Elecsys Anti-HBs II

cobas®

REF		Σ	SYSTEM
08498598160	08498598501	100	**cobas e** 601

English

For use in the USA only

System information

For **cobas e** 601 analyzer: Application Code Number 765

Warning

- Federal law restricts this device to sale by or on the order of a physician.
- Assay performance characteristics have not been established when the Elecsys Anti-HBs II assay is used in conjunction with other manufacturers' assays for specific HBV serological markers. Users are responsible for establishing their own performance characteristics.
- This assay has not been FDA licensed for the screening of blood or plasma donors.

Intended use

Immunoassay for the in vitro quantitative determination of total antibodies to the hepatitis B surface antigen (HBsAg) in human adult, pregnant women, and pediatric (ages 2 to 21 years) serum and plasma (K_2-EDTA and K_3-EDTA). Assay results may be used as an aid in the determination of susceptibility to hepatitis B virus (HBV) infection for individuals prior to or following HBV vaccination; or where vaccination status is unknown.

Assay results may be used with other HBV serological markers for the laboratory diagnosis of HBV disease associated with HBV infection. A reactive assay result will allow a differential diagnosis in individuals displaying signs and symptoms of hepatitis in whom etiology is unknown. The detection of anti-HBs is indicative of laboratory diagnosis of seroconversion from hepatitis B virus (HBV) infection or from vaccination.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on the **cobas e** 601 immunoassay analyzer.

Summary

Anti-HBs is a specific (generally IgG) antibody that is directed against the hepatitis B surface antigen (HBsAg).[1,2] Anti-HBs can be detected several weeks after the disappearance of hepatitis B surface antigen.[3,4] Anti-HBs can be formed following a hepatitis B infection or after hepatitis B vaccination.[3,4] Antibodies are formed against the HBsAg determinant a, which is common to all subtypes, and against subtype-specific determinants.[1,5,6]

Anti-HBs assays are used within the scope of hepatitis B vaccination to check the necessity and success of vaccination.[2,4,7] In addition, anti-HBs assays are used to monitor the course of disease following acute hepatitis B infection.[3]

The Elecsys Anti-HBs II assay uses a mixture of purified antigens from human serum (HBsAg subtype ad), and recombinant HBsAg subtype ay from CHO (Chinese Hamster Ovary) cells.

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: Anti-HBs in the sample (40 µL), biotinylated HBsAg (ad/ay), and HBsAg (ad/ay) labeled with a ruthenium complex[a)] react to form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode or e-barcode.

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

Reagents - working solutions

The reagent rackpack (M, R1, R2) is labeled as A-HBS 2.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 HBsAg~biotin (gray cap), 1 bottle, 10 mL: Biotinylated HBsAg (ad/ay) human/recombinant, > 0.5 mg/L; MES[b)] buffer 85 mmol/L, pH 6.5; preservative.

R2 HBsAg~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 8 mL: HBsAg (ad/ay) human/recombinant, labeled with ruthenium complex > 0.3 mg/L; MES buffer 85 mmol/L, pH 6.5; preservative.

b) MES = 2-morpholino-ethane sulfonic acid

A-HBSII Cal1 Calibrator 1 (white cap), 2 bottles of 1.3 mL each: Anti-HBs (human) in human serum; preservative.

A-HBSII Cal2 Calibrator 2 (black cap), 2 bottles of 1.3 mL each: Anti-HBs (human) in human serum; preservative.

Precautions and warnings

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

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

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

Warning

H317 May cause an allergic skin reaction.

Prevention:

P261 Avoid breathing dust/fume/gas/mist/vapours/spray.

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.

Product safety labeling follows EU GHS guidance.

Contact phone: 1-800-428-2336

All human material should be considered potentially infectious. The calibrators (A-HBSII Cal1 and A-HBSII Cal2) 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 used assays approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

The HBsAg starting material used was inactivated prior to labeling with biotin or ruthenium by heating to 60 °C for 15 hours. In addition, any virus particles remaining were removed by ultracentrifugation.

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.[8,9]

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

Reagent handling

The reagents in the kit are ready-for-use and are supplied 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.

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

Storage and stability

Store at 2-8 °C.

Do not freeze.

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

Stability of the reagent rackpack	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	8 weeks
on **cobas e** 601 analyzer	8 weeks

Stability of the calibrators	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	8 weeks
on **cobas e** 601 analyzer 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

Only the specimens listed below were tested and found acceptable.

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

K_2-EDTA and K_3-EDTA plasma. K_2-EDTA plasma tubes containing separating gel can be used.

Stable for 4 days at 20-25 °C, 6 days at 2-8 °C, 4 months at -20 °C (± 5 °C). The samples may be frozen 6 times.

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

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.

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

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

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Materials provided

See “Reagents – working solutions” section for reagents.

- 2 x 6 bottle labels

Materials required (but not provided)

- REF 11876317160, PreciControl Anti-HBs, for 8 x 1.3 mL
- REF 05192943190, Diluent Universal 2, 2 x 36 mL sample diluent
- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles
- General laboratory equipment
- **cobas e** 601 analyzer

Additional materials for **cobas e** 601 analyzer:

- REF 04880340190, ProCell M, 2 x 2 L system buffer
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- REF 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- REF 12102137001, AssayTip/AssayCup, 48 magazines x 84 reaction cups or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M
- REF 11298500160, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

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

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

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

Place the calibrators in the sample zone.

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

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

After calibration has been performed, discard used vials.

Calibration

Traceability: This method has been standardized against the 1st WHO Reference Standard 1977.

Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using the relevant CalSet.

Calibration frequency: Calibration must be performed once per reagent lot using A-HBSII Cal1, A-HBSII Cal2 and fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer).

Renewed calibration is recommended as follows:

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

Range (in mIU/mL) for the calibrators: 4-15 for calibrator 1 (A-HBSII Cal1) and 200-700 for calibrator 2 (A-HBSII Cal2).

Quality control

For quality control, use PreciControl Anti-HBs.

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

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

If necessary, repeat the measurement of the samples concerned.

