Elecsys Anti-HBe

cobas®

REF		Σ	SYSTEM
11820613160	11820613501	100	**cobas e** 602

English

For use in the USA only

System information

For **cobas e** 602 analyzer: Application Code Number 066

Intended use

Immunoassay for the in vitro qualitative detection of total antibodies to hepatitis B e antigen (anti-HBe) in human adult serum or plasma (potassium EDTA, lithium heparin, sodium citrate, sodium heparin) from individuals with symptoms of hepatitis or at risk for hepatitis B virus (HBV) infection. Assay results, in conjunction with other laboratory results and clinical information may be used as an aid in the diagnosis of hepatitis B virus (HBV) infection in patients with symptoms of hepatitis or who may be at risk for HBV infection. A reactive test is presumptive laboratory evidence of HBV seroconversion. Further HBV serological marker testing is required to define the specific disease state.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on the **cobas e** 602 immunoassay analyzer.

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 the cases 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 250 million chronically infected patients and a serious threat to blood transfusion safety, especially in highly endemic countries.[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]

The hepatitis B e antigen (HBeAg) is a product of the pre-C/C gene that has been found in hepatocytes during proliferation of the hepatitis B virus (HBV) and is an important diagnostic tool to determine the status of ongoing HBV infections. The detection of HBeAg is generally associated with the presence of large quantities of virus as it is a surrogate of viral replication.[8,9] During acute HBV infection HBeAg can be detected in serum shortly after hepatitis B surface antigen (HBsAg) and usually disappears before HBsAg, when alanine aminotransferase (ALT) levels peak, followed by the presence of the corresponding antibody (anti-HBe).[8,9,10] HBeAg can usually be detected when viral replication is high; its presence for more than 10 weeks is indicative of a persistent infection. HBeAg seroconversion to anti-HBe suggests the end of active viral replication and is therefore associated with clinical resolution (self-limited) or remission (chronic disease).[6,8,9,11] HBV infections can occur without detectable HBeAg due to infection with HBV variants containing precore stop codon mutants; while the virus can no longer produce HBeAg, disease activity is ongoing and anti-HBe may be present.[8,12,13]

The anti-HBe test, therefore, is meaningful in association with the HBeAg test for monitoring the course of a HBV infection and the effect of treatment for chronic hepatitis B.[6,8,9,11] The Elecsys Anti-HBe assay uses recombinant HBeAg and monoclonal anti-HBe antibodies to detect anti-HBe.

Test principle

Competition principle. Total duration of assay: 18 minutes.

- 1st incubation: Anti-HBe in the sample (35 µL) binds to the added HBeAg.
- 2nd incubation: After addition of biotinylated antibodies and ruthenium complex[a] -labeled antibodies specific for HBeAg, together with streptavidin-coated microparticles, the still-free binding sites on the HBe-antigens become occupied. The entire complex is then 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 automatically by the software by comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by calibration.

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-HBE.

M	Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
R1	HBeAg (gray cap), 1 bottle, 12 mL: HBeAg (E. coli, rDNA) > 7 ng/mL; HEPES[b] buffer 36 mmol/L, pH 7.4; preservative.
R2	Anti-HBeAg-Ab~biotin; anti-HBeAg-Ab~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 12 mL: Biotinylated monoclonal anti-HBe antibody (mouse) > 0.8 mg/L; monoclonal anti-HBe antibody (mouse) labeled with ruthenium complex > 0.2 mg/L; HEPES buffer 36 mmol/L, pH 7.4; preservative.

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

A-HBE Cal1	Negative calibrator 1 (white cap), 2 bottles of 1.0 mL each: Human serum, preservative.
A-HBE Cal2	Positive calibrator 2 (black cap), 2 bottles of 1.0 mL each: Anti-HBe (human) approximately 3 IU/mL 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 negative calibrator (A-HBE Cal1) has 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 positive calibrator (A-HBE Cal2) containing anti-HBe was tested for HIV and hepatitis C infections. The findings were negative. The serum containing anti-HBe was inactivated using β-propiolactone and UV-radiation.

However, as no inactivation or testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[14,15]

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 analyzers, 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 the **cobas e** 602 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** 602 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.

Li-heparin, Na-heparin, K_2-EDTA, K_3-EDTA, and Na-citrate plasma.

Plasma tubes containing separating gel can be used.

Criterion: Samples with a COI (cutoff index) > 1.0: ± 20 % recovery; samples with a COI ≤ 1.0: ± 0.2 COI recovery.

Stable for 7 days at 20-25 °C, 14 days at 2-8 °C, 3 months at -20 °C (± 5 °C). The samples may be frozen 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, thawed samples, and samples for repeat measurements before performing the assay.

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 and calibrators on the analyzers should be analyzed/measured within 2 hours.

