Elecsys Anti-HBc II

cobas®

Materials provided

REF			IVD	Rx only	SYSTEM
09014926162	09014926502	10 x 300			**cobas pro** serology solution

For reagents, refer to the "Reagents" section.

Materials required (but not provided)

REF	Description
04927931162	PreciControl Anti-HBc II, 16 x 1.3 mL
09367039190	PreciControl Release Anti-HBc II, 16 x 1.3 mL
11776576322	CalSet Vials, 2 x 56 empty snap-cap vials
	General laboratory equipment
	The **cobas pro** serology solution is a combination of the **cobas pro** serology controller, **cobas pro** integrated solutions (**cobas** e 801 analytical units only), and applicable licensed or cleared donor screening assays.

Additional materials for **cobas** e 801 analytical unit:

REF	Description
06908799190	ProCell II M, 2 × 2 L system solution
04880293190	CleanCell M, 2 × 2 L measuring cell cleaning solution
07485409001	Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
06908853190	PreClean II M, 2 × 2 L wash solution
05694302001	AssayTip/AssayCup tray, 6 magazines × 6 magazine stacks × 105 assay tips and 105 assay cups, 3 wasteliners
07485425001	Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution / Elecsys SysClean for Liquid Flow Cleaning Detection Unit
07485433001	PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution / Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
11298500160	ISE Cleaning Solution / Elecsys SysClean, 5 × 100 mL system cleaning solution

For use in the USA only

System information

Short name	ACN (application code number)
AHBC2B	10505
AHBC2BE (embedded application)	11505
AHBC2BR (for use with **cobas** e flow)	12505

Intended use

Elecsys Anti-HBc II is an in vitro immunoassay for the qualitative detection of antibodies to hepatitis B core antigen (anti-HBc) in human serum and plasma. Elecsys Anti-HBc II is intended to screen individual human donors, including volunteer donors of whole blood and blood components. The assay is also intended to be used to screen organ, tissue and cell donors, when donor samples are obtained while the donor's heart is still beating and in testing serum specimens to screen cadaveric donors when specimens are obtained after the donor's heart has stopped beating.

It is not intended for use on cord blood specimens.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use with the **cobas pro** serology solution equipped with a **cobas** e 801 analytical unit.

Summary

The hepatitis B virus consists of an outer envelope containing host-derived lipids and all S gene polypeptides, the large (L), middle (M), and small (S) surface proteins, also known as pre-S1, pre-S2 and HBsAg. The nucleocapsid contains core proteins HBcAg, a 3.2 kb, circular, partially double stranded viral DNA genome, an endogenous DNA polymerase (reverse transcriptase) enzyme, and protein kinase activity. The hepatitis core antigen comprises 183-185 amino acids.[1]

During an infection with the hepatitis B virus, antibodies to HBcAg are generally formed, which often persist for life. Anti-HBc appears shortly after the onset of infection with hepatitis B virus and can usually be detected in serum soon after the appearance of HBsAg. Anti-HBc antibodies persist both in persons who have recovered from a hepatitis B infection and in those who develop HBsAg-carrier status. Accordingly, they are an indicator of existing or past hepatitis B infection.[2]

In rare cases, an HBV infection can also run its course without the appearance of immunologically detectable anti-HBc (usually in immunosuppressed patients).[3]

Due to the long persistence of anti-HBc following a hepatitis B viral infection, screening for HBV infection may be accompanied by testing for the presence of hepatitis B core antibodies as long as those who test positive are further tested for both HBsAg and anti-HBs to differentiate infection from immunity.[4]

In the absence of other hepatitis B markers (HBsAg-negative persons), anti HBc may be the only indication of an existing hepatitis B viral infection.[5]

Test principle

Competition principle. Total duration of test: 27 minutes.

- First incubation: Pretreatment of 24 µL of sample with reducing agent.
- Second incubation: After addition of HBc recombinant antigens, a complex is formed with anti-HBc antibodies in the sample.
- Third incubation: After addition of biotinylated antibodies and ruthenium complex[a)]-labeled antibodies specific for HBcAg, together with streptavidin-coated microparticles, the still-free binding sites on the HBc antigens become occupied. The entire 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 obtained by the HBc embedded calibration. The Elecsys Anti-HBc II result is calculated automatically based on signal to cutoff ratio (cutoff index, COI).

