HBsAg

Hepatitis B surface antigen

Elecsys® 2010 System

820532

100 tests

WARNING

- *This assay has not been FDA cleared or approved for the screening of blood or plasma donors.*
- *Assay performance characteristics have not been established when the Elecsys HBsAg assay is used in conjunction with other manufacturers' assays for specific HBV serological markers. Users are responsible for establishing their own performance characteristics.*
- *Assay performance characteristics have not been established for testing of newborns.*
- *Federal law restricts this device to sale by or on the order of a physician.*
- *Prenatal testing specificity has been minimally established, users may wish to establish their own specificity for prenatal screening.*

Intended use

Immunoassay for the in vitro qualitative detection of hepatitis B surface antigen (HBsAg) in human serum and plasma (sodium heparin, EDTA-K_3, sodium citrate). Assay results, in conjunction with other serological and clinical information, may be used for the laboratory diagnosis of individuals with acute or chronic hepatitis B. In addition, this assay may be used to screen for hepatitis B infection in pregnant women to identify neonates who are at high risk of acquiring HBV during the perinatal period.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Roche Elecsys 2010 immunoassay analyzer.

Summary*

The hepatitis B surface antigen, a polypeptide of varying size, is a component of the external envelope of the hepatitis B virus particle (HBV).[1] The blood of persons infected with HBV contains, in addition to intact infectious HBV particles, smaller non-infectious "empty" envelope particles, which are formed in great excess and also contain the hepatitis B surface antigen.[2] The HBsAg determinant a, against which the immune response is mainly directed, is common to all HBsAg particles. In addition, either the main determinants d or y and w or r are present.[3] The detection of HBsAg in human serum or plasma indicates an infection by the hepatitis B virus. HBsAg is the first *immunological* marker and is generally present some days or weeks before clinical symptoms begin to appear. HBsAg is observed in persons with acute and chronic hepatitis B infections. In rare cases an HBV infection can also take place without HBsAg being detectable.[4]

HBsAg tests are used within the scope of diagnostic procedures to identify persons infected with HBV and to prevent the transmission of the hepatitis B virus.

The Elecsys HBsAg test uses mouse monoclonal anti-HBs antibodies for the HBsAg determination.

Test principle*

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 50 µl of sample, a biotinylated monoclonal HBsAg-specific antibody and a monoclonal HBsAg-specific antibody labeled with a ruthenium complex** react to form a sandwich complex.
- 2nd incubation: after the 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. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined automatically by the Elecsys software by comparing the electrochemiluminescence signal obtained from the sample with the cutoff value previously obtained by HBsAg calibration.

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

Reagents - contents and concentrations

Elecsys HBsAg reagent kit, Cat. No. 1820532 - 100 tests

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 ml:
Streptavidin-coated microparticles, 0.72 mg/ml, binding capacity: 470 ng biotin/mg microparticles; preservative.

R1 Anti-HBsAg Ab~biotin (gray cap), 1 bottle, 10 ml:
Biotinylated monoclonal anti-HBsAg antibodies (mouse-directed to the "a" region determinant) > 0.5 mg/l; phosphate buffer 100 mmol/l, pH 7.4; preservative.

R2 Anti-HBsAg Ab~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 10 ml:
Monoclonal anti-HBsAg antibodies (mouse-directed to the "a" region determinant) labeled with ruthenium complex > 0.8 mg/l; phosphate buffer 100 mmol/l, pH 8.0; preservative.

Cal1 Negative calibrator (white cap), 2 bottles of 1.3 ml each:
Human serum; preservative.

Cal2 Positive calibrator (black cap), 2 bottles of 1.3 ml each:
HBsAg approx. 0.5 IU/ml in human serum; preservative.
Non-reactive for anti-HBs, anti-HCV and anti-HIV 1+2.

Precautions and warnings

For in vitro diagnostic use.

Disposal of all waste material should be in accordance with local guidelines.

Exercise the normal precautions required for handling all laboratory reagents.

The calibrators have been prepared exclusively from the blood of donors tested individually and shown by FDA-approved methods to be free from HBsAg (Cal1 only) and antibodies to HIV 1+2 and HCV.

The serum containing HBsAg used for the positive calibrator (Cal2) has been cold-sterilized

Reagent handling*

The reagents in the kit are ready for use and are supplied in bottles compatible with the system. The calibrators Cal1 and Cal2 should only be left on the analyzers during calibration at 20–25°C. After use, close the bottles as soon as possible and store at 2–8°C. Ensure that no calibrator solution is trapped in the opened snap-cap. Because of possible evaporation effects, not more than 5 calibration procedures per calibrator bottle set should be performed.

The reagents may not be used after the stated expiration date.

All information required for correct operation is automatically read in via the reagent bar code.

Storage and stability*

Store at 2–8°C.

Store the Elecsys HBsAg reagent kit (M, R1, R2) **upright** in order to ensure complete availability of the microparticles during the automatic mixing prior to use.

Stability:

unopened at 2–8°C	up to the stated expiration date
M, R1, R2 after opening on Elecsys 2010	twelve weeks at 2–8°C four weeks
Cal 1, Cal 2 after opening on the analyzer	twelve weeks at 2–8°C five hours in total.

Store calibrators upright. Ensure that calibrator solution does not adhere to snap-cap.

Specimen collection and preparation*

None other than the specimens listed below were tested in sufficient amounts.

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

Plasma treated with sodium heparin, EDTA-K_3, or sodium citrate.

Lithium heparin plasma tubes containing separating gel cannot be used.

Stable for five days at 2-8° C, three months at -20° C. The samples may be frozen and thawed six times.[7]

For information on the stability of serum obtained with tubes containing separating gel, please note the data provided by the tube manufacturer.

Samples containing precipitates must be centrifuged before performing the assay. Heat-inactivated samples may be used. Samples and controls stabilized with azide cannot be used.

Ensure the patients samples, calibrators and controls are at ambient temperature (20–25°C) before measurement.

Elecsys HBsAg testing procedure*

Materials provided

Cat. No. 1820532, Elecsys HBsAg reagent kit for 100 tests contains:

- M Streptavidin-coated microparticles
- R1 Anti-HBsAg-Ab~biotin
- R2 Anti-HBsAg-Ab~$Ru(bpy)_3^{2+}$
- Cal1 Negative calibrator
- Cal2 Positive calibrator

Materials required (but not provided)

- Cat. No. 1876309, Elecsys PreciControl HBsAg, for 8 x 1.3 ml each of PreciControl HBsAg 1 and 2
- Cat. No. 1820648, Elecsys HBsAg Confirmatory Test, 2 x 1 ml each of confirmatory reagent and control reagent.
- Cat. No. 1732277, Elecsys Diluent Universal, 2 x 18 ml sample diluent or
  Cat. No. 3183971, Elecsys Diluent Universal, 2 x 40 ml sample diluent
- Elecsys 2010 analyzer
- Cat. No.1662988, Elecsys ProCell, 6 x 380 ml system buffer
- Cat. No. 1662970, Elecsys CleanCell, 6 x 380 ml measuring cell cleaning solution
- Cat. No. 1930346, Elecsys SysWash, 1 x 500 ml additive for washing water
- Cat. No. 1298500, Elecsys SysClean, 5 x 100 ml system cleaning solution
- Cat. No. 1933159, Adapter for SysClean
  Cat. No. 1706802, Elecsys 2010 Assay Cup, 60 x 60 reaction vessels
- Cat. No. 1706799, Elecsys 2010 Assay Tip, 30 x 120 pipette tips
- General laboratory equipment

Assay*

For optimal performance of the assay it is important to follow the directions given for the analyzer used, and to check that the system's inventory of assay materials and other consumables is adequate.