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

The claims, including those pertaining to sample stability made in the labeling of the cleared/approved reagents of Roche Diagnostics are part of the clearance/approval of the overall IVD test system (assay). Sample stability was tested only for the temperatures/time frame as claimed by the manufacturer under the conditions claimed 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 4 bottle labels

Materials required (but not provided)

- REF 11876384160, PreciControl Anti-HBe, for 16 x 1.3 mL
- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles
- General laboratory equipment
- **cobas e** 602 analyzer

Additional materials for **cobas e** 602 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.

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.

After calibration has been performed, discard the calibrator vials.

Calibration

Traceability: This method has been standardized against the WHO 1st International Standard for detection of antibodies to anti-hepatitis B virus "e" antigen (anti-HBe), code 129095/12 of the Paul-Ehrlich-Institute, Langen (Germany).

Calibration frequency: Calibration must be performed once per reagent lot using A-HBE Cal1, A-HBE 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-HBe outside the defined limits

Range for the electrochemiluminescence signals (counts) for the calibrators:
Negative calibrator (A-HBE Cal1): 300000-1500000
Positive calibrator (A-HBE Cal2): 1000-6000

Quality control

For quality control, use PreciControl Anti-HBe.

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.

Cutoff determination

The analyzer automatically calculates the cut-off based on the measurement of A-HBE Cal1 and A-HBE Cal2.

The cutoff is calculated from signals of the negative calibrator (A-HBE Cal1) and the positive calibrator (A-HBE Cal2) according to the following formula:
Cutoff formula
Cutoff = 0.65*counts Cal1 + 0.5*counts 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 the results

Initial output Elecsys Anti-HBe assay	Test result	Interpretation
> 1.00 COI	Non-reactive	Indicates sample is non-reactive for anti-HBe. A negative test result does not exclude the possibility of infection with hepatitis B virus.
≤ 1.00 COI	Reactive	Indicates sample is reactive for anti-HBe.

Limitations - interference

To evaluate the effect of elevated levels of hemoglobin, bilirubin, intralipid, biotin, and total protein on the Elecsys Anti-HBe assay, one negative, one high negative, one low positive, and one positive anti-HBe serum samples were spiked with potential interferents. Each interferent was evaluated at 11 concentrations. All samples were tested in duplicate. Interferences were tested up to the listed concentration and no impact on results was observed.

Endogenous interference

Compound	Concentration tested
Bilirubin	≤ 66 mg/dL
Hemoglobin	≤ 2000 mg/dL
Intralipid	≤ 2000 mg/dL
Albumin	≤ 7 g/dL

Biotin interference

Because this test employs streptavidin technology and may be subject to potential interference by biotin, more extensive interference testing with biotin was performed.

% Bias for samples containing various concentrations of biotin							
Sample (COI)			Biotin concentration (ng/mL)				
			96	112	128	144	160
negative	1.56	relative deviation (%)	-1.8	-5.2	-8.2	-12.5	-17.1
high negative	1.14		-6.2	-6.9	-12.2	-14.3[c)]	-19.8[c)]
low positive	0.892	absolute deviation	-0.025	-0.052	-0.069	-0.108	-0.154
positive	0.371		-0.019	-0.032	-0.043	-0.058	-0.075

c) false positive

% Bias for samples containing various concentrations of biotin						
Sample (COI)			Biotin concentration (ng/mL)			
			200	300	600	1200
negative	1.56	relative deviation (%)	-46.2[c)]	-74.1[c)]	-89.3[c)]	-95.8[c)]
high negative	1.14		-45.5[c)]	-73.7[c)]	-88.4[c)]	-93.1[c)]
low positive	0.892	absolute deviation	-0.361	-0.604	-0.730	-0.765
positive	0.371		-0.151	-0.226	-0.263	-0.273

Specimens with biotin concentrations up to 112 ng/mL demonstrated ≤ 10 % bias in measured anti-HBe s/co. Biotin concentrations greater than 112 ng/mL lead to higher positive bias and in consequence can lead to false positive Elecsys Anti-HBe results in samples with an anti-HBe antibody concentration near the medical decision point. 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[16] and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin.[17]

Drug interference

A drug interference study was performed with 16 common therapeutic drugs. Each drug was spiked into one negative, one high negative, one low positive, and one positive sample. Each sample was tested in triplicate. Each drug was found to be non-interfering at the following claimed concentrations:

Compound	Concentration (mg/L)
Acetyl cysteine	150
Ampicillin-Na	1000
Ascorbic acid	300
Cefoxitin	2500
Heparin	5000 U/L
Levodopa	20
Methyldopa+ 1.5	20
Metronidazole	200
Doxycycline	50
Acetylsalicylic acid	1000
Rifampicin	60
Cyclosporine	5
Phenylbutazone	400
Acetaminophen	200
Ibuprofen	500
Theophylline	100

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.