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

Reagents

The **cobas** e pack (M, R0, R1, R2) is labeled as AHBC2B.

M	Streptavidin-coated microparticles, 1 bottle, 12.4 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
R0	DTT, 1 bottle, 6.3 mL: 1,4-dithiothreitol 110 mmol/L; citrate buffer 50 mmol/L.
R1	HBc recombinant antigens (*E. coli*), 1 bottle, 15.8 mL: HBc recombinant antigens (*E. coli*) > 25 ng/mL; phosphate buffer 100 mmol/L, pH 7.4; preservative.
R2	Anti-HBcAg-Ab~biotin; anti-HBcAg-Ab~$Ru(bpy)_3^{2+}$, 1 bottle, 15.8 mL: Biotinylated monoclonal anti-HBc antibody (mouse) 700 ng/mL; monoclonal anti-HBc antibody (mouse) labeled with ruthenium complex 200 ng/mL; phosphate buffer 100 mmol/L, pH 7.4; preservative.
AHBC2B Cal1	Non-reactive calibrator 1, 2 vials of 1.0 mL each: Human serum, non-reactive for anti-HBc antibodies; preservative.
AHBC2B Cal2	Reactive calibrator 2, 2 vials of 1.0 mL each: Human serum, reactive for anti-HBc antibodies > 8 WHO IU/mL[A)]; preservative.

A) WHO international units

Warnings and precautions

For in vitro diagnostic use.

The test is not intended for use as an aid in diagnosis of hepatitis B infection.

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 safe disposal.

The Safety Data Sheet is available for professional users 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.

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.

Hazardous components:

- 2-methyl-2H-isothiazol-3-one hydrochloride

Product safety labeling follows EU GHS guidance.

Contact phone: +1-866-744-6397

All human material should be considered potentially infectious.

The calibrators (AHBC2B Cal1 and AHBC2B Cal2) have been prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg (AHBC2B Cal1) 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-HBc (AHBC2B Cal2) was inactivated using β_2-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 donor specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[6,7]

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

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 **cobas** e 801 analytical unit	16 weeks

Stability of the calibrators:

unopened at 2-8 °C	up to the stated expiration date
on the **cobas** e 801 analytical unit at 20-25 °C	use only once, stable onboard for up to 5 hours

Store calibrators **upright** in order to prevent the calibrator solution from adhering to the lid of the vials.

Calibration

Traceability: This method has been standardized against the anti-HBc reference material WHO Standard (NIBSC code 95/522).

Calibration frequency: Calibration must be performed once per reagent lot using AHBC2B Cal1, AHBC2B Cal2 and fresh reagent (i.e., not more than 24 hours after the **cobas** e pack was registered on the analytical unit).

Recalibration is required as follows:

- every 12 weeks when using the same reagent lot
- every 28 days when using the same **cobas** e pack on the analytical unit
- as required, such as when quality control findings are outside the defined limits

Quality control

For quality control, use PreciControl Anti-HBc II.

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

PreciControl Anti-HBc II values must be within the ranges specified in the control value sheet.

When the assay control values are within range, sample results are generated, and a valid release control result is required to release test results. If an assay control value is not within range, sample results are not generated for in-process or scheduled samples. For troubleshooting information, refer to User Assistance **cobas pro** serology solution or contact US Customer Technical Support.

Release control

For release control, use PreciControl Release Anti-HBc II.

Result validation is based on test result batches that are concluded by release control measurements. A release control result within defined limits is required to validate a batch of previously measured test results utilizing the **cobas pro** serology controller software. Initial reactive results will not be invalidated by a failed release control and must be retested in duplicate. Repeatedly reactive results will not be invalidated by a failed release control and stay reactive. Other results rendered invalid due to a failed release control result must be retested after resolving the cause for the failed control measurement.

For a valid batch of sample results, the release control is tested at user-defined intervals with a maximum span of every 300 samples or 350 determinations within 24 hours from the PreciControl and must be tested in order to release the test results. Reactive results will not be invalidated.

The release control must meet specifications defined in the PreciControl Release Anti-HBc II value sheet in order to validate the system functionality and release test results.

