Anti-HBs

Antibody to hepatitis B surface antigen (anti-HBs)

Elecsys® 2010 System

11820524 **100 tests**

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

Intended use
Immunoassay for the in vitro qualitative determination of total antibodies to the hepatitis B surface antigen (HBsAg) in human serum and plasma (EDTA). The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Roche Elecsys 2010 immunoassay analyzer. Assay results may be used as an aid in the determination of susceptibility to hepatitis B virus (HBV) infection for individuals prior to or following HBV vaccination, or where vaccination status is unknown. Assay results may be used with other HBV serological markers for the laboratory diagnosis of HBV disease associated with HBV infection. A reactive assay result will allow a differential diagnosis in individuals displaying signs and symptoms of hepatitis in whom etiology is unkown. The detection of anti-HBs is indicative of laboratory diagnosis of seroconversion from hepatitis B virus (HBV) infection.

Summary[1]
Anti-HBs is an antibody that is directed against the hepatitis B surface antigen.[1] Anti-HBs can be formed following a hepatitis B infection or after hepatitis B vaccination. Antibodies are formed against the HBsAg determinant a, which is common to all subtypes, and against subtype-specific determinants.[2]
Anti-HBs tests are used within the scope of hepatitis B vaccination to check the necessity and success of vaccination.[3,4,5] In addition, anti-HBs test are used to monitor the course of disease following acute hepatitis B infection.[3] The Elecsys Anti-HBs assay uses a mixture of purified antigens of the HBsAg subtypes ad and ay from human serum.

Test principle[1]
Sandwich principle. Total duration of assay: 18 minutes.
- 1st incubation: Anti-HBs in the sample (40µl), biotinylated HBsAg (ad/ay) and HBsAg (ad/ay) 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 via a calibration curve which is instrument-specifically generated by two-point calibration and a master curve provided via the reagent bar code.

**Tris(2,2'-bipyridyl)ruthenium(II) complex (Ru(bpy))

Reagents - contents and concentrations
Elecsys Anti-HBs reagent kit, Cat. No. 11820524 - 100 tests

M	Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 ml: Streptavidin-coated microparticles, 0.72 mg/ml, 0.1% BSA binding capacity: 470 ng biotin/mg microparticles; preservative.
R1	HBsAg~biotin (gray cap), 1 bottle, 10 ml: Biotinylated HBsAg (ad/ay), human, >0.5 mg/l; MES*** buffer 85 mmol/l, 0.8% BSA, pH 6.5; preservative.
R2	HBsAg~Ru(bpy) (black cap), 1 bottle, 8 ml: HBsAg (ad/ay) human, labeled with ruthenium complex > 0.3 mg/l; MES buffer 85 mmol/l, 0.8% BSA, pH 6.5; preservative.
Cal1	Calibrator 1 (white cap), 2 bottles of 1.3 ml each: Anti-HBs (human) in human serum; preservative. Non-reactive for HBsAg, anti-HCV or anti-HIV1+2.
Cal2	Calibrator 2 (black cap), 2 bottles of 1.3 ml each: Anti-HBs (human) in human serum; preservative. Non-reactive for HBsAg, anti-HCV and anti-HIV 1+2.

***MES = 2-morpholino-ethanesulfonic acid

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 Cal 1 and Cal 2 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 and HCV.
The HBsAg starting material used was inactivated prior to labeling with biotin and ruthenium by heating to 60°C for 18 hours. In addition, any virus particles remaining were removed by ultracentrifugation. However, as no testing method can rule out the risk of potential infection with absolute certainty, the material must be handled just as carefully as patient specimens. In the event of exposure the directives of the responsible health authorities should be followed.[6,7]
The reagents may not be used after the stated expiration date.

Reagent handling[1]
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 five calibration procedures per calibrator bottle set should be performed.
All information required for correct operation is automatically read in via the reagent bar code.

Storage and stability[1]
Store at 2–8°C.
Store the Elecsys Anti-HBs 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:	eight weeks at 2–8°C
on Elecsys 2010:	four weeks
Cal 1, Cal 2 after opening:	eight weeks at 2-8°C;
Cal 1, Cal 2 on the analyzers:	five hours in total (no more than 5 separate calibrations)

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

Specimen collection and preparation[1]
Some sample collection devices have been reported to be detrimental to the integrity of certain analytes, and could interfere with some method technologies.[8] Because of the variety of sample collection devices available, it is not possible to issue a definitive statement on the performance of *Vitros* Immunodiagnostic Products when used with these devices. Each user should confirm that the chosen device is used according to the manufacturer's instructions and is compatible with this assay.
Serum collected using standard sampling tubes or tubes containing separating gel.
Plasma treated with EDTA-K_3.
Serum is stable for six days at 2-8° C, three months at -20° C. Plasma is stable for two days at 2-8° C, three months at -20° C.[9] The samples may be frozen and thawed six times.[10]
For information on the stability of serum obtained with tubes containing separating gel, please note the data provided by the tube manufacturer.
Frozen samples and samples containing precipitates must be centrifuged before performing the assay. Heat-inactivated samples may be used.
The assay is unaffected by icterus (bilirubin < 30 mg/dl), hemolysis (Hb ,1.6 g/dl), lipemia (triglycerides (Intra-lipid®) <1500 mg/dl) and biotin <50 ng/dl (criterion: recovery within ± 10% of initial values).
Turbidity may affect assay results.