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In case the Elecsys HBsAg II/Anti-HBs and HBeAg/Anti-HBe assay combinations are processed, make sure that these assays are entered in the "Special Wash" section of the system software and "Step1" (wash execute) is checked. Please refer to the operator's manual.

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

Assay performance characteristics have not been established when Elecsys Anti-HBe assay is used in conjunction with other manufacturers' assays for specific HBV serological markers.

Analytical sensitivity

In order to determine assay sensitivity, the anti-HBe concentration which corresponds to the measuring signal of the cutoff value was read off the standard curves of serial dilutions of the reference material, WHO International Standard for Anti-HBe code 129095/12. The reference material was diluted with human serum negative for HBV in nine dilution steps to ten concentrations. The samples were measured in duplicate. The sensitivity at cutoff (= 1.0 COI) was calculated by reading off the concentration at the cutoff from the standard curve.

Sample	WHO concentration (IU/mL)	Mean measured values (COI)
WHO 1	0.000	1.58
WHO 2	0.020	1.42
WHO 3	0.039	1.30
WHO 4	0.078	1.15
WHO 5	0.156	0.943
WHO 6	0.313	0.680
WHO 7	0.625	0.365
WHO 8	1.25	0.101
WHO 9	2.50	0.014
WHO 10	5.00	0.003
Cutoff sensitivity	0.127 IU/mL	

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Repeatability and intermediate precision were determined on the **cobas e** 602 analyzer, using Elecsys reagents and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute). A precision panel consisting of four human sera and two controls was measured. Each sample was separated in two aliquots measured in single determination in two runs per day for 12 days (n = 48). The following results were obtained:

cobas e 602 analyzer					
		Repeatability[d)]		**Intermediate precision[e)]**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS[f)], negative	1.50	0.016	1.0	0.030	2.0
HS, high negative	1.10	0.012	1.1	0.025	2.3
HS, low positive	0.799	0.008	1.0	0.020	2.5
HS, positive	0.023	0.001	2.8	0.002	7.0
PC[g)] A-HBe 1	1.49	0.027	1.8	0.034	2.3
PC A-HBe 2	0.660	0.008	1.2	0.021	3.1

d) Repeatability = within-run precision

e) Intermediate precision = within-laboratory precision

f) HS = Human serum

g) PC = PreciControl

Reproducibility

A precision panel was evaluated in the reproducibility study. The reproducibility results were collected on three **cobas e** 602 analyzers at three sites with three lots of reagents. PreciControl Anti-HBe and the following sample concentrations were tested in 3 replicates per run, 2 runs per day, for 5 days in a modified protocol EP05-A3 of the CLSI (Cinical and Laboratory Standards Institute) (n = 180). The overall reproducibility (imprecision) data are summarized in the following table:

cobas e 602 analyzer							
		Repeatability		**Between-run**		**Between-day**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %	SD COI	CV %
HSP[h)] 01	0.576	0.009	1.5	0.012	2.2	0.015	2.6
HSP 02	0.783	0.012	1.6	0.013	1.6	0.021	2.7
HSP 03	0.885	0.013	1.5	0.011	1.3	0.024	2.7
HSP 04	1.05	0.017	1.6	0.014	1.3	0.030	2.9
HSP 05	1.08	0.019	1.8	0.012	1.1	0.029	2.7
HSP 06	1.22	0.020	1.7	0.013	1.1	0.033	2.8
PC A-HBe 1	1.53	0.029	1.9	0.018	1.2	0.031	2.1
PC A-HBe 2	0.643	0.012	1.8	0.012	1.9	0.013	2.1

h) HSP = human serum pool

cobas e 602 analyzer						
	Between-lot		**Between-site**		**Reproducibility**	
Sample	SD COI	CV %	SD COI	CV %	SD COI	CV %
HSP 01	0.019	3.2	0.024	4.1	0.037	6.4
HSP 02	0.025	3.2	0.025	3.2	0.045	5.7
HSP 03	0.025	2.9	0.023	2.6	0.045	5.1
HSP 04	0.027	2.6	0.034	3.2	0.057	5.5
HSP 05	0.034	3.2	0.022	2.0	0.055	5.1
HSP 06	0.046	3.8	0.026	2.1	0.067	5.5
PC A-HBe 1	0.025	1.6	0.013	0.83	0.054	3.5
PC A-HBe 2	0.012	1.8	0.015	2.4	0.029	4.5

Serum / plasma comparison

Studies were conducted to evaluate the suitability of the following seven sample types: serum/gel separation tubes, sodium heparin plasma, sodium citrate plasma, lithium heparin plasma, K_2-EDTA plasma, K_3-EDTA plasma and plasma tubes containing separation gel, to be used with the Elecsys Anti-HBe assay.