Resuspension of the microparticles before use and the reading in of the test-specific parameters via the reagent bar code take place automatically. No manual input is necessary. If in exceptional cases the bar code cannot be read, enter the 15-digit sequence of numbers.

Bring the cooled reagents to approx. 20°C and place on the reagent disk of the Elecsys 2010 analyzer. Avoid the formation of foam. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Place Elecsys HBsAg Cal1 and Cal2 in the sample zone of the analyzer. Only keep open during calibration. All information necessary for calibration is encoded on the bar-coded bottle labels and is read in automatically. After calibration has been performed, store Elecsys HBsAg Cal1 and Cal2 at 2–8°C.

Calibration*

Elecsys HBsAg has been calibrated against the 1st WHO International Standard for HBsAg, subtype ad (IU/ml), 80/549, 1985. The following reference materials from the Paul Ehrlich Institute, Langen (Germany), were also measured (U/ml) and compared with the WHO standard:
"HBsAg reference material No. 1 (subtype ad; 1987)": 1 U/ml ≙ 2.4 IU/ml (WHO),
"HBsAg reference material No. 1 (subtype ay; 1987)": 1 U/ml ≙ 3.2 IU/ml (WHO),
"HBsAg reference material 1A (1st, 1992)": 1 U/ml ≙ 1.2 IU/ml (WHO).

Calibration frequency:

Calibration must be performed once per reagent lot using Elecsys HBsAg Cal 1, Cal 2 and fresh reagent (i.e. not more than 24 hours since the reagent pack was registered on the analyzer).

Perform renewed calibration as follows:

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Calibration verification: Not necessary. The analyzer's software automatically checks the validity of the curve and draws attention to any deviations.
Range for the electrochemiluminescence signals (counts) for the calibrators: 600–1,200 for the negative calibrator (Cal1) and 3,000–8,000 for the positive calibrator (Cal2).

Quality control*
Elecsys PreciControl HBsAg.
The controls 1 and 2 should be run as single determinations at least once every 24 hours when the test is in use, once per reagent kit and after every calibration. The control intervals should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined ranges.
Each laboratory should establish guidelines for corrective measures to be taken if values fall outside the range. If necessary, measurement of the samples in question should be repeated.
The furnished quality control material is serum based. This material will not adequately control the assay when plasma matrix are used. The user is responsible for establishing their own control material when these matrix are tested.
Additional controls may be tested according to guidelines or requirements of local, state, and/or federal regulations or accrediting organizations.

Calculation*
The Elecsys 2010 automatically calculates the cutoff on the basis of the Cal1 and Cal2 measurements.
The cutoff for the Elecsys 2010 HBsAg immunoassay was established by testing a 175 member panel of well characterized HBsAg specimens with three kit lots followed by testing on two kits lots with over 2,800 specimens including subjects at various risk for HBV infection, sensitivity, specificity and seroconversion panels and dilution series of both international reference materials and HBs Ag positive samples. Using these data, the cutoff value that allowed for optimal discrimination between negative and positive specimens was determined.

Cutoff Formula:
Cutoff value=1.2 x (signal $_{Cal1}$ - background*) + 0.05 x (signal $_{Cal2}$ - background*)
*background = 0.7 x signal $_{Cal1}$

The sample results are reported as reactive or non-reactive, and in the form of a cutoff-index (signal of sample/cutoff).
Interpretation of the results:
Samples having a cutoff-index < 1.0 are not reactive in the Elecsys HBsAg test. These samples are deemed negative for HBsAg and need not be further tested.
Samples having a cutoff-index ≥ 1.0 are reactive in the Elecsys HBsAg test. All samples active in the initial test must be redetermined in duplicate using the Elecsys HBsAg test. If the results from this follow-up test are negative in both cases, then the sample is deemed negative for HBsAg.
If the result in either of the two repeat measurements is reactive, then the sample is deemed repeatedly reactive. Repeatedly reactive samples must be investigated using an independent neutralization test (Elecsys HBsAg Confirmatory Test).
Samples confirmed by neutralization with human anti-HBs are regarded as positive for HBsAg.

- Results obtained with the Elecsys HBsAg assay may not be used interchangeably with values obtained with different manufacturers' assay methods.
- The magnitude of a Elecsys HBsAg assay result cannot be correlated to an endpoint titer.
- The ability of the Elecsys HBs Ag assay to detect HBV mutants has not been determined. Testing using alternative methodologies may be warranted if signs, symptoms, and risk factors are indicative of viral hepatitis and other laboratory tests are nonreactive for the diagnosis of viral hepatitis.
- Heparin and citrate have been shown to lower the signal/cutoff (s/c) values in some HBsAg reactive samples. High negative results (0.80-0.99 s/c) obtained on samples collected with these anticoagulants should be interpreted accordingly. Supplemental tests may be required.

Limitations - Interference*
The assay is unaffected by icterus (bilirubin < 30 mg/dl), hemolysis (Hb < 1.4 g/dl), lipemia (triglycerides < 1500 mg/dl) and biotin < 40 ng/ml (criterion: recovery within ± 10% of initial value).
In patients receiving therapy with high biotin doses (i.e. > 5 mg/day) no sample should be taken until at least 8 hours after the last biotin administration.
No false negative findings due to the high-dose hook effect are observed up to a HBsAg concentration of 1.5 million IU/ml.
As with all tests containing monoclonal mouse antibodies, erroneous findings may be obtained from samples taken from patients who have been treated with monoclonal mouse antibodies or have received them for diagnostic purposes.
In rare cases, interference due to extremely high titers of antibodies to streptavidin and ruthenium can occur.
Elecsys HBsAg contains additives which minimize these effects.
For diagnostic purposes, the Elecsys HBsAg findings should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.
It is recognized that presently available methods for the detection of hepatitis B surface antigen may not detect all potentially infected individuals. A nonreactive test result does not exclude the possibility of exposure to or infection with hepatitis B. Nonreactive test results in individuals with prior exposure to hepatitis B may be due to antigen levels below the detection limit of this assay or lack of antigen reactivity to the antibodies used in this assay.
Individuals recently vaccinated for hepatitis B may give a transient positive result for HBsAg because of its presence in the vaccine.[9]
The analytical sensitivity of the Elecsys HBsAg immunoassay was found to be 0.028 IU/ml using the WHO 1st International Standard (subtype ad, Code 80/549; 1985); 0.010 E/ml using the PEI Reference Material No 1 (subtype ad, 1000 E/ml: 1987).
Assay performance characteristics have not been established for any other specimen matrices than serum, plasma treated with sodium heparin, EDTA-K_3 or sodium citrate.

Expected values
Of 1445 prospective subjects participating in the Elecsys HBsAg clincial study, 41.5% (n = 600) were first time blood donors, asymptomatic for viral hepatitis. All of these subjects were enrolled in Sacramento, CA. The group was Caucasian (61%), African American (10%), Hispanic (2%), Asian (1%) with 26% electing not to provide this information. The group was 58% male and 42% female ranging in age from 17 to 73 years. There were no confirmed positive results for HBsAg by either the reference or the Elecsys test system among these subjects. The table below summarizes the Elecsys HBsAg negative and confirmed positive results by age range and gender.