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

Calculation

The analyzer automatically calculates the analyte concentration of each sample in IU/L (IU/L is equivalent to mIU/mL).

Interpretation of the results

The accepted criterion for immunity to HBV is ≥ 10 mIU/mL of anti-HBs, with mIU defined by the WHO Reference Preparation.

- A result of < 10 mIU/mL indicates that the sample is non-reactive or the titer is below a level consistent with protective immunity against HBV infection.
- A result of ≥ 10 mIU/mL indicates that the sample is reactive for anti-HBs. This result is consistent with levels of anti-HBs at ≥ 10 mIU/mL, which indicates that anti-HBs has been detected at levels consistent with protective immunity against HBV infection.

Elecsys Anti-HBs II result	Result interpretation	Clinical interpretation of HBV immune status
< 10 mIU/mL	Non-reactive	Individual is considered to be not immune to infection with HBV.
≥ 10 mIU/mL	Reactive	Anti-HBs concentration detected at ≥ 10 mIU/mL. Individual is considered to be immune to infection with HBV.

If there is a change in the test used during the monitoring of vaccination protection, then the anti-HBs values obtained upon changing over to the new test must be confirmed by parallel measurements with both methods.

Vaccination strategies in certain risk groups are based on the measured anti-HBs concentration.[10] Respective recommendations are given by national or regional guidelines.

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	≤ 513 µmol/L or ≤ 30 mg/dL
Hemoglobin	≤ 0.62 mmol/L or ≤ 1.00 g/dL
Intralipid	≤ 1500 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Human serum albumin	≤ 7.0 g/dL
Rheumatoid factors	≤ 1200 IU/mL
IgG	≤ 7.0 g/dL
IgA	≤ 1.6 g/dL
IgM	≤ 1.0 g/dL

Criterion: Recovery for samples from Limit of Detection to 10 mIU/mL: ≤ ± 2 mIU/mL or samples > 10 mIU/mL: ≤ ± 20 % of initial value.

This assay has no biotin interference in serum concentrations up to 1200 ng/mL. Pharmacokinetic studies have shown that serum concentrations of biotin can reach up to 355 ng/mL within the first hour after biotin ingestion for subjects consuming supplements of 20 mg biotin per day[11] and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin[12].

A drug interference study was performed with 17 commonly used and 10 special therapeutic drugs. Each drug was found to be non-interfering at the claimed concentrations in the following table.

Compound	Concentration tested mg/L
Acetylcysteine	150
Ampicillin-Na	1000
Ascorbic acid	300
Cyclosporine	5
Cefoxitin	2500
Heparin	5000 U/L
Intralipid	10000
Levodopa	20
Methyldopa	20
Metronidazole	200
Phenylbutazone	400
Doxycycline	50
Acetylsalicylic acid	1000
Rifampicin	60
Acetaminophen	200
Ibuprofen	500
Theophylline	100
Ca-dobesilate	1500
Adefovir	10
Telbivudine	600
Tenovir	245
Lamivudin	300
Entecavir	1
Interferon alfa-2a	9 Mio IU/L
Interferon alfa-2b	20 Mio IU/L
PEG interferon alfa-2a	0.036
PEG interferon alfa-2b	0.036

Drug interferences are measured based on recommendations given in CLSI guidelines EP07 and EP37 and other published literature. Effects of concentrations exceeding these recommendations have not been characterized.

Due to high-dose hook effect[c], results from anti-HBs concentrations with samples > 1000 mIU/mL to 500,000 mIU/mL were properly detected as ≥ 100 mIU/mL. In rare cases, high-dose hook effect cannot be excluded and therefore any unexpected low result should be diluted 1:100 (refer to chapter "Dilution") and tested with dilution.

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

Samples with antibodies to Rubella may cross react and produce false positive results.

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

c) High-dose hook effect: A sample with a true concentration clearly above the measuring range, but found within the measuring range.

Limits and ranges

Measuring range

3.5-1000 mIU/mL (defined by the Limit of Quantitation and the maximum of the master curve). Values below the Limit of Quantitation are reported as < 3.5 mIU/mL. Values above the measuring range are reported as > 1000 mIU/mL (or up to 100000 mIU/mL for 100-fold diluted samples).

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 1.5 mIU/mL

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Limit of Detection = 2.0 mIU/mL

Limit of Quantitation = 3.5 mIU/mL

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of ≤ 20 %.

Dilution

Samples with anti-HBs concentrations above the measuring range can be diluted with Diluent Universal. The recommended dilution is 1:100 (either automatically by the analyzers or manually). The concentration of the diluted sample must be > 10 mIU/mL.

After manual dilution, multiply the result by the dilution factor.

After dilution by the analyzers, the software automatically takes the dilution into account when calculating the sample concentration.

Manual dilution can also be made with negative human serum.

Note: Antibodies to HBsAg are heterogeneous. In some isolated cases, this may lead to non-linear dilution behavior.

Expected values

The expected values were obtained from 2397 subjects at increased risk for hepatitis (asymptomatic and symptomatic), regardless of age or pregnancy status, collected within the United States. The adult subjects were 1 % AIAN (American Indian/Alaskan Native), 0.73 % Asian, 49.6 % African American/Black, 45.9 % Caucasian, 0.19 % Hawaiian Native/Pacific Islander, 2.1 % other and 0.39 % unknown race. The pediatric subjects were 3.1 % Asian, 25.0 % African American/Black, 67.2 % Caucasian, 0.78 % Hawaiian Native/Pacific Islander, 3.1 % other and 0.78 % unknown race. The pregnant subjects were 8.6 % African American/Black and 90.0 % Caucasian. No supplemental samples or ex-US pregnant subjects were included in this study. The following table summarizes the Elecsys Anti-HBs II test results by age and gender.