Samples were collected into matched serum and plasma collection tubes and assayed in single determinations. The study was conducted using negative, high negative, low positive, and positive samples for anti-HBe. The studies support the use of serum/gel separation tubes, and the following plasma types: lithium heparin, K_2-EDTA, K_3-EDTA, sodium heparin, sodium citrate, and plasma tubes containing separating gel.

Analytical specificity

A study was conducted to evaluate the Elecsys Anti-HBe assay for potential cross-reactivity in specimens from individuals with various medical conditions. The specificity of 190 samples with 23 sub-categories of potentially interfering diseases or medical conditions was evaluated with the Elecsys Anti-HBe assay on the **cobas e** 602 immunoassay analyzer and the reference assay. The results are summarized in the following table:

Reactivity of the Elecsys Anti-HBe assay				
Category	Sub-category	RX[i)]	NR[i)]	Total
Immune disorders	ANA	0	12	12
	RF	0	12	12

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Reactivity of the Elecsys Anti-HBe assay				
Category	Sub-category	RX[i]	NR[j]	Total
Infections / disorders	T. pallidum	0	11	11
	Toxoplasmosis	0	11	11
Infectious viral	CMV	0	10	10
	EBV	1	11	12
	HAV	0	12	12
	HCV	2	10	12
	HIV 1/2	0	10	10
	HSV	0	12	12
	Parvo B19	1	11	12
	Rubella	0	12	12
	VZV	0	12	12
Non-viral liver disease	Liver cancer	2	8	10
	Chronic alcoholic liver disease	0	7	7
	Various cirrhosis	0	5	5
	Alcoholic fatty liver	0	4	4
	Alcoholic liver disease	0	4	4
	Abdominal pain / pelvic mass	0	4	4
	Unspecified jaundice	0	2	2
	Liver abscess or lesion	0	2	2
	Fatty infiltrate of liver	0	1	1
	Chronic passive congestion of liver	0	1	1
Total		6	184	190

i) RX = reactive

j) NR = non-reactive

Conclusion: One hundred eighty-four (184) samples were found to be non-reactive in both the Elecsys Anti-HBe assay and FDA-approved reference anti-HBe assay. Six (6) samples of the sub-categories: EBV, Hepatitis C, non-viral liver disease (NVLD) and Parvo, were found to be discrepant reactive in the Elecsys Anti-HBe assay. Ten disease sub-categories were completely concordant between the Elecsys Anti-HBe assay and the FDA-approved reference anti-HBe assay.

Seroconversion sensitivity

Seroconversion sensitivity of the Elecsys Anti-HBe assay on the **cobas e** 602 immunoassay analyzer has been shown by testing 9 commercial seroconversion panels in comparison to a commercially available FDA-approved anti-HBe reference assay. In 4 of the panels the Elecsys Anti-HBe assay shows detection of seroconversion equal to the reference anti-HBe assay. One of the panels did not convert in either the Elecsys Anti-HBe assay or the FDA-approved reference assay. In the 4 remaining panels, the Elecsys Anti-HBe assay reported a reactive outcome earlier than the FDA-approved reference assay. Overall seroconversion performance of the Elecsys Anti-HBe assay was equivalent or better than the reference assay performance.

Panel ID	Bleed day of the last NR[k] test		Bleed day of the first RX[l] test		Difference in days[m] to anti-HBe reactive
	Reference assay	Elecsys Anti-HBe assay	Reference assay	Elecsys Anti-HBe assay	
6281	54	41	N/A	43	>11
6510	56	14	70	28	42
9092	198	134	N/A	141	>57
9093	173	173	182	182	0
11024	54	54	N/A	N/A	N/A
BMX11071	81	69	88	81	7
BMX11072	60	60	74	74	0
BMX11073	78	78	140	140	0

k) NR = non-reactive

l) RX = reactive

m) The dates of the first reactive test results were compared between the Elecsys Anti-HBe assay and the Reference assay

Summary of clinical performance

Study description

A prospective and retrospective multicenter study was conducted on the **cobas e** 602 analyzer to evaluate the Elecsys Anti-HBe assay to detect anti-HBe antibodies in specimens from an intended use population. Fifteen hundred (1500) adult specimens were prospectively obtained from individuals at increased risk of HBV infection due to lifestyle, behavior, occupation, disease state or known exposure event, or from individuals with signs and symptoms of a hepatitis infection (asymptomatic and symptomatic subjects at increased risk for hepatitis). In addition, a supplemental cohort of 300 subjects, which provided an enhanced prevalence of hepatitis B markers such as HBsAg, HBeAg, and anti-HBc IgM, were also tested. The 1500 specimens were collected from seven collection sites located in Los Angeles, CA (32.0 %), San Antonio, TX (24.9 %), Baltimore, MD (17.9 %), Miami, FL (7.9 %), City of Industry, CA (6.9 %), Darby, PA (6.8 %), Minneapolis, MN (3.6 %). The 300 supplemental specimens were obtained from three external vendors. Testing of the specimens was performed at three clinical testing sites located in South Bend, IN, Iowa City, IA and San Diego, CA.

