

Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please call 800-835-4709 or 240-402-8010, extension 1. CBER Consumer Affairs Branch or send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

Elecsys HBsAg II



Materials provided

REF	i	Σ	IVD	Rx only	SYSTEM
08814848162	08814848502	20 x 300			cobas pro serology solution

For reagents, refer to the "Reagents" section.

Materials required (but not provided)

REF	Description
04687876162	PreciControl HBsAg II, 16 x 1.3 mL
09366717190	PreciControl Release HBsAg II, 16 x 1.3 mL
	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 x 2 L system solution
04880293190	CleanCell M, 2 x 2 L measuring cell cleaning solution
07485409001	Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
06908853190	PreClean II M, 2 x 2 L wash solution
05694302001	Assay Tip / Assay Cup tray, 6 magazines x 6 magazine stacks x 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 x 100 mL system cleaning solution

For use in the USA only

System information

Short name	ACN (application code number)
HBSAG2B	10502
HBSAG2BE (embedded application)	11502
HBSAG2BR (for use with cobas e flow)	12502

Intended use

Elecsys HBsAg II is an in vitro immunoassay intended for the qualitative detection of hepatitis B surface antigen (HBsAg) in human serum and plasma. Elecsys HBsAg II is intended to screen individual human donors, including volunteer donors of whole blood, blood components and source plasma. 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 electrochemiluminescence immunoassay "ECLIA" is intended for use with the **cobas pro** serology solution equipped with a **cobas e 801** analytical unit.

Summary

Hepatitis B virus (HBV) is transmitted by percutaneous or mucosal exposure to infected blood and various body fluids including saliva, menstrual, vaginal, and seminal fluids.¹ The majority of adult patients recover completely from their HBV infection, but up to 10 % of them become asymptomatic carriers or develop chronic hepatitis which may lead to cirrhosis and/or liver cancer.^{2,3} Despite immunization, HBV is still prevalent worldwide with approximately 300 million chronically infected patients and a serious threat to blood transfusion safety, especially in highly endemic countries.^{1,4,5} Serological diagnosis of HBV infection involves the detection of HBV specific antigens and/or antibodies to identify different phases of the HBV infection to determine whether a patient has acute or chronic HBV infection, is susceptible to infection, or is immune to HBV as a result of prior infection or vaccination.^{6,7} In addition, some of these HBV markers are routinely used in patient and donor screening.⁷

The external envelope of the hepatitis B virus (HBV) particle is composed of a polypeptide of varying size, namely hepatitis B surface antigen (HBsAg).⁸ Detection of HBsAg in human serum or plasma is the standard serological test to confirm an acute or chronic HBV infection. Particularly, after an acute exposure to HBV, HBsAg appears in serum within 1 to 10 weeks.⁹ After recovery from an acute HBV infection, the level of HBsAg becomes undetectable.¹⁰ Persistence of HBsAg for more than 6 months implies chronic HBV infection, which is conventionally diagnosed by a repeat reactive test for HBsAg, 6 months after the initial reactive test.¹¹

HBsAg assays are used to detect HBV in blood donors to prevent the transmission of the virus by blood and blood products.⁷

HBsAg assays are also used to screen organ and tissue donors.^{12,13} The objective of blood screening is to detect markers of infection to prevent the release of infected blood and blood components for clinical use. Blood screening strategies are designed to assure the safety of blood units, but should not be used for notifying blood donors of reactive test results.¹⁴

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- First incubation: 30 µL of sample, 2 biotinylated monoclonal anti-HBsAg antibodies, and a mixture of monoclonal anti-HBsAg antibody and polyclonal anti-HBsAg antibodies labeled with a ruthenium complex^{a)} form a sandwich complex.
- Second incubation: After streptavidin-coated microparticles have been added, 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 obtained by HBsAg embedded calibration. The Elecsys HBsAg II result is calculated automatically based on signal to cutoff ratio (cutoff index, COI).

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

Reagents

The **cobas** e pack (M, R1, R2) is labeled as HBSAG2B.