For troubleshooting information, refer to User Assistance **cobas pro** serology solution or contact US Customer Technical Support.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Serum and Li-heparin, K2 EDTA, K3 EDTA, CPD and Na-citrate plasma collected using standard sampling tubes.

Serum and Li-heparin and K2 EDTA plasma collected in tubes containing separating gel.

Samples on-the-clot are stable for 7 days at 15-30 °C, 14 days at 2-8 °C. Do not freeze samples on-the-clot.

Samples off-the-clot are stable for 7 days at 20-25 °C, 14 days at 2-8 °C, 3 months at -20 °C (± 5 °C). Samples off-the-clot may be frozen up to 4 times.

Cadaveric samples off-the-clot are stable for 3 days at 15-30 °C, 14 days at 2-8 °C, 12 months at -20 °C (± 5 °C). Samples off-the-clot may be frozen up to 5 times.

All whole-blood samples and samples containing precipitates need to be centrifuged before performing the assay for 10 to 15 minutes at 2000 to 4000 RCF (relative centrifugal force = x g).

The sample types listed were tested with a selection of sample collection tubes or systems that were commercially available at the time of testing. Not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials that 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.

Do not use pools of samples.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

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

Sample stability claims were established by experimental data by the manufacturer only for the temperatures/time frames as stated in the method sheet.

Test procedure

The reagents (M, R0, R1, R2) in the kit are ready for use and are supplied in **cobas** e packs.

For optimum performance of the assay follow the directions given in this document for the analytical unit concerned. Refer to the appropriate user guide for analytical unit 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

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

Read in all the information necessary for calibrating the assay.

Perform **only 1** calibration procedure per vial.

All information required for correct operation is available via **cobas** link.

Place the calibrators in the sample zone.

Calculation

The analytical unit automatically calculates the cutoff based on the measurement of AHBC2B Cal1 and AHBC2B Cal2.

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

Interpretation of results

Initial result

Numeric result	Result	Interpretation / further steps
COI > 1.00	Non-reactive	Non-reactive for HBc-specific antibodies. No further testing needed.
COI ≤ 1.00	Reactive	Reactive in the Elecsys Anti-HBc II assay. All initially reactive samples should be retested in duplicate with the Elecsys Anti-HBc II assay. Redetermination of samples with an initial COI ≤ 1.00 can be performed automatically (see section **cobas** e flow).

Final result

Numeric result	Final Result	Interpretation / further steps
One or both of the duplicate retests have a COI ≤ 1.00	Repeatedly reactive	Repeatedly reactive samples must be confirmed according to supplementary algorithms.
Both of the duplicate retests have a COI >1.00	Non-reactive	Non-reactive for HBc-specific antibodies. No further testing needed.

cobas e flow

A **cobas** e flow is a procedure programmed into the system to enable a fully automated sequence of measurements and the calculation of assay combinations to perform decision algorithms.

A **cobas** e flow is available to perform a repetition of measurements in duplicate automatically for samples with an initial cutoff index ≤ 1.00 (AHBC2BR).

Limitations of the test

A non-reactive test result does not completely rule out the possibility of an infection with HBV. Serum or plasma samples from the very early (pre-seroconversion) phase can occasionally yield non-reactive findings. New HBV variants can also lead to non-reactive HBV results.

The detection of HBc antibodies is not a diagnosis of HBV. It is recommended that repeatedly reactive specimens be confirmed by supplemental testing. Individuals who are repeatedly reactive should be referred for medical evaluation which may include additional testing.

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

Testing of cadaveric serum specimens from patients with plasma dilution due to transfusions of > 2000 mL of blood or colloids within 48 hours, or > 2000 mL of crystalloids within 1 hour (or any combination thereof) prior to collection of the specimens has not been verified.

Specific performance data

Representative performance data is given below. Results obtained in individual laboratories may differ.