Demographics of clinical population

A total of 1800 samples were tested at 3 clinical testing sites with the Elecsys Anti-HBe assay to evaluate clinical performance of the Elecsys Anti-HBe assay. The following tables show the demographics for the adult at increased risk (AIR) and supplemental study cohorts:

Demographics of clinical population by sex

Cohort	Gender	N	% of cohort total
Adult AIR	Female	686	45.7
	Male	814	54.3
	Unknown	0	0.0
	Subtotal	1500	100
Supplemental	Female	117	39.0
	Male	182	60.7
	Unknown	1	0.3
	Subtotal	300	100
Total		1800	

Demographics of clinical population by ethnicity

Cohort	Ethnicity	N	% of cohort total
Adult AIR	Hispanic or Latino	421	28.1
	Not Hispanic or Latino	1073	71.5
	Unknown	6	0.4
	Subtotal	1500	100

Cohort	Ethnicity	N	% of cohort total
Supplemental	Hispanic or Latino	2	0.7
	Not Hispanic or Latino	0	0.0
	Unknown	298	99.3
	Subtotal	300	100
Total		1800	

Demographics of clinical population by race

Cohort	Race	N	% of cohort total
Adult AIR	AIAN	17	1.1
	Asian	9	0.6
	Black or African American	735	49.0
	Caucasian / White	709	47.3
	More than one race	21	1.4
	Nhopi	4	0.3
	Other	1	0.1
	Unknown	4	0.3
	Subtotal	1500	100
Supplemental	AIAN	0	0.0
	Asian	166	55.3
	Black or African American	114	38.0
	Caucasian / White	15	5.0
	More than one race	0	0.0
	Nhopi	0	0.0
	Other	0	0.0
	Unknown	5	1.7
	Subtotal	300	100
Total		1800	

Demographics of clinical population by age

Cohort	Age group (years)	N	% of cohort total
Adult AIR	22-29	176	11.7
	30-39	253	16.9
	40-49	435	29.0
	50-59	481	32.1
	60-69	140	9.3
	70-79	12	0.8
	≥ 80	3	0.2
	Unknown	0	0.0
	Subtotal	1500	100
Supplemental	22-29	73	24.3
	30-39	80	26.7
	40-49	70	23.3
	50-59	50	16.7
	60-69	26	8.7
	70-79	1	0.3
	≥ 80	0	0.0
	Unknown	0	0.0
	Subtotal	300	100
Total		1800	

Results from clinical performance

A total of 1800 samples were tested on the **cobas e** 602 immunoassay analyzer from subjects from the following cohorts:

- adult subjects at increased risk for hepatitis (symptomatic and asymptomatic)
- supplemental cohort

Serological characterization using a complete hepatitis B panel of assays approved by the FDA was performed on the main clinical cohort samples from the prospective at increased risk collection (asymptomatic and symptomatic adults) and the adult supplemental sample cohort. For serological characterization the following HBV markers were evaluated: HBsAg (and HBsAg confirmatory test), Anti-HBc IgM, Anti-HBc, Anti-HBs, Anti-HBe and HBeAg.

Results by specimen classification

Interpretation of test results for all specimens was performed blinded to the Elecsys Anti-HBe test result. The interpretation for the various HBV classifications based on the serological profiles actually observed in this evaluation are 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	(-)	(-)	(-)	(+)	(-), (+)	(-)
Early recovery	(-)	(-)	(+)	(+)	(-)	(-), (+)
Early recovery	(-)	(-)	(+)	(+)	(+)	(-), (+)
Recovery	(-)	(-)	(-)	(-),(+)	(+)	(+)
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 vaccination response	(-)	(-)	(-)	(-)	(-)	(eq)
Not previously infected	(-)	(-)	(-)	(-)	(-)	(-)
Not interpretable	(-)	(+)	(-)	(+)	(-)	(+)
Not interpretable	(-)	(-)	(-)	(-)	(+)	(-)
Not interpretable	(-)	(+)	(-)	(+)	(+)	(-)
Not interpretable	(-)	(+)	(-)	(-)	(-)	(-), (eq), (+)

Disease status of the at increased risk and supplemental cohorts were based on the constellations of the various hepatitis B markers obtained for each specimen. The following table shows the distribution of hepatitis B disease states across serologically characterized cohorts.