M	Streptavidin-coated microparticles, 1 bottle, 14.1 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
R1	Anti-HBsAg-Ab-biotin, 1 bottle, 15.8 mL: 2 biotinylated monoclonal anti-HBsAg antibodies (mouse) > 0.5 mg/L; phosphate buffer 100 mmol/L, pH 7.5; preservative.
R2	Anti-HBsAg-Ab-Ru(bpy) ₃ ²⁺ , 1 bottle, 13.9 mL: Monoclonal anti-HBsAg antibody (mouse), polyclonal anti-HBsAg antibodies (sheep) labeled with ruthenium complex > 1.5 mg/L; phosphate buffer 100 mmol/L, pH 8.0; preservative.
HBSAG2B Cal 1	Non-reactive calibrator 1, 2 vials of 1.3 mL each: Human serum, non-reactive for HBsAg; preservative
HBSAG2B Cal2	Reactive calibrator 2, 2 vials of 1.3 mL each: Human serum, reactive for HBsAg; preservative.

Warnings and precautions

For in vitro diagnostic use.

This 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:



Elecsys HBsAg II

Warning

H317 May cause an allergic skin reaction.

Prevention:

P261 Avoid breathing mist or vapours.

P272 Contaminated work clothing should not be allowed out of the workplace.

P280 Wear protective gloves.

Response:

P333 + P313 If skin irritation or rash occurs: 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 (HBSAG2B Cal1 and HBSAG2B Cal2) have been prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg (HBSAG2B Cal1 only) 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 HBsAg (HBSAG2B 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 donor specimen. In the event of exposure, the directives of the responsible health authorities should be followed.^{15,16}

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 **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 NIBSC standard (code number: 00/588; WHO Second International Standard for HBsAg, subtype adw2, genotype A; IU/mL).

Calibration frequency: Calibration must be performed once per reagent lot using HBSAG2B Cal1, HBSAG2B Cal2 and fresh reagent (i.e., not more than 24 hours since 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 HBsAg II.

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.

PreciControl HBsAg 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 HBsAg 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 HBsAg 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 and 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, and 1 month 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 and 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).

Specimens collected by plasmapheresis, which have not been frozen, do not require centrifugation.

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 Elecsys HBsAg II 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, 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.

Note: Anti-CMV and any HBsAg assay shall not be assigned to the same measuring cell on a **cobas pro** analytical unit, avoiding a potential signal carryover from samples with high CMV antibodies on a measuring cell. When assigned to the same measuring cell as Anti-CMV or HBsAg II, confirmation of HBsAg-reactive samples using HBsAg II Auto Confirm must only be run with all results reported and released (all brackets closed). All samples must be finalized in processing on the instrument (**cobas pro** integrated solution). This is to further reduce a potential signal carryover with high HBsAg II samples on a measuring cell.

Calibrators

Place the calibrators in the sample zone.

Read in all the information necessary for calibrating the assay.

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

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

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

Calculation

The analytical unit automatically calculates the cutoff based on the measurement of HBSAG2B Cal1 and HBSAG2B 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 < 0.90	Non-reactive	Non-reactive for HBsAg. No further testing needed.
COI ≥ 0.90	Reactive	Reactive in the Elecsys HBsAg II assay. All initially reactive samples should be retested in duplicate using Elecsys HBsAg II assay. Redetermination of samples with an initial COI ≥ 0.90 can be performed automatically (see section cobas e flow).

Final result

Numeric result	Result	Interpretation / further steps
One or both of the duplicate retests have a COI ≥ 0.90	Repeatedly reactive	Presumptive evidence of HBV. Repeatedly reactive samples must be confirmed using a neutralization test (Elecsys HBsAg II Auto Confirm).
Both of the duplicate retests have a COI < 0.90	Non-Reactive	Non-reactive for HBsAg. 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.

The **cobas e flow** (short name HBSAG2BR) is available to perform a repetition of measurements in duplicate automatically for samples with an initial cutoff index ≥ 0.90.

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. HBV variants may also lead to non-reactive HBsAg results.

The detection of HBsAg is not a diagnosis of HBV. It is recommended that repeatedly reactive specimens be confirmed by supplemental testing. Vaccination with a recombinant HBsAg Hepatitis B vaccine may cause transient positive results caused by a passive transfer of antigen by vaccination.¹⁷ Individuals who are repeatedly reactive should be referred for medical evaluation which may include additional testing.

The performance of the Elecsys HBsAg 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 HBsAg II assay and 1 lot of PreciControl HBsAg II. Panel members and controls were tested in 4 replicates, 1 run per day for 21 days. The following results were obtained.