Elecsys Anti-HBs II results by age range and sex for individuals at increased risk for hepatitis

		Elecsys Anti-HBs II		
Age	**Sex**	**Reactive**	**Non-reactive**	**Total**
2 to 11	Female	5 (45.5)	6 (54.6)	11
	Male	6 (46.2)	7 (53.9)	13
12 to 21	Female	52 (44.8)	64 (55.2)	116
	Male	18 (38.3)	29 (61.7)	47
22 to 29	Female	149 (62.3)	90 (37.7)	239
	Male	57 (52.3)	52 (47.7)	109
30 to 39	Female	108 (46.2)	126 (53.9)	234
	Male	64 (36.0)	114 (64.0)	178
40 to 49	Female	120 (45.8)	142 (54.2)	262
	Male	111 (32.7)	228 (67.3)	339
50 to 59	Female	124 (47.9)	135 (52.1)	259
	Male	164 (42.9)	218 (57.1)	382
60 to 69	Female	27 (34.2)	52 (65.8)	79
	Male	40 (37.0)	68 (63.0)	108
70 to 79	Female	3 (30.0)	7 (70.0)	10
	Male	2 (25.0)	6 (75.0)	8

Elecsys Anti-HBs II results by age range and sex for individuals at increased risk for hepatitis

		Elecsys Anti-HBs II		
Age	**Sex**	**Reactive**	**Non-reactive**	**Total**
≥ 80	Female	0 (0.00)	3 (100)	3
	Male	0 (0.00)	0 (0.00)	0
Totals	Female	588 (48.5)	625 (51.5)	1213
	Male	462 (39.0)	722 (61.0)	1184
All	All	1050 (43.8)	1347 (56.2)	2397

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

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

Precision

Precision was determined on the **cobas e** 601 analyzer using Elecsys reagents and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute). Results were generated from an 8 member panel and 2 controls, assayed in 2 runs per day in duplicate each for 12 days (n = 48). The following results were obtained:

cobas e 601 analyzer					
		Repeatability[d]		**Intermediate precision**[e]	
Sample[f]	Mean mIU/mL	SD mIU/mL	CV %	SD mIU/mL	CV %
Human serum 1	3.94	0.410	10.4	0.462	11.7
Human serum 2	8.57	0.384	4.5	0.587	6.8
Human serum 3	10.8	0.373	3.5	0.535	5.0
Human serum 4	100	2.10	2.1	3.20	3.2
Human serum 5	12.2	0.455	3.7	0.686	5.6
Human serum 6	13.1	0.303	2.3	0.580	4.4
Human serum 7	577	11.2	1.9	19.1	3.3
Human serum 8	949	14.3	1.5	31.1	3.3
PreciControl A-HBS1	0.239	0.616	258	0.986	413
PreciControl A-HBS2	107	1.58	1.5	3.71	3.5

d) Repeatability = within-run precision

e) Intermediate precision = within-laboratory precision

f) One human serum pool member was excluded as mean recovery was 1.15 mIU/mL

Reproducibility

Reproducibility was determined with a panel of 6 human sera and 2 controls. Samples were measured in triplicate using 3 reagent lots, in 2 runs per day for 5 days at 3 sites, according to CLSI EP15-A2 and CLSI EP05-A3 (n = 180). Variance components were calculated absolutely, as well as in relative contribution to the total size variance. The following results were obtained:

Elecsys Anti-HBs II reproducibility on the **cobas e** 601 analyzer					
		Repeatability		**Between-run**	
Sample	Mean mIU/mL	SD mIU/mL	CV %	SD mIU/mL	CV %
HSP[g]01	8.87	0.252	2.85	0.171	1.93
HSP 06	9.85	0.268	2.72	0.980	0.99
HSP 02	11.22	0.279	2.49	0.191	1.70
HSP 05	77.35	1.11	1.44	0.794	1.03
HSP 03	379.6	4.33	1.14	4.78	1.26

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Elecsys Anti-HBs II reproducibility on the **cobas e** 601 analyzer					
		Repeatability		**Between-run**	
Sample	Mean mIU/mL	SD mIU/mL	CV %	SD mIU/mL	CV %
HSP 04	823.8	10.90	1.32	9.33	1.13
PC[h)]A-HBS1	0.002	0.029	1341	0.000	0.00
PC A-HBS2	95.61	1.20	1.26	1.51	1.58

g) HSP = human serum pool

h) PC = PreciControl

Elecsys Anti-HBs II reproducibility on the **cobas e** 601 analyzer					
		Between-day		**Between-lot**	
Sample	Mean mIU/mL	SD mIU/mL	CV %	SD mIU/mL	CV %
HSP 01	8.87	0.048	0.55	0.478	5.39
HSP 06	9.85	0.193	1.96	0.729	7.40
HSP 02	11.22	0.124	1.11	0.704	6.28
HSP 05	77.35	0.778	1.01	1.86	2.40
HSP 03	379.6	3.21	0.85	12.46	3.28
HSP 04	823.8	6.26	0.76	15.46	1.88
PC A-HBS1	0.002	0.000	0.00	0.000	0.00
PC-A-HBS2	95.61	0.437	0.46	1.65	1.73

Elecsys Anti-HBs II reproducibility on the **cobas e** 601 analyzer					
		Between-lab		**Reproducibility**	
Sample	Mean mIU/mL	SD mIU/mL	CV %	SD mIU/mL	CV %
HSP 01	8.87	0.000	0.00	0.569	6.42
HSP 06	9.85	0.000	0.00	0.806	8.18
HSP 02	11.22	0.000	0.00	0.791	7.05
HSP 05	77.35	2.32	3.00	3.36	4.35
HSP 03	379.6	0.000	0.00	14.40	3.79
HSP 04	823.8	23.52	2.86	32.21	3.91
PC A-HBS1	0.002	0.000	0.00	0.029	1342
PC-A-HBS2	95.61	2.89	3.03	3.88	4.05

Analytical specificity

Analytical specificity with medical conditions and diseases with similar etiology or symptoms to hepatitis B viral infection was tested on 96 samples. These samples were not prescreened for the presence of anti-HBs. Testing with the reference assay shows that these samples were positive for anti-HBs. The presence of potential interferent did not change the reactive result (there were no false negatives observed) with the Elecsys Anti-HBs II assay.