	Elecsys HBsAg Immunoassay Test Systems					
Age	**Gender**	**Pos**	**Percent**	**Neg**	**Percent**	**Total**
< 10	Male	0	NA	0	NA	0
	Female	0	NA	0	NA	0
10 - 19	Male	0	NA	177	100	177
	Female	0	NA	115	100	115
20 - 29	Male	0	NA	71	100	71
	Female	0	NA	42	100	42
30 - 39	Male	0	NA	45	100	45
	Female	0	NA	46	100	46
40 - 49	Male	0	NA	35	100	35
	Female	0	NA	32	100	32
50 - 59	Male	0	NA	16	100	16
	Female	0	NA	13	100	13
60 - 69	Male	0	NA	2	100	2
	Female	0	NA	4	100	4
70 - 79	Male	0	NA	1	100	1
	Female	0	NA	1	100	1
80 - 89	Male	0	NA	0	NA	0
	Female	0	NA	0	NA	0
90 - 99	Male	0	NA	0	NA	0
	Female	0	NA	0	NA	0
Unknown	Male	0	NA	0	NA	0
	Female	0	NA	0	NA	0
Totals	Male	0	NA	347	100	347
	Female	0	NA	253	100	253
	All	0	NA	600	100	600

The 845 remaining subjects were enrolled from populations considered at risk for viral hepatitis due to lifestyle or behavior. Of these, 448 were outpatients of a health screening clinic, 299 were hospitalized patients and 98 were IV drug users. All 98 IV drug users were enrolled in Baltimore, MD. Of the hospitalized and health screening clinic patients, 444 of the subjects were enrolled in Memphis, TN and 303 in Miami, FL. This collective group was African American (26%), Caucasian (19%), Hispanic (5%), Asian (<1%) or other (<1%) with 49% electing not to provide this information. The group was 49% male and 51% female ranging in age from 8 to 94 years. Six (6) of these subjects were confirmed positive by both the reference and the Elecsys assay reference assay. A follow-up specimen taken 28 days later from the same subject and was confirmed positive by both assays showing that the first Elecsys result was correct. The table below summarizes the Elecsys HBsAg negative and confirmed positive results by age range and gender.

	Elecsys HBsAg Immunoassay Test System					
Age	**Gender**	**Pos**	**Percent**	**Neg**	**Percent**	**Total**
< 10	Male	0	NA	1	100	1
	Female	0	NA	0	NA	0
10 - 19	Male	0	NA	7	100	7
	Female	0	NA	10	100	10
20 - 29	Male	1	0.7	135	99.3	136
	Female	3	2.5	117	97.5	120
30 - 39	Male	0	NA	60	100	60
	Female	2	3.1	62	96.9	64
40 - 49	Male	0	NA	56	100	56
	Female	0	NA	65	100	65
50 - 59	Male	0	NA	53	100	53
	Female	0	NA	44	100	44
60 - 69	Male	0	NA	38	100	38
	Female	1	1.9	53	98.1	54
70 - 79	Male	0	NA	33	100	33
	Female	0	NA	46	100	46
80 - 89	Male	0	NA	12	100	12
	Female	0	NA	19	100	19
90 - 99	Male	0	NA	1	100	1
	Female	0	NA	3	100	3
Unknown	Male	0	NA	14	100	14
	Female	0	NA	8	100	8
Totals	Not Given	0	NA	1	100	1

HBsAg

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Specific Performance Data of the Test*

Clinical Performance

A multi-center prospective study was conducted to characterize the performance of the Elecsys 2010 HBsAg immunoassay test system with individuals from defined populations. All subjects were tested using FDA-approved/cleared reference methods in strict accordance with the manufacturer's package insert instructions. The collection sites for the specimens were located in Sacramento, CA (41.5%), Baltimore, MD (6.8%), Memphis, TN (30.7%) and Mianmi, FL (21%). Of the 1445 prospective subjects participating in the Elecsys HBsAg clinical study, 41.5% (n=600) were first time blood donors, asymptomatic for viral hepatitis and 845 subjects were at risk of HBV infection due to lifestyle or behavior. Of the 845 at risk subjects, 53.0% (n=448) were outpatients of a health screening clinic, 35.4% (n=299) were hospitalized patients and 11.6% (n=98) were IV drug users.

The first time blood donors were Caucasian (61%), African American (10%), Hispanic (2%), Asian (1%) with 26% electing not to provide this information. The group was 58% male and 42% female ranging in age from 17 to 73 years. The at risk subjects were African American (26%), Caucasian (19%), Hispanic (5%), Asian (< 1%) or other (<1%) with 49% electing not to provide this information. This group was 49% male and 51% female ranging in age from 8 to 94 years.

The performance of the Elecsys HBsAg immunoassay test system was analyzed relative to the reference HBsAg reported results for all 1445 specimens. Complete testing using FDA approved methods for all 6 HBV markers including HBsAg, HBeAg, anti-HBc, anti-HBc IgM, anti-HBe and anti-HBs, thus allowing single point serological classifications of HBV status, was available for 382 of the subjects.

Results by Specimen Classification

HBV classification were performed based on the constellation of test results from FDA-approved methodologies for various markers of HBV, Elecsys test results were not considered in these classifications. Presented below are the interpretations of HBV classificaitons made for each of the serological profiles observed.

HBV Classification	HBsAg	HBeAg	anti-HBc	anti-HBc IgM	anti-HBe IgG+M	anti-HBs
Acute	pos	+ or -	-	-	-	-
Acute	pos	+ or -	pos	pos	+ or-	-
Chronic*	pos > 6 mo					
Chronic	pos	+ or -	-	pos	+ or -	+ or -
Early Recovery	-	-	pos	pos	+ or -	+ or -
Recovery	-	-	-	pos	pos	+ or -
Recovered	-	-	-	pos	-	+ or -
Vaccinated	-	-	-	-	-	pos
not previously infected	-	-	-	-	-	-
Uninterpretable	pos	-	pos	pos	pos	pos
Uninterpretable	-	pos	-	-	-	-
Uninterpretable	-	pos	-	-	-	pos
Uninterpretable	-	pos	-	pos	-	pos
Uninterpretable	-	-	-	-	pos	pos
Uninterpretable	-	-	-	-	-	equiv

*Subjects known, by testing to have HBsAg persisting for greater than 6 months.

Results by Specimen Classification

The following table compares the Elecsys 2010 HBsAg results with the reference results for the prospective studies first time blood donors by HBV classification.

HBV Classification	Final HBsAg Result Reference Test System				Total
	-		+		
	Elecsys HBsAg Results		Elecsys HBsAg Results		
	-	+	-	+	
Acute	0	0	0	0	0
Chronic	0	0	0	0	0
Early Recovery	1	0	0	0	1
Recovery	2	0	0	0	2
Recovered	1	0	0	0	1
Uninterpretable	1	0	0	0	1
HBV Vaccine Response	86	0	0	0	86
Not Previously Infected	31	0	0	0	31
Incomplete Testing	478	0	0	0	478
Total	600	0	0	0	600

The table below compares the Elecsys 2010 HBsAg results with the reference results for the prospective studies with subjects at risk for HBV infection due to lifestyle or behavior by HBV classification.