Precision

A study was performed based on guidance from CLSI EP05-A3 (n = 84). Testing was conducted at 1 site using 1 lot of the Elecsys Anti-HBc II assay and 1 lot of PreciControl Anti-HBc II. Panel members and controls were tested in 4 replicates, 1 run per day for 21 days. The following results were obtained:

Overall precision for Elecsys Anti-HBc II

Sample	Mean COI	Repeatability SD (COI)	Repeatability % CV	Within-laboratory SD (COI)	Within-laboratory % CV
HSP[A)] 01	2.13	0.032	1.5	0.037	1.7
HSP 02	1.10	0.019	1.7	0.030	2.8
HSP 03	1.01	0.014	1.4	0.029	2.8

Sample	Mean COI	Repeatability SD (COI)	Repeatability % CV	Within-laboratory SD (COI)	Within-laboratory % CV
HSP 04	0.004	0.000	1.2	0.000	2.2
HSP 05	0.92	0.017	1.9	0.029	3.1
HSP 06	1.48	0.024	1.6	0.033	2.2
PC[B)] AHBC1 B	2.41	0.029	1.2	0.044	1.8
PC AHBC2 B	0.64	0.008	1.3	0.018	2.8

A) HSP = human specimens

B) PC = PreciControl

Reproducibility

A study was performed based on guidance from CLSI EP05-A3 (n = 270). Testing was conducted at 3 external sites using 3 lots of the Elecsys Anti-HBc II reagent kit and 1 lot each of PreciControl Anti-HBc II and PreciControl Release Anti-HBc II. Panel members and PreciControl Anti-HBc II were tested in 2 runs per day for 5 days with 3 sample replicates per run. The results for the Elecsys Anti-HBc II assay are presented in the following tables.

Overall repeatability and reproducibility for Elecsys Anti-HBc II

Sample	Mean (COI)	Repeatability SD (COI)	Repeatability % CV	Between run SD (COI)	Between run % CV	Between day SD (COI)	Between day % CV	Intermediate precision SD (COI)	Intermediate precision % CV
HSP 14	0.596	0.011	1.91	0.010	1.63	0.010	1.62	0.018	2.99
HSP 15	0.006	0.000	1.95	0.000	0.391	0.000	0.559	0.000	2.07
PC AHBC1 B	2.33	0.054	2.34	0.000	0.000	0.021	0.910	0.058	2.51
PC AHBC2 B	0.581	0.006	1.06	0.006	1.08	0.006	1.02	0.011	1.83

Overall repeatability and reproducibility for Elecsys Anti-HBc II

Sample	Mean (COI)	Between site SD (COI)	Between site % CV	Between lot SD (COI)	Between lot % CV	Reproducibility SD (COI)	Reproducibility % CV
HSP 14	0.596	0.005	0.816	0.039	6.52	0.043	7.22
HSP 15	0.006	0.000	0.993	0.000	4.18	0.000	4.77
PC AHBC1 B	2.33	0.027	1.14	0.014	0.589	0.066	2.82
PC AHBC2 B	0.581	0.008	1.33	0.019	3.19	0.023	3.91

Results: The precision and reproducibility of the Elecsys Anti-HBc II assay demonstrated minor variability from run to run, day to day and between reagent lots.

Analytical specificity

The effect of the following endogenous substances 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	≤ 753 µmol/L or ≤ 44 mg/dL
Hemoglobin	≤ 0.311 mmol/L or ≤ 500 mg/dL
Intralipid	≤ 2000 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Albumin	≤ 7.0 g/dL

Additionally, naturally elevated samples for bilirubin, rheumatoid factor, triglycerides (lipemic), hemoglobin and albumin were tested; no false reactive results were found.

In rare cases, interference due to extremely high titers of antibodies to immunological components, streptavidin or ruthenium can occur and these effects are minimized by assay formulation and design.

Clinical specificity

A total of 3763 fresh serum specimens and 3904 fresh plasma specimens from volunteer whole blood donors were collected at 3 blood centers. The initial and repeat reactive rates for the serum and plasma specimens were 0.21 % (8/3763) and 0.13 % (5/3904), respectively.

Repeatedly reactive specimens were further tested for 1 or more additional hepatitis B markers using HBV qualitative DNA, HBsAg, and FDA-licensed anti-HBc assays. Based on supplemental test results, 10 specimens were positive and 3 specimens were negative. Samples with a final anti-HBc status of positive were not included in the specificity calculation.