Elecsys HBsAg II



Sample	Mean (COI)	Repeatability		Intermediate precision	
		SD	% CV	SD	% CV
Human specimen 01	0.254	0.018	7.1	0.030	11.7
Human specimen 02	0.784	0.030	3.8	0.038	4.8
Human specimen 03	0.962	0.039	4.0	0.045	4.7
Human specimen 04	1.12	0.038	3.3	0.043	3.9
Human specimen 05	1.22	0.036	2.9	0.046	3.8
Human specimen 06	10.8	0.295	2.7	0.365	3.4
PreciControl HBSAG1B	0.363	0.036	9.9	0.040	11.0
PreciControl HBSAG2B	4.17	0.091	2.2	0.125	3.0

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 HBsAg II reagent kit and 1 lot each of the PreciControl HBsAg II and PreciControl Release HBsAg II. Panel members and PreciControl HBsAg II were tested in 2 runs per day for 5 days with 3 sample replicates per run. The precision and reproducibility for the Elecsys HBsAg II assay are presented in the following tables:

Overall repeatability and reproducibility for Elecsys HBsAg II

Sample	Mean (COI)	Repeatability SD (COI)	Repeatability % CV	Between run SD (COI)	Between run % CV	Between day SD (COI)	Between day % CV
HSP ^{A)} 01	1.74	0.067	3.85	0.009	0.492	0.024	1.38
HSP 02	7.04	0.182	2.59	0.092	1.31	0.145	2.06
PC ^{B)} HBSAG1B	0.411	0.030	7.28	0.000	0.000	0.014	3.45
PC HBSAG2B	3.81	0.098	2.56	0.025	0.642	0.059	1.56

A) HSP = human specimen

B) PC = PreciControl

Overall repeatability and reproducibility for Elecsys HBsAg II

Sample	Mean (COI)	Intermediate precision SD (COI)	Intermediate precision % CV	Between site SD (COI)	Between site % CV	Between lot SD (COI)	Between lot % CV	Reproducibility SD (COI)	Reproducibility % CV
HSP 01	1.74	0.072	4.12	0.030	1.75	0.123	7.07	0.146	8.37
HSP 02	7.04	0.250	3.56	0.149	2.12	0.601	8.54	0.668	9.49
PC HBSAG1B	0.411	0.033	8.06	0.012	2.89	0.018	4.46	0.040	9.65
PC HBSAG2B	3.81	0.117	3.07	0.067	1.76	0.382	10.0	0.405	10.6

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

Analytical sensitivity

For determination of the cutoff sensitivity, a dilution series of 2 HBsAg reference standards (WHO standard 00/588, 2nd International Standard for HBsAg. Subtype adw2. Genotype A, and WHO standard 12/226, 3rd International Standard for HBsAg, HBV genotype B4, HBsAg subtype ayw1/adw2) were prepared. The measurements were performed in duplicate with 3 reagent lots on 1 **cobas** e 801 analytical unit at 1 site. The results from 3 kit lots at the COI of 0.90 were 0.023, 0.027, and 0.028 IU/mL (average 0.026 IU/mL) for NIBSC code 00/588 and 0.025, 0.026, and 0.028 IU/mL (average 0.026 IU/mL) for NIBSC code 12/226.

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.

No false non-reactive result due to high-dose hook effect was found with the Elecsys HBsAg II assay up to a concentration of 1.5 million IU/mL.

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.

Seroconversion

Seroconversion panels

Seroconversion sensitivity of the Elecsys HBsAg II assay was demonstrated by testing 20 commercially available seroconversion panels comparing Elecsys HBsAg II results to commercially licensed product. Results are summarized in the table below.

Panel ID	Elecsys HBsAg II first reactive result (bleed number)	Reactivity status by Elecsys HBsAg II Auto Confirm	Reference method first reactive result (bleed number)	Difference in number of bleeds (+/-)
HBV6271	3	Reactive	3	0
HBV6272	20	Reactive	20	0
HBV6274	1	Reactive	1	0
HBV6276	7	Reactive	7	0
HBV6277	6	Reactive	6	0
HBV6279	6	Reactive	6	0
HBV6286	5	Reactive	5	0
HBV6292	7	Reactive	7	0
HBV9072	12	Reactive	12	0
HBV9073	14	Reactive	14	0
HBV9074	17	Reactive	17	0
HBV11002	3	Reactive	3	0
HBV11011	9	Reactive	9	0
HBV11012	4	Reactive	4	0
HBV11016	6	Reactive	6	0
HBV11024	11	Reactive	11	0
HBV11029	9	Reactive	9	0
HBV11058	5	Reactive	5	0
HBV11059	5	Reactive	6	+1
HBV11069	9	Reactive	9	0