HBV Classification	Final HBsAg Result Reference Test System				Total
	-		+		
	Elecsys HBsAg Results		Elecsys HBsAg Results		
	-	+	-	+	
Acute	0	0	0	3	3
Chronic	0	0	0	2	2
Early Recovery	4	0	0	0	4
Recovery	36	0	0	0	36
Recovered	31	0	0	0	31
Uninterpretable	8	0	0	0	8
HBV Vaccine Response	140	0	0	0	140
Not Previously Infected	35	1*	0	0	36
Incomplete Testing	584	0	0	1	585
Total	838	1	0	6	845

* This specimen was tested using the Roche Molecular Systems HBV Monitor Test and yielded a count of >9600 copies of HBV DNA/ml. A follow-up sample from the same patient taken 28 days after the first sample was confirmed positive on both the reference and Elecsys HBsAg immunoassay test systems.

Percent Agreement

The table below summarizes the percent agreement between the Elecsys 2010 HBsAg Immunoassay Test System and the HBsAg reference assay test system with first time blood donors by specimen classification. The table also provides the upper and lower 95% Exact confidence bounds.

HBV Classification	Positive Percent Agreement	95% Exact Confidence Interval	Negative Percent Agreement	95% Exact Confidence Interval
Acute	NA	NA	NA	NA
Chronic	NA	NA	NA	NA
Early Recovery	NA	NA	100.0 (1/1)	2.5 - 100
Recovery	NA	NA	100 (2/2)	15.9 - 100
Recovered	NA	NA	100 (1/1)	2.5 - 100
Uninterpretable	NA	NA	100 (1/1)	2.5 - 100
HBV Vaccine Response	NA	NA	100 (86/86)	95.8 - 100
Not Previously Infected	NA	NA	100 (31/31)	88.8 - 100
Incomplete Testing	NA	NA	100 (478/478)	99.2 - 100
Overall	NA	NA	100 (600/600)	99.4 - 100

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ıe table below summarizes the percent agreement between the Elecsys 2010 HBsAg .ınmunmoassay Test System and the HBsAg reference assay test system with subjects at risk for HBV infection due to lifestyle or behavior by specimen classification. The table also provides the upper and lower 95% Exact confidence bounds.

HBV Classification	Positive Percent Agreement	95% Confidence Interval	Negative Percent Agreement	95% Confidence Interval
Acute	100 (3/3)	29.5-100.0	NA	NA
Chronic	100 (2/2)	15.9 - 100	NA	NA
Early Recovery	NA	NA	100.0 (4/4)	40.0-100.0
Recovery	NA	NA	100 (36/36)	90.3-100.0
Recovered	NA	NA	100 (31/31)	88.8 - 100.0
Uninterpretable	NA	NA	100 (8/8)	63.2-100.0
HBV Vaccine Response	NA	NA	100 (140/140)	97.4-100.0
Not Previously Infected	NA	NA	97.2 (35/36)	85.5-99.9
Incomplete Testing	100 (1/1)	2.5-100.0	100 (584/584)	99.4-100.0
Overall	100 (6/6)	54.3-100.0	98.7 (838/838)	97.7-99.3

Percent Agreement of the Elecsys HBsAg Immunoassay for Subjects at Various Discrete Stages of HBV Infection or Recovery

The performance of the Elecsys 2010 HBsAg Immunoassay test system was studied with archived specimens representing various discrete stages of HBV infection or recovery. The table below compares the Elecsys HBsAg immunoassay test system results with the HBsAg reference assay test system results by specimen classification.

HBV Classification	Final HBsAg Results Reference Test System				Total
	-		+		
	Elecsys HBsAg Results		Elecsys HBsAg Results		
	-	+	-	+	
Acute	0	0	0	151	151
Chronic	0	0	0	111	111
Chronic-HBsAG >6 mo*	0	0	0	74	74
Early Recovery	4	1°	0	0	5
Recovery	35	0	0	0	35
Recovered	24	0	0	0	24
Uninterpretable	4	0	0	1	5
HBV Vaccine Response	6	0	0	0	6
Not Previously Infected	9	0	0	0	9
Total	82	1	0	337	420

* Subjects known, by testing, to have HBsAg persisting for greater than 6 months.
° This specimen by the reference method was repeatedly within 10% of cut-off and showed 100% acutralization but was classified as negative in accordance with reference test's approved package insert instructions since the initial test was below cut-off at 0.94 COI.

The following table summarizes the percent agreement between the Elecsys 2010 HBsAg Immunoassay Test System and the HBsAg reference assay test system by specimen classification, and provides the upper and lower 95% Exact confidence bounds.

HBV Classification	Positive Percent Agreement	95% Confidence Interval	Neg Percent Agreement	95% Confidence Interval
Acute	100 (151/151)	97.6-100.0	NA	NA
Chronic	100 (111/111)	96.8-100.0	NA	NA
Chronic - HBsAg >6 mo	100 (74/74)	95.1-100.0	NA	NA
Early Recovery	NA	NA	80 (4/5)	28.6-99.5
Recovery	NA	NA	100 (35/35)	90.0-100.0
Recovered	NA	NA	100 (24/24)	85.8-100.0
Uninterpretable	100 (1/1)	2.5 - 100	100 (4/4)	40.0-100.0
HBV Vaccine Response	NA	NA	100 (6/6)	54.3-100.0

Seroconversion Panels

A total of nine seroconversion panels from commercial vendors were tested at one of the clinical sites by the Elecsys HBsAg immunoassay and the reference HBsAg assay.
The table below presents a summary of the Elecsys HBsAg immunoassay test system results for the nine panels in comparison to the reference method.

Panel ID	Days to HBsAg Confirmed Reactive result from Initial Draw Date		Difference in days to HBsAg Reactive Result (Reference-Elecsys)
	Reference HBsAg Assay	Elecsys HBsAg Assay	
01005	16	16	0
11004	26	26	0
40565L	5	5	0
51005	0	0	0
21469D	0	0	0
22663D*	17	17	0
PHM902	71	71	0
PHM907	50	50	0
PHM919**	19	19	0
PHM920	26	26	0

*Initial reactive results only, quantity not sufficient to perform confirmatory with either assay
** Sample was reactive on Day 14 by Elecsys only, but without confirmation

Clinical Performance in Pregnant Women

A total of 81 pregnant women were reported from among all subjects in the Elecsys 2010 HBsAg clinical study. All were considered to be at low risk for HBV infection. The table below summarizes the Elecsys 2010 HBsAg final result in comparison to the reference method by age and ethnic group. Information on trimester stage was not available.

Ethnicity	Age	N	Reference HBsAg Assay Final Result		Elecsys 2010 HBsAg Final Result	
			Positive	Negative	Positive	Negative
African-American	10-19	5	0	5	0	5
	20-29	8	1	7	1	7
	30-39	2	0	2	0	2
	40-49	0	0	0	0	0
Caucasian	10-19	1	0	1	0	1
	20-29	7	0	7	0	7
	30-39	8	0	8	0	8
	40-49	1	0	1	0	1
Not Provided	10-19	3	0	3	0	3
	20-29	29	1	28	1	28
	30-39	15	1	14	1	14
	40-49	1	0	1	0	1
	not given	1	0	1	0	1
		81	3 (3.7%)	78 (96.3%)	3 (3.7%)	78 (96.3%)

The table below summarizes the percent agreement between the Elecsys HBsAg Immunoassay Test System and the HBsAg reference assay test system with pregnant women. The table also provides the upper and lower 95% Exact confidence bounds.