HBV classification	Adult AIR	Supplemental
Acute	7	128
Chronic	32	172
Early recovery	197	0
Not previously infected	555	0
Recovered	242	0
Recovery	132	0
Vaccination	335	0
Total	1500	300

Adult at increased risk cohort

Specimens were tested using the Elecsys Anti-HBe assay on the **cobas e** 602 immunoassay analyzer and a FDA-approved reference assay to establish the clinical performance characteristics of the Elecsys Anti-HBe assay. The study was performed at 3 clinical laboratories. The following table compares the Elecsys Anti-HBe results with the results obtained on an FDA-approved anti-HBe reference assay by HBV disease classification for the adult at increased risk cohort.

HBV classification	FDA-approved reference assay				Total
	Reactive		Non-reactive		
	Elecsys Anti-HBe		Elecsys Anti-HBe		
	RX[n]	NR[o]	RX	NR	
	n	n	n	n	
Acute	0	0	0	7	7
Chronic	25	0	0	7	32
Early recovery	40	2	16	139	197
Not previously infected	0	0	1	554	555
Recovered	0	0	47	195	242
Recovery	129	3	0	0	132
Vaccination	0	0	0	335	335
Total	194	5	64	1237	1500

n) RX = reactive

o) NR = non-reactive

The following table reflects the percent agreement between the Elecsys Anti-HBe assay and the reference assay for each disease classification for the adult at increased risk cohort.

Percent agreement between Elecsys Anti-HBe and FDA-approved reference assay by HBV classification for adults at increased risk cohort				
	PPA[p]		NPA[q]	
HBV classification	% (n/N)	95 % Exact CI[r]	% (n/N)	95 % Exact CI
Acute	N/A (0/0)	N/A	100 (7/7)	59.0 to 100
Chronic	100 (25/25)	86.3 to 100	100 (7/7)	59.0 to 100
Early recovery	95.2 (40/42)	83.8 to 99.4	89.7 (139/155)	83.8 to 94.0
Not previously infected	N/A (0/0)	N/A	99.8 (554/555)	99.0 to 100
Recovered	N/A (0/0)	N/A	80.6 (195/242)	75.0 to 85.4
Recovery	97.7 (129/132)	93.5 to 99.5	N/A (0/0)	N/A
Vaccination	N/A (0/0)	N/A	100 (335/335)	98.9 to 100
Total	97.5 (194/199)	94.2 to 99.2	95.1 (1237/1301)	93.8 to 96.2

p) PPA = positive percent agreement

q) NPA = negative percent agreement

r) CI = confidence interval

Supplemental cohort

Specimens were tested using the Elecsys Anti-HBe assay on the **cobas e** 602 immunoassay analyzer and an FDA-approved reference assay to establish the clinical performance characteristics of the Elecsys Anti-HBe assay. The study was performed at 3 clinical laboratories. The following table compares the Elecsys Anti-HBe results with the results obtained on an FDA-approved anti-HBe reference assay by HBV disease classification for the supplemental cohort.

HBV classification	FDA-approved reference assay				Total
	Reactive		Non-reactive		
	Elecsys Anti-HBe		Elecsys Anti-HBe		
	RX	NR	RX	NR	
	n	n	n	n	
Acute	7	0	97	24	128
Chronic	45	0	10	117	172
Total	52	0	107	141	300

The following table reflects the percent agreement between the Elecsys Anti-HBe assay and the reference assay for each disease classification for the supplemental cohort.

Percent agreement between Elecsys Anti-HBe and FDA-approved reference assay by HBV classification in supplemental cohort				
	PPA		NPA	
HBV classification	% (n/N)	95 % Exact CI	% (n/N)	95 % Exact CI
Acute	100 (7/7)	59.0 to 100	19.8 (24/121)	13.1 to 28.1
Chronic	100 (45/45)	92.1 to 100	92.1 (117/127)	86.0 to 96.2

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Percent agreement between Elecsys Anti-HBe and FDA-approved reference assay by HBV classification in supplemental cohort				
	PPA		NPA	
HBV classification	% (n/N)	95 % Exact CI	% (n/N)	95 % Exact CI
Total	100 (52/52)	93.2 to 100	56.9 (141/248)	50.4 to 63.1

Evaluation of reactive and non-reactive samples

In order to demonstrate the presence or absence of anti-HBe antibody activity, an internal confirmatory assay was developed. The confirmatory principle used HBeAg covalently coupled to sepharose to bind to anti-HBeAg (anti-HBe) antibodies in the sample. Depletion of anti-HBeAg antibodies in the sample distinguished a confirmed reactive or positive result from false-positive or unconfirmed reactive results.

After testing was completed at the 3 external sites, samples were transfered to Roche for storage. An internal study was then conducted testing all Elecsys Anti-HBe reactive samples (N = 421) and approximately 1/3 of the concordant non-reactive samples (N = 476). The concordant non-reactive samples were randomly selected for testing from the remaining samples with enough sample volume to complete testing.