Clinical specificity

A total of 5569 fresh serum specimens and 5713 fresh plasma specimens from volunteer blood donors and 3002 plasmapheresis samples were collected at 4 donor centers. The initial and repeat reactive rates were 0.02 % (1/5569) for the serum specimens, 0.07 % (4/5713) and 0.05 % (3/5713), respectively, for the plasma specimens, and 0.07 % (2/3002) for the plasmapheresis samples. Repeatedly reactive specimens were further tested using the Elecsys HBsAg II Auto Confirm; 1 specimen was confirmed positive and 5 specimens were not confirmed. The 1 confirmed positive specimen was positive by a FDA-licensed HBV Qualitative DNA assay.

Specificity of Elecsys HBsAg II

Elecsys HBsAg II



Specimen category	Number tested	Initially reactive (% of total)	Repeatedly reactive (RR) (% of total)	Reactive by Elecsys HBsAg II Auto Confirm (% of RR)	Number confirmed positive ^{A)} (% of RR)	Specificity (%) (95 % CI ^{B)})
Volunteer blood donors - serum	5569	1 (0.02)	1 (0.02)	0 (0.00)	0 (0.00)	99.98 (5568/5569) (99.90, 100.00)
Volunteer blood donors - plasma	5713	4 (0.07)	3 (0.05)	1 (33.33)	1 (33.33)	99.96 (5710/5712) (99.87, 99.99)
Total volunteer blood donors	11282	5 (0.04)	4 (0.04)	1 (25.00)	1 (25.00)	99.97 (11278/11281) (99.92, 99.99)
Plasmapheresis donors - plasma	3002	2 (0.07)	2 (0.07)	0 (0.00)	0 (0.00)	99.93 (3000/3002) (99.76, 99.98)
Total donors	14284	7 (0.05)	6 (0.04)	1 (16.67)	1 (16.67)	99.96 (14278/14283) (99.92, 99.99)

A) Number confirmed positive by supplemental testing

B) CI = confidence interval

Specificity based on assumed zero prevalence of HBsAg in whole blood and plasmapheresis donors was estimated in this study to be 99.96 % (14278/14283) with a 95 % confidence interval of 99.92 % to 99.99 %.

Clinical sensitivity

A total of 582 specimens from the categories shown in the table below were tested using the Elecsys HBsAg II assay. All repeatedly reactive specimens were tested using the Elecsys HBsAg II Auto Confirm assay. Sensitivity was estimated to be 100 % (582/582) with a 95 % confidence interval of 99.34 % to 100 % for preselected positive specimens.

Sensitivity of Elecsys HBsAg II

Specimen category	Number tested	Repeatedly reactive (RR) (% of total)	Reactive by Elecsys HBsAg II Auto Confirm (% of RR)	Sensitivity (95 % CI ^{A)})
Acute HBV	80	80 (100)	80 (100)	100 (80/80) (95.42, 100)
Chronic HBV	186	186 (100)	186 (100)	100 (186/186) (97.98, 100)
HBsAg (Genotypes A-H)	19	19 (100)	19 (100)	100 (19/19) (83.18, 100)
HBsAg positive	297	297 (100)	297 (100)	100 (297/297) (98.72, 100)
Total	582	582 (100)	582 (100)	100 (582/582) (99.34, 100)

A) CI = confidence interval

A total of 462 specimens from individuals at increased risk for hepatitis and from individuals recovered from HBV infection were tested to demonstrate assay performance in an untested population of specimens which could potentially provide more positive outcomes than in a donor population.

Elecsys HBsAg II



Specimen category	Number tested	Repeatedly reactive (RR) (% of total)	Reactive by Elecsys HBsAg II Auto Confirm (% of total)	Number confirmed positive ^{A)} (% of RR) ^{B)}
Increased risk for hepatitis infection	409	4 (0.98)	2 (50.0)	2 (50.0)
HBV recovered	53	1 (1.89)	0 (N/A)	0 (N/A)
Total	462	5 (1.08)	2 (40.0)	2 (40.0)

A) Number confirmed positive by supplemental testing

B) The sensitivity and 95% confidence intervals are not estimated due to the small sample size

