	–	+ 8.6 days	–	+ 17.9 days	–	+ 21.9 days

Clinical sensitivity[20,21]

Clinical sensitivity of the Elecsys® HCV Duo assay was determined in 257 samples from a reference center with a characterized HCV antibody and RNA status. All samples except one 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. Sensitivity of the Elecsys® HCV Duo assay was higher than that of the comparator, a registered HCV Ag/anti-HCV combination assay, which only detected 11 samples in the antibody-negative/RNA-positive (assumed early infection) and 88 samples in the antibody-positive/RNA-negative (assumed resolved infection) cohort.

Cohort	Samples total	Non-Reactive	Elecsys® HCV Duo Specificity (95% CI)	Non-Reactive	Monolisa HCV Ag-Ab ULTRA V2 Specificity (95% CI)
HCV RNA positive / anti-HCV negative	19	1	94.7 % (74.0 – 99.9 %)	8	57.9 % (33.5 – 79.8 %)
HCV RNA positive / anti-HCV positive	148	0	100 % (97.5 – 100 %)	0	100 % (97.5 – 100 %)
HCV RNA negative /anti-HCV positive	90	0	100 % (96.0 – 100 %)	2	97.8 % (92.2 – 99.7 %)
Overall	**257**	**256**	**99.6 % (97.9 – 100 %)**	247	96.1 % (93.0 – 98.1 %)

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

Cohort	N	Non-Reactive	Elecsys® HCV Duo Sensitivity (95% CI)
HCV infected persons with different stages of disease	386	0	100 % (99.1 – 100 %)
HCV genotypes 1 – 6	100	0	100 % (96.4 – 100 %)
Overall	**486**	**0**	100 % (99.2 – 100 %)

The overall (N = 743) clinical sensitivity of the Elecsys® HCV Duo assay was **99.87 % (95 % CI 99.25 – 100 %)**.