- Immune disorders (Systemic Lupus Erythematosis - SLE, ANA antibody and Rheumatoid Factor - RF) showed specificity of 100 %
- Viral infections (CMV, EBV, HAV, HCV, HEV, Herpes Simplex Virus, HTLV, Parvovirus B19, Rubella, Varicella Zoster) showed specificity of 100 %
- Non-viral disorders (Syphilis and Toxoplasmosis) showed specificity of 100 %
- Non-viral liver disease (various cirrhosis, other chronic non-alcoholic liver disease, non-alcoholic steatohepatitis, acute liver failure, fatty infiltrate liver, autoimmune hepatitis, chronic passive congestion liver, jaundice, abdominal pain/pelvic mass, liver abscess, liver lesion, malignant neoplasm of liver and intrahepatic bile ducts) showed specificity of 100 %
- Flu vaccination showed specificity of 100 %

96 positive anti-HBs samples tested by the reference method, Elecsys Anti-HBs assay, were tested for potentially cross-reactive medical conditions or diseases with similar etiology or symptoms to hepatitis B viral infection using the Elecsys Anti-HBs II assay. The following results were observed.

Reactivity of the Elecsys Anti-HBs II assay in individuals with various medical conditions				
		Elecsys Anti-HBs II		
Category	**Subcategory**	**RX[i)]**	**NR[j)]**	**Total**
Immune disorders	ANA	3	0	3
	RF	1	0	1
	SLE	1	0	1
Infections/disorders	T. pallidum	5	0	5
	Toxoplasmosis	9	0	9
Infectious viral	CMV	8	0	8
	EBV	5	0	5
	HAV	6	0	6
	HCV	2	0	2
	HIV	6	0	6
	HSV	9	0	9
	HTLV	4	0	4
	Parvo B19	7	0	7
	Rubella	10	0	10
	VZV	6	0	6
Non-viral liver disease	Alcohol liver disease	2	0	2
	Other non-viral liver disease	5	0	5
	Primary biliary cirrhosis	1	0	1
Vaccination	Influenza	6	0	6
Total		96	0	96

i) RX = reactive

j) NR = non-reactive

Cross-reactivity

A total of 187 negative anti-HBs samples tested by the reference method, Elecsys Anti-HBs assay, were tested for potentially cross-reactive medical conditions or diseases with similar etiology or symptoms to hepatitis B viral infection using the Elecsys Anti-HBs II assay. The following percent of cross-reactivity was observed: SLE 9 %, EBV 10 %, HCV 9 %, HEV 5 %, Rubella 20 %, VZV 11 %. The following results were observed.

Reactivity of the Elecsys Anti-HBs II assay in individuals with various medical conditions				
		Elecsys Anti-HBs II		
Category	**Subcategory**	**RX[k)]**	**NR[l)]**	**Total**
Immune disorders	ANA	0	12	12
	RF	0	14	14
	SLE	1	10	11
Infections/disorders	T. pallidum	0	10	10
	Toxoplasmosis	0	6	6
Infectious viral	CMV	0	7	7
	EBV	1	9	10
	HAV	0	4	4

Reactivity of the Elecsys Anti-HBs II assay in individuals with various medical conditions				
	HCV	1	10	11
	HEV	1	18	19
	HIV	0	9	9
	HSV	0	6	6
	HTLV	0	10	10
	Parvo B19	0	8	8
	Rubella	1	4	5
	VZV	1	8	9
Non-viral liver disease	Alcohol liver disease	0	4	4
	Other non-viral liver disease	0	2	2
	Primary biliary cirrhosis	0	26	26
Vaccination	Influenza	0	4	4
Total		6	181	187

k) RX = reactive

l) NR = non-reactive

Seroconversion sensitivity

Seroconversion sensitivity was evaluated by testing 11 commercially available seroconversion panels and comparing the Elecsys Anti-HBs II assay and the reference, Elecsys Anti-HBs assay.

Days to evidence of seroconversion for Elecsys Anti-HBs II compared to the reference assay, Elecsys Anti-HBs					
	Elecsys Anti-HBs		Elecsys Anti-HBs II		
Panel ID	NR[m)]	RX[n)]	NR[m)]	RX[n)]	
Initially negative/non-reactive, converted to positive/reactive					**Difference in days to Elecsys Anti-HBs II reactivity (Reference - Test)**
6281	43	50	43	50	0
6506	41	55	55	69	+14
6508	70	84	70	84	0
6510	70	84	70	84	0
6529	42	56	42	56	0
6534	14	29	29	43	+14
PHM 935B[o)]	231	262	246	262	0
Initially positive/reactive, converted to negative/non-reactive					**Difference in days of sustained initial reactivity (Reference - Test)**
6272	108	104	104	101	-3
11000[p)]	26	19	21	19	0

m) NR = non-reactive

n) RX = reactive

o) Elecsys Anti-HBs II was negative on day 246, while Elecsys Anti-HBs was indeterminate on day 246

p) Elecsys Anti-HBs II was negative on day 21, while Elecsys Anti-HBs was indeterminate

Seven panels demonstrated conversion of negative/non-reactive to positive/reactive status. Performance in 5 of the panels was equivalent, while the Elecsys Anti-HBs II assay showed conversion to reactivity 1 draw later (+14 days later) in 2 panels. Two panels demonstrated conversion from positive/reactive to negative/non-reactive status in both assays. Performance in 1 panel was equivalent, while the Elecsys Anti-HBs II assay showed conversion to negative/non-reactive 1 draw earlier (-3 days earlier) in the other panel. Two panels did not convert to positive/reactive status. Panels 9092 and RP-017 were negative/non-reactive throughout in both assays. Overall seroconversion performance was equivalent to the reference performance.