Subjects	Positive Percent Agreement	95% Exact Confidence Interval	Negative Percent Agreement	95% Exact Confidence Interval
Pregnant	100 (3/3)	29.5-100.0	100 (78/78)	95.4-100.0

HBsAg

Hepatitis B surface antigen

Elecsys® System 2010

Analytical Specificity

No crossreactivity was seen in specimens from patients having HAV, HCV, HAV/HCV co-infection, or HEV. Additionally, no crossreactivity was seen in patients with CMV (n=10), EBV (n=10), E-Col (n=10), HIV (n=9), HSV (n=14), Parvovirus B19 (n=10), Rubella (n=10), Syphilis (n=10), Toxoplasmosis (n=13). Samples from patients with non-viral liver disease, influenza vaccination and gammopathies were found non-reactive with the Elecsys HBsAg immunoassay. The results from the analytical specficity studies are shown in the table below.

Elecsys HBsAg Immunoassay	Neg	Neg	Pos	Pos	Total Samples
HBV Status	Neg	Pos	Neg	Pos	n
Other Viral Hepatitis Infections	46	0	0	0	46
Other Infectious Diseases	87	1*	0	8**	96
Non-Viral Liver Diseases	24	0	0	0	24
Autoimmune Diseases	19	0	0	1[a]	20
High Risk Populations	30	0	0	1[b]	31
Post Influenza Vaccination	5	0	0	0	5
Gammopathy	10	0	0	0	10
Total	221	1	0	10	232

*Patient with HSV infection
**Patients with HIV (n=4), Parvovirus B19 (n=3), Toxoplasmosis infection (n=1)
[a] Rheumatoid Factor+
[b] IV drug user

A database search of the "BLAST" database (http://www.ncbi.nlm.nih.gov/blast) was performed for the two mouse monoclonal antibodies (Mabs) used in the Elecsys 2010 HBsAg immunoassay. The biotinylated Mab was found to be highly specific to a conformational epitope of HBsAg "a" region determinant while the ruthenylated-Mab showed no relevant sequence homology with any known virus other than its designated target. The results of the search are interpreted as evidence that cross-reactivity by the kit Mabs to other non-HBV viruses is highly remote.

Specific Performance Data of the Test*[11]

Precision

In a three-center precision study based on the NCCLS draft guideline EP5-T2, results from a series of negative and positive samples run on the Elecsys 2010 analyzer at three centers had within run precision ranging from 1.3 to 7.5% CV.[11] Between day precision, which also included within run and between run, ranged from 4.6 to 16.3% CV; total precision, which included all precision components, ranged from 6.0 to 22.3% CV.

Panel Member	Mean COI	Within Run SD	Within Run CV	Between Day[a] SD	Between Day[a] CV	Total[b] SD	Total[b] CV
1	0.419	0.0314	7.5%	0.0685	16.3%	0.0946	22.6%
2	0.767	0.0517	6.7%	0.0632	8.2%	0.1050	13.7%
3	1.78	0.0434	2.4%	0.1088	6.1%	0.1486	8.3%
4	19.13	0.2536	1.3%	0.8971	4.7%	1.1390	6.0%
5	51.25	0.6723	1.3%	2.4349	4.7%	3.1569	6.2%
6	100.9	1.2761	1.3%	4.6727	4.6%	6.0313	6.0%

[a] Includes within run, between run and between day components
[b] Includes within run, between run, between day, between site/lot interaction, between lot and between site components.

Analytical Sensitivity

In dilution experiments of international reference standards, the analytical sensitivity of the Elecsys HBsAg immunoassay was found to be 0.028 IU/ml using the WHO 1st International Standard (subtype ad, Code 870/549; 1985); 0.010 E/ml using the PEI Reference Material No 1 (subtype ad, 1000 E/ml; 1987). Duplicate determinations of each panel member were obtained.

Reference Standard	Elecsys HBsAg Immunoassay	95% Confidence Interval
WHO 1st Intl Standard, subtype ad, Code 80/549	0.028 IU/ml	0.024 - 0.032 IU/ml
PEI reference material No. 1, subtype ad, 1987	0.010 E/ml	0.009 - 0.011 E/ml

References

1 Gerlich W. Viral Hepatitis. Section 2, Churchill Livingstone, Ed. Zuckermann AJ, Thomas HC, 1993:83–113.
2 Hollinger FB. Hepatitis B virus In Fields BN, Knipe DM (eds). Virology 2nd ed. New York Raven Press 1990;2:2171–2236.
3 Couroucé-Pauty AM, Plancon A, Soulier JP. Distribution of HBsAg Subtypes in the World. Vox Sang 1983;44:197–211.
4 Frösner G. Moderne Hepatitisdiagnostik. Kilian Verlag,Marburg 1996.
5 Hoofnagle JH DI Bisceglie AM. Serologic Diagnosis of Acute and Chronic Viral Hepatitis, Seminars in Liver Disease 1991; 11(2); 73-83.
6 Frösner G, Schomerus H; Wiedmann KH et al. Diagnostic significance of quantitative HBsAg determination in acute and chronic hepatitis B infection. Eur J Clin Microbiol 1982; 1:52-58.
7 Department of Labor, Occupational Safety and Health Administration - 29 CFR Part 1910.1030. Occupational Exposure to Bloodborne Pathogens; Final Rule. Fed. Register 1991;56:64175-64182.
8 Council Directive (90/679/EEC). Official Journal of the European Communities No. L374 from Dec. 31, 1990.
9 National Committee for Clinical Standards (NCCLS). Evaluation of Precision Performance of Clinical Chemistry Devices - NCCLS document EP5-T2. NCCLS, 771 East Lancaster Avenue, Villanova, Pennsylvania 19085, 1992.
10 Data on file at Roche.
11 Kloster B, Kramer R, Eastlund T, Grossman B, Zarvan B. Hepatitis B surface antigenemia in blood donors following vaccination. Transfusion. 35:475-477; 1995.

* For more detailed information consult the operators' manual for the Elecsys 2010, and the package inserts for the system reagents, Elecsys HBsAg Confirmatory Test, Diluent Universal and PreciControl HBsAg.

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2001 - 07

Roche Diagnostics GmbH, D-68298 Mannheim

For USA:
US Distributor: Roche Diagnostics Corporation, Indianapolis, IN, USA

Elecsys HbsAg Assay

Elecsys®

HBsAg

For the qualitative determination of HBsAg
Zur qualitativen Bestimmung von HBsAg
Pour la détermination qualitative des Ag HBs
Para la determinacion cualitativa de HBsAg
Per la determinazione qualitativa del HBsAg

1820532

Sensitivity/Sensitivität/
Sensibilité/Sensibilidad/
Sensibilità < 0.1 IU/ml

IN VITRO DIAGNOSTICUM

Store at/Lagern bei/Conservation/
Conservar/Conservare a: 2 - 8°C
Contents/Inhalt/Contenu/Contenido/
Componenti:
M | R1 | R2 for/für/pour 100 Tests
M : 6.5 ml, cont./enth.: Streptavidin(e) Microparticle(s) 0.72 mg/ml
R1: 10 ml, cont./enth.: anti-HBsAg-AB/AK/AC (monoclon., mouse/Maus/souris/raton/topo)–biotin(e) > 0.5 mg/l
R2: 10 ml, cont./enth.: anti-HBsAg-AB/AK/AC (monoclon., mouse/Maus/souris/raton/topo)–Ru(bpy) $^{2+}_{3}$ > 0.8 mg/l
Cal 1: 2 x 1.3 ml, cont./enth.: Serum/suero/siero (hum.); 600 - 1200 counts/coups
Cal 2: 2 x 1.3 ml, cont./enth.: HBsAg; Serum/suero/siero (hum.); 3000 - 8000 counts/coups