The following algorithm was employed to obtain a composite method result for the above subset:

Confirmatory assay result	FDA-approved Reference assay result	Composite result interpretation
Confirmed non-reactive	Non-reactive	Non-reactive
Confirmed non-reactive	Reactive	Reactive
Confirmed positive	Non-reactive	Reactive
Confirmed positive	Reactive	Reactive

False positive results are considered non-reactive for the purposes of this analysis.

Verification bias analysis

Because only a subset of the clinical samples were tested by the confirmatory assay, a verification bias analysis was employed to impute the results for those samples that were not tested by confirmatory assay. The following results were obtained for the Adult AIR cohort and the Supplemental cohort.

Adult AIR cohort

HBV classification	Composite comparator				Total
	Reactive		Non-reactive		
	Elecsys Anti-HBe		Elecsys Anti-HBe		
	RX[s)]	NR[t)]	RX	NR	
	n	n	n	n	
Acute	0	0	0	7	7
Chronic	25	0	0	7	32
Early recovery	56	10	0	131	197
Not previously infected	0	0	0	554	554
Recovered	1	0	1	155	157
Recovery	174	43	0	0	217
Vaccination	0	0	0	335	335
Not interpretable	1	0	0	0	1
Total	257	53	1	1189	1500

s) RX = reactive

t) NR = non-reactive

HBV classification	PPA (95 % CI, Wilson score)	NPA (95 % CI, Wilson score)
Acute	N/A (0/0)	100 % (7/7)
Chronic	100 % (25/25)	100 % (7/7)
Early recovery	84.8 % (56/66)	100 % (131/131)
Not previously infected	N/A (0/0)	100 % (554/554)
Recovered	100 % (1/1)	99.4 % (155/156)
Recovery	80.2 % (174/217)	N/A (0/0)
Vaccination	N/A (0/0)	100 % (335/335)
Not interpretable	N/A (0/0)	N/A (0/0)
Total	82.9 % (257/310)	99.9 % (1189/1190)

Supplemental cohort

HBV classification	Composite comparator				Total
	Reactive		Non-reactive		
	Elecsys Anti-HBe		Elecsys Anti-HBe		
	RX[s)]	NR[t)]	RX	NR	
	n	n	n	n	
Acute	103	2	2	21	128
Chronic	54	4	1	113	172
Total	157	6	3	134	300

HBV classification	PPA (95 % CI, Wilson score)	NPA (95 % CI, Wilson score)
Acute	98.1 % (103/105)	91.3 % (21/23)
Chronic	93.1 % (54/58)	99.1 % (113/114)
Total	96.3 % (157/163)	97.8 % (134/137)

Overall summary of clinical study results

The percent agreements for the Elecsys Anti-HBe assay, the FDA-approved reference assay, and the confirmatory assay for at increased risk and supplemental subjects (n = 897) are summarized in the following table.

		Composite result		
		Reactive	Non-reactive	Total
Elecsys Anti-HBe	Reactive	399	14	413
	Non-reactive	20	464	484
Total		419	478	897

The percent agreements were calculated as follows:

	% Agreement	95 % CI[u)]
Positive percent agreeement	95.2	92.7 to 96.9
Negative percent agreement	97.1	95.1 to 98.2

u) CI = confidence interval

Comparator method

At increased risk (AIR) cohort

For the at increased risk cohort, the results were further analyzed to assess the perfomance of the FDA-approved reference assay and the Elecsys Anti-HBe assay as compared to the confirmatory assay. The results showing the comparison of the FDA-approved reference assay and the confirmatory assay are shown in the following table.

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FDA-approved reference assay versus confirmatory assay using comparator method			
FDA-approved reference assay	Confirmatory assay		Total
	Confirmed reactive	Confirmed non-reactive	
Positive	197	2	199
Negative	211	1090	1301
Total	408	1092	1500

The results showing the comparison of the Elecsys Anti-HBe assay and the confirmatory assay are shown in the following table.

Elecsys Anti-HBe assay versus confirmatory assay using comparator method			
Elecsys Anti-HBe assay	Confirmatory assay		Total
	Reactive	Non-reactive	
Positive	255	3	258
Negative	50	1192	1242
Total	305	1195	1500

A summary of performance, including percent agreements, of the Elecsys Anti-HBe assay and the FDA-approved reference assay compared to confirmatory assay for the adult at increased risk cohort are presented in the following table.

Summary of performance of Elecsys Anti-HBe assay and the FDA-approved assay compared to the confirmatory assay				
	PPA (%)	95 % CI	NPA (%)	95 % CI
Elecsys Anti-HBe assay	83.6	79.0-87.3 %	99.7	99.3-99.9 %
FDA-approved reference assay	48.3	43.5-53.1 %	99.8	99.3-99.9 %

Supplemental cohort

For the supplemental cohort, the results were further analyzed to assess the perfomance of the FDA-approved reference assay and the Elecsys Anti-HBe assay as compared to the confirmatory assay. The results showing the comparison of the FDA-approved reference assay and the confirmatory assay are shown in the following table.