Clinical performance

A multi-center study was conducted to characterize the performance of the Elecsys Anti-HBs II assay on the **cobas e** 601 analyzer against the reference assay, Elecsys Anti-HBs, with individuals from defined populations. Performance of the Elecsys Anti-HBs II assay was assessed by testing a total of 4047 samples from adult, pediatric and pregnant subjects at increased risk, and vaccination subjects, at 3 different study sites. All subjects were tested using FDA-approved reference methods. The 4047 subjects were comprised of 2067 adult subjects at increased risk (45.6 % female and 54.4 % male), 128 pediatric subjects (53.1 % female and 46.9 % male), 218 pregnant at increased risk subjects, and 70 vaccination subjects (45.7 % female and 54.3 % male), along with 692 supplemental samples (18.5 % female and 81.4 % male), 588 pregnant at low risk subjects and 284 specificity samples (57.0 % female and 27.5 % male), and were tested with the Elecsys Anti-HBs II assay and the Elecsys Anti-HBs assay. The supplemental cohort was used to provide an adequate number for both acute and chronic individuals. The 3 sites tested the at-risk and supplemental specimens with a full panel of anti-HBc IgM, anti-HBc, HBsAg, HBeAg, anti-HBe and anti-HBs (reference) for serological characterization. The study included the following races: Caucasian, African-American/Black, Asian, American Indian/Alaskan Native and Hawaiian Native/Pacific Islander.

Serological classification

HBV classifications were determined based on the constellation of test results from FDA-approved methodologies for the various HBV markers. The interpretation of HBV classification made for each of the serological profiles observed is presented in the following table:

Serological classification by FDA-approved HBV panel						
	HBsAg	HBeAg	Anti-HBc IgM	Anti-HBc	Anti-HBe	Anti-HBs
Acute	(+)	(+)	(+)	(+)	(-), (+)	(-)
Acute	(+)	(+)	(-), (+)	(-)	(-)	(-)
Acute	(+)	(-)	(-)	(-)	(-)	(-)
Acute	(+)	(+)	eq	(+)	(-), (+)	(-)
Acute	(+)	(-)	(+)	(+)	(-)	(-)
Acute	(+)	(-)	eq	(+)	(+)	(-)
Acute (late)	(+)	(-)	(+)	(+)	(+)	(-), (+)
Chronic	(+)	(+)	(+)	(+)	(+)	(+)
Chronic	(+)	(-)	(-)	(+)	(+)	(-), (+)
Chronic	(+)	(-)	(-)	(+)	eq	(-)
Chronic	(+)	(-)	(-)	(+)	(-)	(-), (+)
Chronic	(+)	(+)	(+)	(+)	(-)	(+)
Chronic	(+)	(+)	(-)	(+)	(-)	(-), (+)
Chronic	(+)	(+)	(-)	(+)	(+)	(-)
Early recovery	(-)	(-)	(-)	(+)	(-), eq, (+)	(-)
Early recovery	(-)	(-)	(+)	(+)	(-)	(-), (+)
Early recovery	(-)	(-)	(+)	(+)	(+)	(-), (+)
Recovery	(-)	(-)	(-)	(-), (+)	(+)	(+)
Recovery	(-)	(-)	(-)	(+)	(+)	eq
Recovery	(-)	(-)	(-)	(+)	eq	(+)

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Serological classification by FDA-approved HBV panel						
	HBsAg	HBeAg	Anti-HBc IgM	Anti-HBc	Anti-HBe	Anti-HBs
Recovered or immune due to natural infection	(-)	(-)	(-)	(+)	(-)	(+), eq
HBV vaccine response	(-)	(-)	(-)	(-)	(-)	(+)
HBV vaccine response	(-)	(-)	(-)	(-)	(-)	eq
Not previously infected	(-)	(-)	(-)	(-)	(-)	(-)
Not interpretable	(-)	(+)	(-)	(+)	(-)	(+)
Not interpretable	(-)	(-)	(-)	(-)	(+)	(-)
Not interpretable	(-)	(+)	(-)	(+)	(+)	(-)
Not interpretable	(-)	(+)	(-)	(-)	(-)	(-), eq, (+)

Results by specimen classification

Prospective adult subjects

The following table compares the Elecsys Anti-HBs II assay results on the **cobas e** 601 analyzer with results from the reference, Elecsys Anti-HBs assay, for the 2067 prospectively collected adult subjects at increased risk for hepatitis.

	Elecsys Anti-HBs						
	Pos[q)]		Ind[r)]		Neg[s)]		
	Elecsys Anti-HBs II		Elecsys Anti-HBs II		Elecsys Anti-HBs II		
HBV classification	**RX[t)]**	**NR[u)]**	**RX[t)]**	**NR[u)]**	**RX[t)]**	**NR[u)]**	**Total**
Acute	0	0	0	0	0	7	7
Chronic	1	0	0	0	0	31	32
Early recovery	5	0	0	0	26	167	198
Recovery	130	0	1	0	0	0	131
Recovered	239	3	4	2	0	0	248
HBV vaccination	491	5	1	0	0	0	497
Not previously infected	0	0	0	0	10	934	944
Not interpretable	2	1	0	1	0	6	10
Total	1868	9	6	3	36	1145	2067

q) Pos = positive for Elecsys Anti-HBs

r) Ind = indeterminate for Elecsys Anti-HBs

s) Neg = negative for Elecsys Anti-HBs

t) RX - reacitve

u) NR = non-reacitve

Percent agreement prospectively collected adult subjects

The table below summarizes the positive and negative percent agreement between the Elecsys Anti-HBs II assay on the **cobas e** 601 analyzer and the reference, Elecsys Anti-HBs assay, for the 2067 prospectively collected adult subjects for each disease classification. The table provides the upper and lower 95 % exact confidence intervals (CI). The reactive HBsAg cohorts represented the low prevalence of acute and chronic subjects.