Prod.:Roche Diagnostics GmbH, D-68298 Mannheim, Zul.-Nr. 101a/97
Roche Diagnostics Corp., Indianapolis, IN, U.S.A.
Distributeur en France: Roche Diagnostics S.A.,
2 Avenue du Vercors, F-38240 Meylan, ADM n°RS7472

Roche

2102048(1) 01

Lot./Ch.-B.: 15526501 1820532
Exp./Verw.bis: 2002 - 04

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Presidio medico chirurgico
nr. 18269 del Ministero della Sanità.
Rappresentante per l'Italia: Roche Diagnostics S.p.A., I-20131 Milano

02 122

HBsAg

Elecsys

HBSAG

Elecsys®

1820532

M 6.5 ml
R1 10 ml
R2 10 ml

8268
IN VITRO
DIAGNOSTICUM

Roche

2 - 8°C

Lot./Ch.-B.:
155265 01
Exp./Verw.bis:
2002 - 04

03

HBSAG CAL 1

Elecsys®

1820532 1.3 ml

In Vitro
Diagnosticum

Roche

2 - 8°C
Lot./Ch.-B.:
123456 12
Exp./Verw.bis:
2000 - 00 02

1820532 1.3 ml

In Vitro
Diagnosticum

Roche

2 - 8°C
Lot./Ch.-B.:
123456 12
Exp./Verw.bis:
2000 - 00 02

HBsAg Confirmatory Test

Elecsys® 2010 System

820648 **2 x 10–15 tests**

WARNING
- *This assay has not been FDA cleared or approved for the screening of blood or plasma donors.*
- *Assay performance characteristics have not been established when the Elecsys HBsAg assay is used in conjunction with other manufacturers' assays for specific HBV serological markers. Users are responsible for establishing their own performance characteristics.*
- *Assay performance characteristics have not been established for testing of newborns.*

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

Intended use
Immunoassay for in vitro qualitative confirmation of the presence of hepatitis B surface antigen in human serum and plasma (sodium heparin, EDTA-K3, sodium citrate) samples repeatedly reactive when tested with Elecsys 2010 HBsAg Immunoassay.

Summary*
The Elecsys HBsAg confirmatory test is based on the principle of specific antibody neutralization.[1] Polyclonal HBsAg-specific antibodies bind to immunodominant epitopes of the hepatitis B surface antigen and thereby block the binding sites for the antibodies used in the Elecsys HBsAg assay.

Test principle*
The test principle is based on pretreatment of the samples with confirmatory reagent and control reagent followed by the assay procedure using the HBsAg test. The positive control, PreciControl HBsAg 2, should be run in parallel as a performance check.

Pretreatment of the samples:
- Samples found to be repeatedly reactive in the Elecsys HBsAg test are treated in parallel with confirmatory reagent and control reagent and then incubated. The excess anti-HBs antibodies in the confirmatory reagent neutralize any HBsAg in the sample. In the subsequent Elecsys HBsAg test this leads to a reduction in the cutoff Index (COI) value (signal of sample/cutoff) in comparison to the value originally obtained for the sample.

HBsAg test:
- 1st incubation: the two pretreated sample preparations react with a biotinylated, monoclonal HBsAg-specific antibody and a monoclonal HBsAg-specific antibody labeled with a ruthenium complex** to form a sandwich complex.
- 2nd incubation: after the 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. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined automatically by the Elecsys software by comparing the electrochemiluminescence signal obtained from the sample with the cutoff value previously obtained by HBsAg calibration. This is followed by manual verification of the validity of the test and interpretation of the findings.

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

Reagents - contents and concentrations
Elecsys HBsAg Confirmatory Test kit, Cat. No. 1820648 - 2 x 10–15 tests

Bottle 1	Confirmatory reagent (black cap), 2 bottles, 1.3 ml: Anti-HBs (human) > 200,000 IU/l in human serum; non-reactive for HBsAg, anti-HCV, anti-HIV 1+2; preservative.
Bottle 2	Control reagent (white cap), 2 bottles, 1.3 ml: Human serum, anti-HBs < 3 IU/l, negative for HBsAg, anti-HCV and anti-HIV 1+2; preservative.

Precautions and warnings
For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents. The confirmatory and control reagents have been prepared exclusively from the blood of donors tested individually and shown by FDA-approved methods to be free from HBsAg and antibodies to HIV 1+2 and HCV. However as no test method can rule out the potential risk of infection with absolute certainty, the material should be treated just as carefully as patient specimen.
In the event of exposure the directives of the responsible health authorities should be followed.[2,3]
Disposal of all waste material should be in accordance with local guidelines.
The reagents may not be used after the stated expiration date.

Reagent handling*
The reagents in the kit are ready for use. Avoid contamination. Store at 2–8°C after use.

Storage and stability*
Store at 2–8°C.
Stability of solutions 1 and 2:

unopened at 2–8°C	up to the stated expiration date
after opening	eight weeks at 2–8°C

Specimen collection and preparation*
Samples that were repeatedly reactive in the Elecsys HBsAg test. The conditions regarding stability and specimen collection described for Elecsys HBsAg also apply here.

Elecsys HBsAg testing procedure*
Materials provided
Cat. No. 1820648, Elecsys HBsAg Confirmatory Test, kit for 2 x 10–15 tests contains:
- Bottle 1 Confirmatory reagent
- Bottle 2 Control reagent

Materials required (but not provided)
- Cat. No. 1820532, Elecsys HBsAg reagent kit for 100 tests
- Cat. No. 1876309, Elecsys PreciControl HBsAg, for 8 x 1.3 ml each of PreciControl HBsAg 1 and 2
- Cat. No. 1732277, Elecsys Diluent Universal, 2 x 18 ml sample diluent or Cat.-No. 3183971, Diluent Universal Elecsys, 2 x 40 ml sample diluent
- Elecsys 2010 analyzer
- Cat. No. 11662988, Elecsys ProCell, 6 x 380 ml system buffer
- Cat. No. 1662970, Elecsys CleanCell, 6 x 380 ml measuring cell cleaning solution
- Cat. No. 1930346, Elecsys SysWash, 1 x 500 ml additive for wash water
- Cat. No. 1298500, Elecsys SysClean, 5 x 100 ml system cleaning solution
- Cat. No. 1933159, Adapter for SysClean
  Cat. No. 1706802, Elecsys 2010 Assay Cup, 60 x 60 reaction vessels
- Cat. No. 1706799, Elecsys 2010 Assay Tip, 30 x 120 pipette tips
- General laboratory equipment

Assay*
Pretreatment of the samples:
Selection of the reactant volumes is dependent on the magnitude of the respective cutoff index of the samples which were reactive in the Elecsys HBsAg test. The following volumes are pipetted into Elecsys sample cups:

- For positive samples having a cutoff index < 7.0
  180 µl sample + 20 µl confirmatory reagent
  180 µl sample + 20 µl control reagent

or

- For positive samples having a cutoff index between 7.0 and 30
  100 µl sample + 100 µl confirmatory reagent
  100 µl sample + 100 µl control reagent

or

- For positive samples having a cutoff index > 30
  Predilute samples 1:20 with Diluent Universal
  100 µl diluted sample + 100 µl confirmatory reagent
  100 µl diluted sample + 100 µl control reagent

PreciControl HBsAg 2, the positive control, should always be run in parallel as a check on performance:
180 µl PreciControl HBsAg 2 + 20 µl confirmatory reagent
180 µl PreciControl HBsAg 2 + 20 µl control reagent

Incubation of the reactants: 30–60 minutes at 15–25°C or overnight at 2–8°C.