Other specimen conditions or disease states

A total of 311 samples containing potentially interfering substances were tested with the Elecsys HBsAg II assay comprising specimens:

- containing antibodies against acute HIV, HCV, HTLV-I/II, HDV, VZV, HAV, HSV, EBV, HEV
- from pregnant women with both single and multiparous pregnancy
- containing heterophilic autoantibodies (ANA), EBV, or human anti-mouse antibodies (HAMA)
- containing antibodies against *Candida* sp., *Escherichia coli*, *Treponema pallidum* (syphilis), *Toxoplasma gondii*, *Chlamydia trachomatis*, parvovirus, and rubella virus
- after vaccination against hepatitis A (HAV) and influenza
- for hyper-IgG / IgM interference
- containing autoimmune antibodies for Morbus Crohn and Colitis Ulcerosa
- from patients with alcohol induced hepatitis /cirrhosis
- from patients with systemic lupus erythematosus (SLE)

Only one false reactive sample (antibody against infectious agent of chlamydia) was found in samples with potentially cross-reacting factors.

Mutant detection

A total of 20 recombinant HBsAg proteins with mutations and 21 native samples with HBsAg mutations (including different HBV genotypes) were tested with the Elecsys HBsAg II assay to determine correct antigenic recognition of the HBsAg structure. The mutants contained important epitope clusters within amino acids 100-160, including the "a determinant" region (amino acid 124-147). All mutations were recognized with Elecsys HBsAg II.

Recombinant HBsAg proteins with mutations

Sample	Mutation	Elecsys HBsAg II reactivity
Mutant 1	F8L, R24K, N40S, G43R, L94S, M103I, 113A114, M133T, P142L, D144G	+
Mutant 2	T/A45S, C107R, M195I	+
Mutant 3	S132Y, P142S, G145R	+
Mutant 4	T123N	+
Mutant 5	G145K	+
Mutant 6	D144G	+
Mutant 7	D144A	+
Mutant 8	G145R	+
Mutant 9	I22RA123	+
Mutant 10	Q129P, F134R, P142L, D144E, G145K, S171F, L175S	+
Mutant 11	R122I	+
Mutant 12	M125T, T127P, P142A, G145R	+
Mutant 13	T131I	+
Mutant 14	C147S	+
Mutant 15	K141E	+
Mutant 16	S143L	+
Mutant 17	P142L	+

Sample	Mutation	Elecsys HBsAg II reactivity
Mutant 18	Y134S	+
Mutant 19	E164D	+
Mutant 20	I126S	+

Native samples with HBsAg mutation

Sample	Mutation	Elecsys HBsAg II reactivity
Mutant 1	A128V	+
Mutant 2	G145R	+
Mutant 3	S143T	+
Mutant 4	M133L	+
Mutant 5	G130R	+
Mutant 6	T125M, S143M	+
Mutant 7	G130N	+
Mutant 8	T125M	+
Mutant 9	S143L	+
Mutant 10	G145A	+
Mutant 11	M133I	+
Mutant 12	Q129H	+
Mutant 13	T140I	+
Mutant 14	G145V	+
Mutant 15	P127T	+
Mutant 16	S132F, G145R	+
Mutant 17	T126A	+
Mutant 18	S132Y	+
Mutant 19	M133T	+
Mutant 20	F134L	+
Mutant 21	T126I	+

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 24 hours after death.¹⁸ 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 Δ COI]	0.0233	-0.0377	-0.0551	0.00299
Cadaveric reactive [mean % recovery]	97.9	99.4	95.6	98.3

Reproducibility

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

Overall reproducibility for Elecsys HBsAg II

Specimen category	Number tested	Mean (COI)	Reproducibility SD (COI)	Reproducibility % CV
Cadaveric donor ^{A)}	360	1.81	0.104	5.76
Living donor	360	1.80	0.094	5.23

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 HBsAg II assay.