HBV classification				
	Positive percent agreement		Negative percent agreement	
	% (ratio)	95 % Exact CI	% (ratio)	95 % Exact CI
Acute	n/a (0/0)	n/a (0/0)	100 (7/7)	59.0 to 100
Chronic	100 (1/1)	2.50 to 100	100 (31/31)	88.8 to 100
Early recovery	100 (5/5)	47.8 to 100	86.5 (167/193)	80.9 to 91.0
Recovery	100 (130/130)	97.2 to 100	0.00 (0/1)	0.00 to 97.5
Recovered	98.0 (239/244)	95.3 to 99.3	0.00 (0/4)	0.00 to 60.2
HBV vaccination	99.0 (491/496)	97.7 to 99.7	0.00 (0/1)	0.00 to 97.5
Not previously infected	n/a (0/0)	n/a (0/0)	98.9 (934/944)	98.1 to 99.5
Not interpretable	50.0 (2/4)	6.76 to 93.2	100 (6/6)	54.1 to 100
Total	98.6 (868/880)	97.6 to 99.3	96.5 (1145/1187)	5.3 to 97.4

Retrospective adult subjects

The following table compares the Elecsys Anti-HBs II assay results on the **cobas e** 601 analyzer with results from the reference, Elecsys Anti-HBs assay, for the 692 retrospectively collected adult subjects at increased risk for hepatitis. These supplemental specimens were aquired to enhance the low prevalence reactive hepatitis B markers and disease states.

	Elecsys Anti-HBs						
	Pos		Ind		Neg		
	Elecsys Anti-HBs II		Elecsys Anti-HBs II		Elecsys Anti-HBs II		
HBV classification	**RX[v)]**	**NR[w)]**	**RX[v)]**	**NR[w)]**	**RX[v)]**	**NR[w)]**	**Total**
Acute	3	0	0	0	2	70	75
Chronic	7	4	0	0	2	305	318
Early recovery	0	0	0	0	5	11	16
Recovery	197	0	1	1	0	0	199
Recovered	80	0	3	0	0	0	83
Not previously infected	0	0	0	0	0	1	1
Total	287	4	4	1	9	387	692

v) RX = reactive

w) NR = non-reactive

Percent agreement retrospectively collected adult subjects

The table below summarizes the positive and negative percent agreement between the Elecsys Anti-HBs II assay on the **cobas e** 601 analyzer and the reference, Elecsys Anti-HBs assay, for the 692 retrospectively collected adult subjects for each disease classification. The table provides the upper and lower 95 % exact confidence intervals (CI).

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HBV classification				
	Positive percent agreement		Negative percent agreement	
	% (ratio)	95 % Exact CI	% (ratio)	95 % Exact CI
Acute	100 (3/3)	29.2 to 100	97.2 (70/72)	90.3 to 99.7
Chronic	63.6 (7/11)	30.8 to 89.1	99.4 (305/307)	97.7 to 99.9
Early recovery	n/a (0/0)	n/a (0/0)	68.8 (11/16)	41.3 to 89.0
Recovery	99.5 (197/198)	97.2 to 100	0.00 (0/1)	0.00 to 97.5
Recovered	100 (80/80)	95.5 to 100	0.00 (0/3)	0.00 to 70.8
Not previously infected	n/a (0/0)	n/a (0/0)	100 (1/1)	2.50 to 100
Total	98.3 (287/292)	96.05 to 99.4	96.8 (387/400)	94.5 to 98.3

Combined results of prospective and retrospective adult subjects

The following table compares the Elecsys Anti-HBs II assay results on the **cobas e** 601 analyzer with results from the reference, Elecsys Anti-HBs assay, for both the prospective and retrospective specimens for HBV classification.

	Elecsys Anti-HBs						
	Pos		Ind		Neg		
	Elecsys Anti-HBs II		Elecsys Anti-HBs II		Elecsys Anti-HBs II		
HBV classification	**RX[x)]**	**NR[y)]**	**RX[x)]**	**NR[y)]**	**RX[x)]**	**NR[y)]**	**Total**
Acute	3	0	0	0	2	77	82
Chronic	8	4	0	0	2	336	350
Early recovery	5	0	0	0	31	178	214
Not interpretable	2	1	1	1	0	6	10
Not previously infected	0	0	0	0	10	935	945
Recovered	319	3	2	2	0	0	331
Recovery	327	0	1	1	0	0	330
Vaccination	491	5	0	0	0	0	497
Total	1155	13	4	4	45	1532	2759

x) RX = reactive

y) NR = non-reactive

Combined prospective and retrospective adult subject percent agreement

The table below summarizes the positive and negative percent agreement between the Elecsys Anti-HBs II assay on the **cobas e** 601 analyzer and the reference, Elecsys Anti-HBs assay, for the 2759 prospective and retrospective specimens for HBV classification. The table provides the upper and lower 95 % exact confidence intervals (CI).

HBV classification				
	Positive percent agreement		Negative percent agreement	
	% (ratio)	95 % Exact CI	% (ratio)	95 % Exact CI
Acute	100 (3/3)	29.2 to 100	97.5 (77/79)	91.2 to 99.7
Chronic	66.7 (8/12)	34.9 to 90.1	99.4 (336/338)	97.9 to 99.9
Early recovery	100 (5/5)	47.8 to 100	85.2 (178/209)	79.6 to 89.7
Recovery	99.7 (327/328)	98.3 to 100	0.00 (0/2)	0.00 to 84.2
Recovered	98.5 (319/324)	96.4 to 99.5	0.00 (0/7)	0.00 to 41.0
Not previously infected	n/a (0/0	n/a	98.9 (935/945)	98.1 to 99.5
Vaccination	n/a (0/0)	97.7 to 99.7	0.00 (0/1)	0.00 to 97.5
Not interpretable	50.0 (2/4)	6.76 to 93.2	100 (6/6)	54.1 to 100
Total	98.6 (1155/1172)	97.7 to 99.2	96.5 (1532/1587)	5.5 to 97.4

Clinical performance with individuals having received hepatitis B vaccine

Pre- and post-vaccination samples were collected from a minimum of 71 subjects who were inoculated with 1 of 3 US-approved hepatitis B vaccines. Testing of the pre-vaccination samples found all 71 samples to be negative for anti-HBs, but 1 subject was anti-HBc positive and was therefore, excluded. All 17 nonresponder specimens were negative/non-reactive in another FDA-approved anti-HBs assay. Results of the concordance for the vaccinated subjects are shown in the following table:

	Elecsys Anti-HBs								
	Pre-vaccination			Post-vaccination			Total		
Elecsys Anti-HBs II	**Pos**	**Ind**	**Neg**	**Pos**	**Ind**	**Neg**	**Pos**	**Ind**	**Neg**
Reactive	0	0	0	52	0	0	52	0	0
Non-reactive	0	0	70	1	0	17	1	0	87
Total	0	0	70	53	0	17	53	0	87
PPA[z)]	(0/0)			98.1 (52/53)			98.1 (52/53)		
95 % CI[aa)]	n/a			89.9 to 100.0			89.9 to 100.0		
NPA[ab)]	100 (70/70)			100 (17/17)			100 (87/87)		
95 % CI	94.9 to 100			80.5 to 100			95.9 to 100		

z) PPA = positive percent agreement

aa) CI = confidence interval

ab) NPA = negative percent agreement

Clinical performance with pediatric population

The pediatric increased-risk for hepatitis subgroup was acquired from the US-prospective sample collection to demonstrate the clinical performance of the Elecsys Anti-HBs II assay in subjects from 2 years, through and including 21 years of age. A total of 128 samples were collected. The following table summarizes the positive and negative percent agreement.

	Elecsys Anti-HBs		
Elecsys Anti-HBs II	**Pos**	**Ind**	**Neg**
Reactive	55	1	1
Non-reactive	3	0	68
Total	58	1	69
PPA	94.8 (55/58)		

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	Elecsys Anti-HBs		
Elecsys Anti-HBs II	**Pos**	**Ind**	**Neg**
95 % CI	85.6 to 98.9		
NPA	97.1 (68/70)		
95 % CI	90.0 to 99.7		

In addition, there were 59 specimens from pregnant young women that met the age criteria as pediatric from subjects at increased risk for hepatitis obtained in the prospective collection. Thirty-four of these specimens were concordantly negative between the Elecsys Anti-HBs II assay and the Elecsys Anti-HBs assay, while 23 were concordantly positive. There was 1 positive and 1 negative in the test assay that was indeterminate in the reference assay. The NPA for the pregnant pediatric sub-group was 97.1 % based on a ratio of 34/35 with confidence limits of 85.1 to 99.9 %. The PPA was 95.8 % based on a ratio of 23/24 with confidence limits of 78.9 to 99.9 %.

Clinical performance with pregnant population

Pregnant subjects at increased risk for hepatitis (US prospective [n = 202] and ex-US with retrospective [n = 16] collections) and with low risk for hepatitis (remnant samples n = 588) were tested with the Elecsys Anti-HBs II assay and the reference assay, Elecsys Anti-HBs assay on the **cobas e** 601 analyzer. The following table shows the comparison of the results from the 2 assays to demonstrate the clinical performance in terms of percent agreement for these groups.

	Elecsys Anti-HBs		
Elecsys Anti-HBs II	**Pos**	**Ind**	**Neg**
Reactive	420	4	8
Non-reactive	3	3	368
Total	423	7	376
PPA	98.6 (420/426)		
95 % CI	97.0 to 99.5		
NPA	96.8 (368/380)		
95 % CI	94.6 to 98.4		

References

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

Symbols

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

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

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

Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336

Roche

PreciControl Anti-HBs

cobas®

REF 11876317160 **16 x 1.3 mL**

English

For use in the USA only

Intended use

PreciControl Anti-HBs is used for quality control of the Elecsys Anti-HBs immunoassay on the **cobas e** immunoassay analyzers and of the Elecsys Anti-HBs II immunoassay on the **cobas e** 601 immunoassay analyzer. The performance of PreciControl Anti-HBs has not been established with any other anti-HBs assay.

Summary

PreciControl Anti-HBs is a ready-for-use control serum based on human serum both in the negative and positive concentration range.

The controls are used for monitoring the accuracy of the Elecsys Anti-HBs and Elecsys Anti-HBs II immunoassays.

Reagents - working solutions

- PC A-HBS1: 8 bottles, each containing 1.3 mL of control serum Human serum, negative for anti-HBs; preservative.
  Target concentration range for anti-HBs: ≤ 5 mIU/mL.
- PC A-HBS2: 8 bottles, each containing 1.3 mL of control serum Anti-HBs antibodies (human) approximately 100 mIU/mL in human serum; preservative.
  Target concentration range for anti-HBs: 60-150 mIU/mL.

cobas e 801 analyzer: The exact lot-specific target values and ranges are available as an electronic barcode and value sheet provided via the **cobas** link.
All other analyzers: The exact lot-specific target values and ranges are encoded in the barcodes as well as printed on the enclosed (or electronically available) value sheet.
Please note: The value sheets for the **cobas e** 801 analyzer are only available electronically via the **cobas** link.

Target values and ranges

The target values and ranges were determined and evaluated by Roche. They were obtained using the Elecsys Anti-HBs assay reagents and analyzers available at the time of testing.

If the target values and control ranges are updated, this information is conveyed either via the reagent barcodes, or control barcodes (or provided electronically) and in an additional value sheet included in the reagent kit. This value sheet lists all control lots to which the new values apply. If some of the values remain unchanged, the original values conveyed via the CBC (Control Barcode), and in the value sheet included in the control kit (or provided electronically), remain valid.

cobas e 801 analyzer: Updated target values and ranges are available both as an electronic barcode and as a value sheet provided via the **cobas** link.

Results must be within the specified ranges. In the event that increasing or decreasing trends, or any other suddenly occurring deviations beyond the range limits are observed, all test steps must be checked.

When necessary, measurement of the patient sample tested should be repeated.

Traceability information is given in the Method Sheet of the relevant Elecsys assay.

Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Precautions and warnings

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

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

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

Warning

H317	May cause an allergic skin reaction.

Prevention:

P261	Avoid breathing dust/fume/gas/mist/vapours/spray.
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.

Product safety labeling follows EU GHS guidance.

Contact phone: 1-800-428-2336

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods used assays approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

However, as no 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.[1,2]

The quality control material furnished is in a serum matrix. It may not adequately control the Elecsys Anti-HBs immunoassay for plasma specimens. The user should provide alternative control material for plasma specimens.

The controls may not be used after the expiration date.

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

Handling

The controls are supplied ready-for-use in bottles compatible with the system. The controls should only be left on the analyzer during performance of quality control. After use, close the bottles as soon as possible and store upright at 2-8 °C.