Specificity based on assumed zero prevalence of antibody to HBc in whole blood donors was estimated in this study to be 99.96 % (7654/7657) with a 95 % confidence interval of 99.88 % to 99.99 %.

Specificity of Elecsys Anti-HBc II

Specimen category	Number tested	Number initially reactive (% of tested)	Number repeatedly reactive (% of tested)	Number positive by supplemental testing	Specificity (%) (95 % CI)
Volunteer blood donors - serum	3763	8 (0.21)	8 (0.21)	6 (75.00)	99.95 3755/3757 (99.81, 99.99)
Volunteer blood donors - plasma	3904	5 (0.13)	5 (0.13)	4 (80.00)	99.97 3899/3900 (99.85, 100)
Total volunteer blood donors	7667	13 (0.17)	13 (0.17)	10 (76.92)	99.96 7654/7657 (99.88, 99.99)

Clinical sensitivity

A total of 898 specimens from 4 categories shown in the table below were tested using the Elecsys Anti-HBc II assay. 2 specimens were repeatedly reactive on the comparator test and non-reactive on the Elecsys Anti-HBc II assay. Repeatedly reactive specimens from individuals were further tested for 1 or more additional HBV markers using HBV qualitative DNA, HBsAg, and FDA licensed anti-HBc assays. The final status of both samples was confirmed reactive. Sensitivity was estimated to be 99.78 % (896/898) with a 95 % confidence interval of 99.19 % to 99.94 % for preselected positive specimens.

Sensitivity of Elecsys Anti-HBc II

Specimen category	Number tested	Number positive	Number repeatedly reactive (% of total)	Number repeatedly reactive that were positive (% of repeatedly reactive)	Sensitivity (%) (95 % CI)
Acute HBV	45	45	45 (100)	45 (100)	100 45/45 (92.13, 100)
Anti-HBc positive	483	483	481 (99.59)	481 (100)	99.59 481/483 (98.50, 99.89)
Chronic HBV	113	113	113 (100)	113 (100)	100 113/113 (96.71, 100)
HBV recovered	257	257	257 (100)	257 (100)	100 257/257 (98.53,100)
Total	898[A)]	898	896 (99.78)	896 (100)	99.78 896/898 (99.19, 99.94)

A) 2 Elecsys Anti-HBc II non-reactive specimens were positive by supplemental testing.

An additional 409 specimens from a cohort at increased risk of infection were tested using the Elecsys Anti-HBc II assay at 3 clinical sites. There were 307 specimens non-reactive with the Elecsys Anti-HBc II assay and 100 specimens repeatedly reactive with the Elecsys Anti-HBc II assay. 2 specimens were repeatedly reactive with the Elecsys Anti-HBc II assay and non-reactive with the comparator assay. 1 of the repeatedly reactive specimens tested non-reactive on supplemental testing and the final status was confirmed as negative. The other repeatedly reactive specimen with the Elecsys Anti-HBc II assay was interpreted as inconclusive. Sensitivity was not analyzed in this cohort and only the comparative results are presented.

Reactivity of the Elecsys Anti-HBc II assay in individuals at increased risk for hepatitis

Specimen category	Number tested	Number initially reactive (% of total)	Number repeatedly reactive (% of total)	Number positive by supplemental testing (% of repeatedly reactive)
Increased risk for HBV	409	102 (24.94)	102 (24.94)	100 (98.04)

Analytical sensitivity

Analytical sensitivity of the Elecsys Anti-HBc II assay was evaluated using the WHO First International Standard for anti-Hepatitis B core antigen (anti-HBc), plasma, human NIBSC code number: 95/522. A six-dilution series of WHO International Standard 95/522 was prepared in anti-HBc negative serum and tested in duplicate with the Elecsys Anti-HBc II assay. Sensitivity was calculated using the mean of both duplicate measurements tested by reading off the concentration at the cutoff of 1.0 from the anti-HBc reference standard curve. The analytical sensitivity of Elecsys Anti-HBc II as measured by WHO International Standard NIBSC code 95/522 was shown to be ≤ 0.8 IU/mL. Using Elecsys Anti-HBc II, the result for NIBSC code 95/522 was determined to be 0.451 IU/mL.