FDA-approved reference assay versus confirmatory assay using comparator method			
FDA-approved reference assay	Confirmatory assay		Total
	Confirmed reactive	Confirmed non-reactive	
Positive	50	2	52
Negative	143	105	248
Total	193	107	300

The results showing the comparison of the Elecsys Anti-HBe assay and the confimatory assay are shown in the following table.

Elecsys Anti-HBe assay versus confirmatory assay using comparator method			
Elecsys Anti-HBe assay	Confirmatory assay		Total
	Confirmed reactive	Confirmed non-reactive	
Positive	144	15	159
Negative	7	134	141
Total	151	149	300

A summary of performance, including percent agreements, of the Elecsys Anti-HBe assay and the FDA-approved reference assay compared to confirmatory assay for the supplemental cohort are presented in the following table.

Summary of performance of Elecsys Anti-HBe assay and the FDA-approved assay compared to the confirmatory assay				
	PPA (%)	95 % CI	NPA (%)	95 % CI
Elecsys Anti-HBe assay	95.4	90.7-97.7 %	89.9	84.1-93.8 %
FDA-approved reference assay	25.9	20.2-32.5 %	98.1	93.4-99.5 %

Overall (combined AIR and supplemental cohorts) results

The overall analysis of the study results, combining the at increased risk and supplemental cohorts, comparing the FDA-approved reference assay and the confirmatory assay. Results are summarized in the following table.

FDA-approved reference assay versus confirmatory assay using comparator method			
FDA-approved reference assay	Confirmatory assay		Total
	Confirmed reactive	Confirmed non-reactive	
Positive	247	4	251
Negative	415	1134	1549
Total	662	1138	1800

The overall analysis of the study results, combining the at increased risk and supplemental cohorts, comparing the Elecsys Anti-HBe assay and the confirmatory assay. Results are summarized in the following table.

Elecsys Anti-HBe assay versus confirmatory assay using comparator method			
Elecsys Anti-HBe assay	Confirmatory assay		Total
	Confirmed reactive	Confirmed non-reactive	
Positive	399	18	417
Negative	57	1326	1383
Total	456	1344	1800

The overall percent agreements for the Elecsys Anti-HBe assay and the FDA-approved reference assay as compared to the confirmatory assay for the study are summarized in the following table.

Summary of performance of Elecsys Anti-HBe assay and the FDA-approved assay compared to the confirmatory assay				
	PPA (%)	95 % CI	NPA (%)	95 % CI
Elecsys Anti-HBe	87.5	84.1-90.2 %	98.7	97.9-99.2 %
FDA-approved reference assay	37.3	33.7-41.1 %	99.6	99.1-99.9 %

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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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PreciControl Anti-HBe

cobas®

REF 11876384160 **16 x 1.3 mL**

English

For use in the USA only

Intended use

PreciControl Anti-HBe is used for quality control of the Elecsys Anti-HBe immunoassay on the **cobas e** 602 immunoassay analyzer. The performance of PreciControl Anti-HBe has not been established with any other anti-HBe assay.

Summary

PreciControl Anti-HBe 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-HBe immunoassay.

Reagents - working solutions

- PC A-HBE1: 8 bottles, each containing 1.3 mL of control serum Human serum, negative for anti-HBe; preservative.
  Target range for the cutoff index: 1.2-2.1
- PC A-HBE2: 8 bottles, each containing 1.3 mL of control serum anti-HBe antibodies (human) approximately 0.25 IU/mL (WHO Standard) in human serum; preservative.
  Target range for the cutoff index: 0.30-0.90

The exact ranges, given in the form of a cutoff index (COI), are encoded in the barcodes as well as printed on the enclosed (or electronically available) value sheet.

Target values and ranges

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

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.

Note:
Always refer to the value sheet included in the reagent kit or PreciControl kit to make sure that the correct target values are used.
When a new reagent or control lot is used, the analyzer will use the original values encoded in the control barcodes.

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.

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.

All human material should be considered potentially infectious.

PC A-HBE1 has 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.

Materials of human origin used for the positive control (PC A-HBE2) were tested for HIV and hepatitis C infections. The findings were negative. The serum containing anti-HBe was inactivated using β-propiolactone and UV-radiation.

However, as no inactivation or testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[1,2]

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.

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
on the analyzers at 20-25 °C	up to 6 hours

Materials provided

- PreciControl Anti-HBe

Materials required (but not provided)

- **cobas e** 602 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.

PreciControl Anti-HBe

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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