Elecsys HBsAg test:
The pretreated samples are placed in the sample zone and registered by entering the sample identification data.
The Elecsys HBsAg assay is performed in accordance with the instructions given in the package insert of the test reagent kit.

Calibration*
For calibration, calibration frequency and calibration verification, see data given in the package insert for the Elecsys HBsAg test reagent kit.

HBsAg Confirmatory Test

Quality control*
Elecsys PreciControl HBsAg 2 should always be run in parallel with the samples needing confirmation. Verification is by the user.
For the Elecsys HBsAg test the conditions given in its package insert apply.

Calculation*
The Elecsys 2010 calculates the cutoff automatically on the basis of measurements on the two HBsAg calibrators (Cal 1 and Cal 2) contained in the kit.
The sample result is reported as either reactive or non-reactive, and as a cutoff index (COI) = signal of sample/cutoff.
The cutoff index is needed for selection of the correct sample pretreatment volumes for the confirmatory test.

Evaluation and interpretation of the results
In order to confirm a reactive result for a sample, the cutoff index for the sample with the confirmatory reagent must be < 50% of that with the control reagent, which must have a cutoff index of > 1.0. This indicates ≥ 50% neutralization of the HBsAg in the sample.

Assay Evaluation:
Neutralization of PreciControl 2 should be ≥ 50% using the fhe following formula
% Neutralization of PreciControl 2 =[(COI of PC2 + Control Reagent) - (COI of PC2 + Confirmatory reagent)]/(COI of PC2 + Control reagent) * 100
The COI of the patient sample diluted with the Control reagent must be ≥ 1.0
% Neutralization of Sample =[(COI of Sample+ Control Reagent) - (COI of Sample+ Confirmatory reagent)]/(COI of Sample+ Control reagent) * 100

Interpretation:
% Neutralization ≥ 50% = Confirmed positive sample or confirmed positive control
% Neutralization < 50% = Negative (False positive) result
Once the validity of the run is established, neutralization of the patient ample is calculated (using the formula above). Samples with neutralization ≥ 50% using the Elecsys HBsAg Confirmatory test are regarded as confirmed positive for HBsAg.

Due to the high-dose hook effect, samples having very high HBsAg concentrations (> 1 mg/ml) can give a cutoff index < 30 in the Elecsys HBsAg test. Such samples are not adequately neutralized by the confirmatory reagent at the stated volume, and are therefore not confirmed as positive. These samples can be recognized by the fact that the COI in the test with the control reagent is higher than the COI for the samples in the original HBsAg test (dilution effect). The confirmatory test for these samples must be repeated at a higher predilution (1:100).

Limitations - interference**
For the Elecsys HBsAg test the data given in the package insert of the test reagents on "Limitations - interference" apply.
For diagnostic purposes, the Elecsys HBsAg findings should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Specific performance data of the test*
Method comparison
The Elecsys HBsAg Confirmatory Test was evaluated with all specimens throughout the Elecsys HBsAg clinical study that had been confirmed positive by the FDA-approved reference HBsAg confirmatory assay. The table below compares the Elecsys HBsAg Confirmatory Test results with the reference HBsAg confirmed positive result on the Elecsys 2010 Immunoassay Analyzer.

Sample Sources	N	Reference HBsAg Reactive and Confirmed Positive by Neutralization	Elecsys HBsAg Confirmatory Test Confirmed Positive by Neutralization
First time blood donors	0	NA	NA
Subjects at risk for HBV infection due to lifstyle or behavior	6	6	6
Serologically classified acute HBV infection (archived)	151	151	151
Serologically classified chronic HBV infection (archived)	111	111	111
Chronic HBV infection determined by persistent HBsAg for > 6 months (archived)	74	74	74
Pregnant women	3	3	3
Total	**345**	**345**	**345 (100%)**

Precision
Reproducibility of the manual test steps was determined using 3 sera of differing HBsAg concentrations (8–10 times per sample with both the control and confirmatory reagents). After a 30-minute period of incubation at 20°C the pretreated samples were determined on Elecsys 2010 analyzers using Elecsys 2010 reagents, calibrators and controls.
Representative data for manual sample pretreatment followed by assay on Elecsys 2010 analyzers are shown below. Results obtained in individual laboratories may differ.

Results from original HBsAg test - without sample pretreatment (intra-assay, n = 8–10):

Sample	Mean COI	SD COI	%CV
HS, COI < 7.0	1.65	0.04	2.4
HS, COI 7.0 - < 30	11.3	0.11	1.0
HS, COI > 30	669	17.7	2.6

HS = human serum COI = Cutoff index
CV = coefficient of variation

Results after manual sample pretreatment

	Control reaction			Confirmatory reaction		
Sample	Mean COI	SD COI	%CV	Mean COI	SD COI	%CV
HS, COI < 7.0	1.57	0.04	2.6	0.42	0.04	9.5
HS, COI 7.0 - < 30	4.85	0.10	2.1	0.40	0.02	5.0
HS, COI > 30	1321	12.8	1.0	1.31	0.10	7.6

References
1 Gerlich W. Viral Hepatitis. Section 2, Churchill Livingstone, Ed. Zuckermann AJ, Thomas HC, 1993:83–113.
2 Department of Labor, Occupational Safety and Health Administration - 29 CFR Part 1910.1030 - Occupational Safety and Health Standards. Bloodborne Pathogens. Fed. Register July 1, 1998;6:267–280.
3 Council Directive (90/679/EEC). Official Journal of the European Communities No. L 374 from December 31, 1990:1-12.
4 Data on file at Roche.

* For more detailed information please consult the operators' manuals for the Elecsys 2010, and the package inserts for the system reagents, Diluent Universal and PreciControl HBsAg.

Roche Diagnostics GmbH, D-68298 Mannheim

For USA:
US Distributor: Roche Diagnostics Corporation, Indianapolis, IN, USA
US Customer Technical Support 1-800-428-2336

Made in Germany

HbsAg Confirmatory Test

HBsAg Confirmatory Test

Elecsys®

HBsAg Bestätigungstest
Test de confirmation de l'Ag HBs
Test de confirmacion de HBsAg
Test di conferma di HBsAg

1820648

For confirming results from samples giving a positive reaction with Elecsys HBsAg. Zur Bestätigung der mit Elecsys HBsAg reaktiven Proben. Pour la confirmation des resultats positifs obtenus avec Elecsys HBsAg. Para la confirmación de los resultados positivos obtenidos con Elecsys HBsAg. Per la conferma dei risultati positivi ottenuti con Elecsys HBsAg.

Cont.