Due to possible evaporation effects, not more than 7 quality control procedures per bottle should be performed.

Please note for **cobas e** 602 and **cobas e** 801 analyzers: Both the vial labels, and the additional labels (if available) contain 2 different barcodes. Please turn the vial cap 180° into the correct position so that the barcode between the yellow markers can be read by the system. Place the vial on the analyzer as usual.

Storage and stability

Store at 2-8 °C.

Store controls **upright** in order to prevent the control solution from adhering to the snap-cap.

Stability:	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	8 weeks

PreciControl Anti-HBs

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Stability:	
on **cobas e** 411 analyzer at 20-25 °C	up to 5 hours
on **cobas e** 601, **cobas e** 602 and **cobas e** 801 analyzers at 20-25 °C	up to 4 hours

Materials provided

- PreciControl Anti-HBs, 2 barcode cards, control barcode sheet

Materials required (but not provided)

- **cobas e** immunoassay analyzer and assay reagents.

See the assay Method Sheet and the operator's manual for additionally required materials.

Assay

Treat the control serum in the system-compatible labeled bottles for analysis in the same way as patient samples.

Read the data into the analyzer.

Ensure the controls are at 20-25 °C prior to measurement.

Run controls daily in parallel with patient samples, once per reagent kit, and whenever a calibration is performed. The control intervals and limits should be adapted to each laboratory's individual requirements.

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

References

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

2 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.

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

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

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US Customer Technical Support 1-800-428-2336

Roche

Anti-HBs CalCheck

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Order information

REF	CONTENT		SYSTEM
04985354160	Check 1	→1 x 1.0 mL	**cobas e** 411 **cobas e** 601 **cobas e** 602 **cobas e** 801
	Check 2	→1 x 1.0 mL	
	Check 3	→1 x 1.0 mL	

For use in the USA only

Intended use

Anti-HBs CalCheck is an assayed control material for use in the verification of the calibration established by the Elecsys Anti-HBs immunoassay on the **cobas e** immunoassay analyzers and by the Elecsys Anti-HBs II immunoassay on the **cobas e** 601 immunoassay analyzer.

Summary

Anti-HBs CalCheck calibration verification solutions comprise three levels – low, mid and high – each with a defined Anti-HBs concentration. The low solution concentration is near the lower detection limit of the assay. The mid solution is in the middle or at a clinically critical point of the measuring range. The high solution is near the upper limit of the measuring range.

Principle

"Calibration verification is the assaying of calibration materials in the same manner as patient samples to confirm that the calibration of the instrument kit or test system has remained stable throughout the laboratory's reportable range for patient test results."[1]

Calibration verification is not a requirement of the Elecsys and **cobas e** immunoassay systems based on the manufacturer's recommendations. However, in instances where such a test procedure is required by certification agencies, or where the user wishes to document calibration verification, these CalCheck solutions provide an appropriate material for such testing.

Reagents - working solutions

Check 1 - 3
Each set contains 3 lyophilized levels
Each bottle, reconstituted to 1.0 mL
Reactive ingredient (after reconstitution):
Anti-HBs antibodies (human) in anti-HBs negative human serum matrix
Nonreactive ingredients:
Preservatives

Target values and ranges

Traceability: The assayed value of each level was standardized against the 1st WHO Reference Standard 1977.[2]

The exact lot-specific target values and ranges are printed on the lot-specific value sheet.

Results must be within the specified ranges. If results are out of range then all test steps must be checked.

Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Refer to the lot-specific value sheet for specified limits. Values below the Limit of Detection (REF 11820524160) or the Limit of Quantitation (REF 08343594160, REF 08498598160 or REF 08498601160) are reported as < 3.50 mIU/mL. Values above the measuring range are reported as > 1000 mIU/mL.

Precautions and warnings

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

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

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

Warning

H317	May cause an allergic skin reaction.
H412	Harmful to aquatic life with long lasting effects.

Prevention:

P261	Avoid breathing dust/fume/gas/mist/vapours/spray.
P273	Avoid release to the environment.
P280	Wear protective gloves/ protective clothing/ eye protection/ face protection.

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.

Product safety labeling follows EU GHS guidance.

Contact phone: 1-800-428-2336

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods used assays approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.
However, as no 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.[3,4]

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

Handling

Reconstitute the contents of each CalCheck vial with exactly 1.0 mL distilled or deionized water. Allow the bottle to stand closed for 15 minutes. Mix gently by inversion to ensure homogeneity.

Storage and stability

Store unopened at 2-8 °C.
Stability unopened: up to the printed expiration date on the bottle labels at 2-8 °C.

Stability reconstituted: 4 hours at 20-25 °C.

Materials provided

See "Order information" section

Materials required (but not provided)

- **cobas e** analyzer
- Elecsys Anti-HBs reagent kit, REF 11820524160 or REF 08343594160 or Elecsys Anti-HBs II reagent kit, REF 08498598160 or REF 08498601160
- Distilled or deionized water

Anti-HBs CalCheck

cobas®

- General laboratory equipment (e.g. volumetric pipette)

See the assay Method Sheet and the operator's manual for additionally required materials.

Assay

1. Run each CalCheck level in triplicate on the Elecsys or **cobas e** analyzer. Program the nine samples as you would patient samples.
2. Determine the median value for each level and compare it to the appropriate acceptable range listed on the lot-specific value sheet. The median value should fall within the specified limits. If the median value falls outside the specified limits, and repetition excludes error in technique, contact your Local Customer Technical Support.

Limitations

This CalCheck is intended for use in the confirmation of assay calibration. This product is not intended to replace calibration or quality control materials. Refer to the appropriate operator's manual and/or package insert for analyzer specific limitations.

References

1 42 Code of U.S. Federal Regulations. Part 493.1217. Standard; Calibration and calibration verification procedures.

2 Calam RR. Specimen Processing Separator Gels: An Update. J Clin Immunoassay; 11;86-90:1988.

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

4 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.

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

Symbols

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

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

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be 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.

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