Overall specificity for Elecsys HBsAg II

Specimen category ^{A)}	Number tested	Number non-reactive (% of tested)	Number repeatedly reactive (% of tested)	Specificity (%) (95 % CI)
Cadaveric donor - Lot 1	55	55 (100)	0 (0.00)	100 (93.47, 100)
Cadaveric donor - Lot 2	55	55 (100)	0 (0.00)	100 (93.47, 100)
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 23 hours after death

Analytical sensitivity

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

Specimen category ^{A)}	Number tested	Mean (COI)	Number positive (% of tested)	Sensitivity (%) (95 % CI)
Cadaveric donor - Lot 1	55	1.99	55 (100)	100 (93.47, 100)
Cadaveric donor - Lot 2	55	1.78	55 (100)	100 (93.47, 100)
Cadaveric donor - Lot 3	55	2.10	55 (100)	100 (93.47, 100)
Living donor - Lot 1	55	2.13	55 (100)	100 (93.47, 100)
Living donor - Lot 2	55	2.00	55 (100)	100 (93.47, 100)
Living donor - Lot 3	55	2.09	55 (100)	100 (93.47, 100)

A) Cadaveric serum specimens were collected up to 24 hours after death

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



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 World Health Organization (WHO), 2022. Hepatitis B Fact sheet. Available at: <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b>
- 2 Kim DY, Han KH. Epidemiology and Surveillance of Hepatocellular Carcinoma. *Liver Cancer* 2012;1(1):2-14.
- 3 Liang TJ. Hepatitis B: The Virus and Disease. *Hepatology* 2009;49(5 Suppl):S13-21
- 4 Schweitzer A, Horn J, Mikolajczyk RT, et al. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. *Lancet* 2015;386(10003):1546-1555
- 5 Song Y, Bian Y, Petzold M, et al. Prevalence and Trend of Major Transfusion-Transmissible Infections among Blood Donors in Western China, 2005 through 2010. *PLoS One*. 2014 Apr 8;9(4):e94528.
- 6 Elgouhari HM, Abu-Rajab Tamini TI, Carey WD. Hepatitis B virus infection: understanding its epidemiology, course, and diagnosis. *Cleve Clin J Med* 2008;75(12):881-889
- 7 World Health Organization (WHO), 2009. Screening Donated Blood for Transfusion-Transmissible Infections. Recommendations. Available at: <https://apps.who.int/iris/handle/10665/44202> (last access May, 2022)
- 8 Trépo C, Chan HL, Lok A. Hepatitis B virus infection. *Lancet* 2014;384(9959):2053-2063.
- 9 Song JE, Kim DY. Diagnosis of hepatitis B. *Ann Transl Med* 2016;4(18):338. doi:10.21037/atm.2016.09.11
- 10 Yuen MF, Chen DS, Dusheiko GM, et al. Hepatitis B virus infection. *Nature Reviews Disease Primers* 2018;4:18035. doi: 10.1038/nrdp.2018.35.
- 11 European Association for Study of Liver & Asociacion Latinoamericana para el Estudio del Hígado. EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis. *Journal of Hepatology* 2015;63(1):237-264.
- 12 Seem DL, Lee I, Umscheid CA. PHS guideline for reducing human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission through organ transplantation. *Public Health Reports*. 2013;128(4):247–343.
- 13 FDA. Guidance for Industry. Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps). 2007. Available at: <https://www.fda.gov/files/vaccines,%20blood%20&%20biologics/published/Eligibility-Determination-for-Donors-of-Human-Cells--Tissues--and-Cellular-and-Tissue-Based-Products--Guidance-for-Industry.pdf>. Accessed 17 March 2022
- 14 WHO. Blood Donor Selection. Guidelines on Assessing Donor Suitability for Blood Donation. 2012. Available at: http://apps.who.int/iris/bitstream/handle/10665/76724/9789241548519_eng.pdf?ua=1?sequence=1. Accessed 17 March 2022
- 15 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.
- 16 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.
- 17 Rysgaard, C. D., Morris, C. S., Drees, D., Bebbler, T., Davis, S. R., Kulhavy, J., & Krasowski, M. D. (2012). Positive hepatitis B surface antigen tests due to recent vaccination: a persistent problem. *BMC Clinical Pathology*, 12(1). <https://doi.org/10.1186/1472-6890-12-15>
- 18 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

Additional information

For further information, refer to the User Guide for the corresponding analyzer, to the corresponding application sheets, and to the Method Sheets of all necessary components.

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.

COBAS, ELECSYS, NAVIFY, and PRECICONTROL are trademarks of Roche.

INTRALIPID is a trademark of Fresenius Kabi AG.

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

Elecsys HBsAg II



© 2026 Roche

Rx only



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

+800 5505 6606



Roche Diagnostics
9115 Hague Road
Indianapolis, IN 46256, USA
+1 866 744 6397



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. Several editorial and layout updates were made.
---------------	--