Seroconversion

Seroconversion sensitivity of the Elecsys Anti-HBc II assay was shown by testing 10 commercially available seroconversion panels with a total of 159 panel members and comparing the Elecsys Anti-HBc II assay to a comparator assay. There was 1 discordant panel member in each of 3 panels, where the Elecsys Anti-HBc II assay detected seroconversion 1 bleed later than the comparator assay.The summary of the results obtained from 10 commercially available seroconversion panels is in the following table.

Elecsys Anti-HBc II assay reactivity in seroconversion panels

Panel ID	Elecsys Anti-HBc II reactive on bleed	Comparator assay reactive on bleed	Differences in bleeds[A)]
SCP-HBV-001	5	5	0
SCP-HBV-002	8	7	+1
SCP-HBV-004	14	14	0
PHM941	7	7	0
HBV-6278	11	10	+1
HBV-6281	9	9	0
HBV-9093	11	10	+1
PHM933	6	6	0
PHM934	6	6	0
PHM935A	13	13	0

A) -1 = Elecsys Anti-HBc II 1 bleed earlier, 0 = equal, + 1 = Elecsys Anti-HBc II 1 bleed later

Other specimen conditions and disease states

293 samples containing potentially interfering substances were tested with the Elecsys Anti-HBc II assay comprising specimens:

- containing antibodies against HIV, HAV, HCV, Rubella, HSV, EBV, HBV, HEV, VZV, HTLV-I/II, HDV, parvovirus
- containing autoantibodies (ANA) and human anti-murine antibodies (HAMA)
- containing antibodies against *Escherichia coli*, *Candida sp.*, *Chlamydia trachomatis*, *Treponema pallidum* (syphilis), *Plasmodium*
- after vaccination against HAV and influenza
- from patients with monoclonal gammopathy, Morbus Crohn, Colitis ulcerosa, systemic lupus erythematosus, non-viral liver disease, autoimmune disorder
- from pregnant women and multiparous pregnancies

Results showed no interference from the above agents.

Performance characteristics of cadaveric specimen testing

Storage

Performance has been established for the use of cadaveric serum specimens (including specimens collected post-mortem, non-heart-beating) that have been collected up to 16 hours after death.[8] Follow general standards and/or regulations for collection, storage, and handling.

If specimens are not processed directly after initial centrifugation, it is recommended to remove the supernatant from the clot, red blood cells, or separator gel until further processing.

Cadaveric samples off-the-clot are stable for 3 days at 15-30 °C, 14 days at 2-8 °C and 12 months at -20 °C (± 5 °C). Samples off-the-clot may be frozen up to 5 times.

Specimen category	Storage at 15-30 °C 3 days Recovery vs. t=0	Storage at 2-8 °C 14 days Recovery vs. t=0	Storage at -20 °C (± 5 °C) 12 months Recovery vs. t=0	Freeze/Thaw 5 cycles Recovery vs. t=0
Cadaveric non-reactive [mean % recovery]	93.2	91.5	102	98.8
Cadaveric reactive [mean Δ COI]	-0.015	-0.009	-0.007	0.033

Reproducibility

20 cadaveric donor serum specimens and 20 living donor serum specimens were spiked with human plasma reactive for antibodies to anti-HBc to create low-level reactive specimens. Each specimen was tested once per day for 6 days using 3 lots of the Elecsys Anti-HBc II assay. Reproducibility in % CV of each specimen category was determined.

Overall reproducibility for Elecsys Anti-HBc II

Specimen category[A)]	Number tested	Mean (COI)	Reproducibility SD (COI)	Reproducibility % CV
Cadaveric donor	360	0.588	0.0760	12.93
Living donor	360	0.639	0.0746	11.68

A) Cadaveric serum specimens were collected up to 1 hour after death

Clinical specificity

Specificity was determined by testing 55 cadaveric serum specimens and 55 living donor serum specimens. Each specimen was tested once using 3 lots of the Elecsys Anti-HBc II assay. There was 1 false repeatedly reactive post-mortem specificity sample observed in all 3 lots of Elecsys Anti-HBc II.