1 2 x 1.3 ml, Anti-HBs (hum.) > 200.000 IU/l; serum/suero/siero (human/humain/humano/umano)
2 2 x 1.3 ml, Anti-HBs < 3 IU/l; serum/suero/siero (human/humain/humano/umano) negative for/negativ für/negatif pour/negativo para/negativo per HBsAg, Anti-HCV, Anti-HIV 1+2

IVD 2-8°C

Roche Diagnostics GmbH,
D-68298 Mannheim, Zul.-Nr. 145a/97
Distribution in USA:
Roche Diagnostics Corporation, Indianapolis, IN, USA
Made in Germany
Distributeur en France:
Roche Diagnostics, 2 Avenue du Vercors,
F-38240 Meylan, AFSSAPS n°S67892

Roche

HBsAg Conf./Best. Test

Elecsys®
1820648 122

LOT 000 000-00
Lot/Ch.-B.:

Exp./Verw.bis: ---

Presidio medico chirurgico
n. 18269 del Ministero della Sanità
Rappresentante per l'Italia:
Roche Diagnostics S.p.A.,
I-20131 Milano 01

Roche

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HBsAg Conf./Best. Test_1

Elecsys®
1820648
Conf./Best. reagent/Reagenz/reactif/reattivo
1.3 ml
IVD 01

Roche

2 - 8°C
LOT 000 000-00
Lot/Ch.-B.:
Exp./Verw.bis: ---

HBsAg Conf./Best. Test_2

Elecsys®
1820648
Conf./Kont. reagent/Reagenz/reactif/reattivo
1.3 ml
IVD 01

Roche

2 - 8°C
LOT 000 000-00
Lot/Ch.-B.:
Exp./Verw.bis: ---

PreciControl HBsAg

Elecsys® 2010 System

'1876309 **16 x 1.3 ml**

Intended use
PreciControl HBsAg is used for quality control of the Elecsys HBsAg immunoassay on the Elecsys 2010 immunoassay System when testing human serum.
The performance of the PreciControl HBsAg has not been established with any other HBsAg assay.

Summary*
PreciControl HBsAg contains control serum based on human serum in the negative and positive concentration range. The controls are used for monitoring the accuracy of Elecsys HBsAg immunoassays.

Reagents - contents and concentration
Elecsys PreciControl HBsAg, Cat. No. 11876309
- *PC HBSAG1:* 8 bottles, each containing 1.3 ml control serum
  Human serum, negative for HBsAg; preservative.
  Target range for cutoff index: 0.0–0.70.
- *PC HBSAG2:* 8 bottles, each containing 1.3 ml control serum
  HBsAg (human; positive for the "a" region determinant of HBsAg) approx. 0.2 IU/ml in human serum; preservative.
  Target range for cutoff index: 2.16–5.04.

The exact ranges, given in the form of a cutoff index, are encoded on the bar code cards.

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.
The controls have been prepared exclusively from the blood of donors tested individually and shown by FDA-approved methods to be free from HBsAg (PC HBSAG 1 only) and antibodies to HCV and HIV 1+2. The serum containing HBsAg used for the positive control (PC HBSAG 2) was cold-sterilized using β-propiolactone and UV radiation. However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled just as carefully as patient specimens. In the event of exposure the directives of the responsible health authorities[1,2] should be followed.
The quality control material furnished is in a serum matrix. It may not adequately control the Elecsys HBsAg immunoassay for sodium heparin, EDTA-K, or sodium citrate specimens.
The user should provide alternative control material for plasma specimens.
The controls may not be used after the expiration date.

Handling of the controls
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. Because of possible evaporation effects, not more than 7 quality control procedures per bottle should be performed.
Ensure the controls are at ambient temperature (20–25°C) before measurement.

Storage and stability
Store controls at 2–8°C. Store upright in order to prevent the control solution adhering to the snap-cap.
Stability:

unopened at 2–8°C:	up to the stated expiration date
after opening: eight weeks at 2–8°C	
on the analyzer:	five hours in total

Procedure
Materials provided
- Elecsys PreciControl HBsAg, 2 bar code cards

Materials required (but not provided)
- Elecsys 2010 assay reagent. See package insert and operator's manual for additionally required materials.

Use the control serum in the system-compatible labeled bottles for analysis in the same way as the patient samples. The information given on the bar-coded label and the corresponding bar code card is read into the system automatically. No manual input of quality control data is necessary.
Run controls daily in parallel with patient samples and whenever calibration is performed. The control intervals should be adapted to the individual requirements of each laboratory.

Results[3]
The target values and ranges given on the bar code card were determined and evaluated by Roche. They were obtained using the Elecsys HBsAg test reagents and Elecsys analyzers available at the time. Results must be within the specified ranges. All test steps must be checked when increasing or decreasing trends or suddenly occurring deviations beyond the range limits are seen. When necessary, measurement of the patient samples involved should be repeated.
Each laboratory should establish corrective measures to be taken if values lie outside the range.

References

1 Department of Labor, Occupational Safety and Health Administration - 29 CFR Part 1910.1030 - Occupational Safety and Health Standards. Bloodborne Pathogens. Fed. Register July 1, 1998;6:267-280.
2 Council Directive (90/679/EEC). Official Journal of the European Communities No. L374 from Dec. 31, 1990.
3 Data on file at Roche.

* For more detailed information, please consult the Elecsys 2010 operator's manual and the package insert.

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2001-06

Roche Diagnostics GmbH, D-68298 Mannheim

CE 0123

For USA:

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PreciControl HbsAg

PreciControl HBsAg

Elecsys®

1876309

For quality control of the Elecsys HBsAg immunoassay.
Zur Qualitätskontrolle des HBsAg Elecsys Immunoassays.
Pour le controle de qualite du test immunologique Elecsys HBsAg.
Para el control de calidad del inmunoensayo HBsAg Elecsys.
Per il controllo della qualità del test immunologico HBsAg Elecsys.

Cont.

1 PC HBSAG 1: 8 x 1.3 ml, serum/suero/siero (human/humain/humano/umano); 0 - 0.7 c.o.i.
2 PC HBSAG 2: 8 x 1.3 ml, HBsAg (human/humain/humano/umano); serum/suero siero (human/humain/humano/umano); 2.16 - 5.04 c.o.i.

IVD 2-8°C

Roche Diagnostics GmbH, D-68298 Mannheim, Germany, Zul.-Nr. 107a/97
Distribution in USA:
Roche Diagnostics Corporation, Indianapolis, IN, USA
Made in Germany
Distributeur en France:
Roche Diagnostics, 2 Avenue du Vercors, F-38240 Meylan, AFSSAPS n°R57482

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PreciControl HBsAg

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LOT Lot./Ch.-B.: 156 160-01

Exp./Verw.bis: 2002 - 08

PC HBSAG 1: LOT Lot./Ch.-B.: 15585999

PC HBSAG 2: LOT Lot./Ch.-B.: 15586099 03

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Rappresentante per l'Italia:
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PC HBSAG 1

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Lot./Ch.-B.:

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PC HBSAG 2

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Lot./Ch.-B.:

123456 12

PC HBSAG 1 Elecsys®

1876309 1.3 ml
In Vitro Diagnosticum
Roche
2 - 8°C
Lot./Ch.-B.:
155859 99
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2002 - 06 02

PC HBSAG 2 Elecsys®

1876309 1.3 ml
In Vitro Diagnosticum
Roche
2 - 8°C
Lot./Ch.-B.:
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Exp./Verw.bis:
2002 - 08 02