Specificity of Elecsys Anti-HBc II

Specimen category[A)]	Number tested	Number non-reactive (% of tested)	Number repeatedly reactive (% of tested)	Specificity (%) (95 % CI)
Cadaveric donor - Lot 1	55	54 (98.18)	1 (1.82)	98.18 (90.39, 99.68)
Cadaveric donor - Lot 2	55	54 (98.18)	1 (1.82)	98.18 (90.39, 99.68)
Cadaveric donor - Lot 3	55	54 (98.18)	1 (1.82)	98.18 (90.39, 99.68)
Living donor - Lot 1	55	55 (100)	0 (0.00)	100 (93.47, 100)
Living donor - Lot 2	55	55 (100)	0 (0.00)	100 (93.47, 100)
Living donor - Lot 3	55	55 (100)	0 (0.00)	100 (93.47, 100)

A) Cadaveric serum specimens were collected up to 16 hours after death.

Analytical sensitivity

Cadaveric serum specimens and living donor serum specimens were spiked with human plasma reactive for antibodies to anti-HBc to create low-level reactive specimens. Each specimen was tested once using each of 3 lots of the Elecsys Anti-HBc II assay. All specimens were reactive on all 3 reagent lots.

Sensitivity of Elecsys Anti-HBc II

Specimen category[A)]	Number tested	Mean (COI)	Number positive (% of tested)	Sensitivity (%) (95 % CI)
Cadaveric donor - Lot 1	80	0.657	80 (100)	100 (95.42, 100)
Cadaveric donor - Lot 2	80	0.730	80 (100)	100 (95.42, 100)
Cadaveric donor - Lot 3	80	0.635	80 (100)	100 (95.42, 100)

Specimen category[A)]	Number tested	Mean (COI)	Number positive (% of tested)	Sensitivity (%) (95 % CI)
Living donor - Lot 1	110	0.672	110 (100)	100 (96.63, 100)
Living donor - Lot 2	110	0.742	110 (100)	100 (96.63, 100)
Living donor - Lot 3	110	0.650	110 (100)	100 (96.63, 100)

A) Cadaveric serum specimens were collected up to 16 hours after death.

Additional information

For further information, refer to the User Guide for the corresponding analytical unit and to the Method Sheets of all necessary components (if available in your country).

Report any serious incident that has occurred in relation to the device to the manufacturer and the competent authority of the member state in which the user and/or patient is established.

FOR US CUSTOMERS ONLY: LIMITED WARRANTY
Roche Diagnostics warrants that this product meets the specifications stated in the labeling when used in accordance with the labeling and is free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL, OR CONSEQUENTIAL DAMAGES.

Symbols

For definition of symbols used, refer to navifyportal.roche.com.

In addition to the ISO 15223-1 standard, Roche Diagnostics uses the following symbols and signs:

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

References

1 Sällberg M, Ruden U, Magnius LO, et al. Characterisation of a Linear Binding Site for a Monoclonal Antibody to Hepatitis B Core Antigen. J Med Virol 1991;33:248-252.

2 Hoofnagle JH. Type B hepatitis: virology, serology and clinical course. Semin Liver Dis. 1981 Feb;1(1):7-14.

3 Kumar S, Pound DC. Serologic diagnosis of viral hepatitis. Postgraduate Medicine 1992;92(4):55-65.

4 Lok A, McMahon B. AASLD Practice Guidelines, Chronic Hepatitis B: Update 2009. Hepatology 2009; September: 2.

5 Gerlich WH, Caspari G, Uy A, et al. A critical appraisal of anti-HBc, HBV DNA and anti-HCV in the diagnosis of viral hepatitis. Biotest Bulletin 1991;4:283-293.

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

7 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.

8 U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research. Guidance for Industry Recommendations for Obtaining a Labeling Claim for Communicable Disease Donor Screening Tests Using Cadaveric Blood Specimens from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps), November 2004. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommendations-obtaining-labeling-claim-communicable-disease-donor-screening-tests-using-cadaveric Accessed Feb, 2025

Rx only

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Change log

Due to technical reasons, changes that have been made since the last version of this document are listed in the following table instead of indicated by change bars in the margin.

Document Revision Information

Doc. Rev. 4.0	Cadaveric claims were added to the following new and existing sections: Intended use, Specimen collection and preparation, Limitations of the test, Performance characteristics of cadaveric specimen testing, and References Editorial and layout updates due to change in software.