Elecsys Anti-HBs testing procedure[1]
Materials provided
Cat. No. 11820524, Elecsys Anti-HBs reagent kit for 100 tests contains:
- M Streptavidin-coated microparticles
- R1 HBsAg~biotin
- R2 HBsAg~Ru(bpy)
- Cal1 Calibrator 1
- Cal2 Calibrator 2

Anti-HBs

Antibody to hepatitis B surface antigen (anti-HBs) **Elecsys® 2010 System**

Materials required (but not provided)
- Cat. No. 11876317, Elecsys PreciControl Anti-HBs, for 8 x 1.3 ml each of PreciControl Anti-HBs 1 and 2
- Elecsys 2010 analyzer
- Cat. No.11662988, Elecsys ProCell, 6 x 380 ml system buffer
- Cat. No. 11662970, Elecsys CleanCell, 6 x 380 ml measuring cell cleaning solution
- Cat. No. 11930346, Elecsys SysWash, 1 x 500 ml additive for washing water
- Cat. No. 11298500, Elecsys SysClean, 5 x 100 ml system cleaning solution
- Cat. No. 11933159, Adapter for SysClean
  Cat. No. 11706802, Elecsys 2010 Assay Cup, 60 x 60 reaction vessels
- Cat. No. 11706799, Elecsys 2010 Assay Tip, 30 x 120 pipette tips
- General laboratory equipment

Assay[1]

For optimal performance of the assay it is important to follow the directions given for the Elecsys 2010 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 of the test-specific parameters via the reagent barcode take place automatically. No manual input is necessary. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers. Bring the cooled reagents to approximately 20°C and place on the reagent disk 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 Anti-HBs Cal1 and Cal2 in the sample zone of the analyzer. Only keep open during calibration. All information necessary for calibration is encoded on the barcoded bottle labels and is read in automatically. After calibration has been performed, store Elecsys Anti-HBs Cal1 and Cal2 at 2–8°C.

Calibrators[1]

The Elecsys Anti-HBs assay has been calibrated against the 1st WHO Reference Standard 1977.[10] Every Anti-HBs reagent set has a barcoded label containing the specific information for calibration of the particular reagent lot. The pre-defined master curve is adapted to the analyzer by the use of Cal 1 and Cal 2.

Calibration frequency:

Calibration must be performed once per reagent lot using Elecsys Anti-HBs 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:
- after one month (when using the same reagent lot)
- after seven days (when using the same reagent kit on the analyzer)
- as required, e.g., quality control findings with Elecsys PreciControl Anti-HBs outside the specified range.
- more frequently when this is required by pertinent regulations.

Range (mIU/ml) for the calibrators: 4-15 for calibrator 1 (Cal 1) and 350-600 for calibrator 2 (Cal 2).

Quality control[1]

Elecsys PreciControl Anti-HBs.

The controls 1 and 2 should be run as single determinations at least once every 24 hours when the test is in use and after every calibration. The control intervals should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined ranges. If control values fall outside of the expected range(s), patient results should not be reported and samples and controls should be retested. The negative and positive controls are intended to monitor for substantial reagent failure. The positive control will not ensure precision at the assay cutoff. The user is responsible for furnishing controls that monitor assay precision at the assay's critical decision point. The recommended quality control material is serum based. The user is responsible for establishing their own control material when plasma samples are tested. Additional controls may be tested according to guidelines or requirements of local, state and/or federal reuglations or accrediting organizations.

Interpretation and Calculation[1]

Calibration of the Elecsys Anti-HBs assay is traceable to the 1st WHO Reference Standard 1977. The accepted criterion for immunity to HBV is ≥10 mIU/ml of anti-HBs, with IU defined by the WHO Reference Preparation.

A result <85% of cutoff indicates that a sample is "Negative" for anti-HBs. A negative result indicates that anti-HBs has not been detected at levels consistent with immunity.

A result ≥115% of cutoff indicates that a sample is "Positive" for anti-HBs. This result is consistent with levels of anti-HBs at >10 mIU/ml, which indicates that anti-HBs has been detected at levels consistent with protective immunity against HBV infection.

A specimen with a result of ≥85% and <115% indicates that a sample is "Indeterminate" for Anti-HBs and should be retested in duplicate. If both repeats are <85%, the specimen is negative for Anti-HBs. If one or both repeats are ≥115%, the specimen is positive for anti-HBs. If a result remains indeterminate it is reported as indeterminate. The immune status of the individual should be further assessed by associated risk factors, and the use of additional diagnostic information or another sample may be collected and tested.

Results obtained with the Elecsys Anti-HBs assay may not be used interchangeably with values obtained with different manufacturers' assay methods. The magnitude of Elecsys Anti-HBs assay result cannot be correlated to an endpoint titer.

The results from this or any other diagnostic kit should be used and interpreted only in the context of the overall clinical picture.

This assay does not differentiate between a vaccine-induced immune response and an immune response induced by natural infection with HBV.

To determine if the anti-HBs response is due to vaccine or HBV infections, the total anti-HBc assay may be performed.

Expected values

Of 1350 prospective subjects participating in the Elecsys Anti-HBs clincial study, 44.4% (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. The following table summarizes the Elecsys Anti-HBs test results by age range and gender.

Elecsys Anti-HBs Immunoassay					
Age	**Gender**	**Pos**	**Equiv**	**Neg**	**Total**
< 10	Male	0	0	0	0
	Female	0	0	0	0
10 - 19	Male	21	1	155	177
	Female	19	1	95	115
20 - 29	Male	11	0	60	71
	Female	6	0	36	42
30 - 39	Male	7	0	38	45
	Female	7	0	39	46
40 - 49	Male	5	0	30	35
	Female	9	0	23	32
50 - 59	Male	1	0	15	16
	Female	2	0	11	13
60 - 69	Male	0	0	2	2
	Female	1	0	3	4
70 - 79	Male	0	0	1	1
	Female	0	0	1	1
80 - 89	Male	0	0	0	0
	Female	0	0	0	0
90 - 99	Male	0	0	0	0
	Female	0	0	0	0
Unknown	Male	0	0	0	0
	Female	0	0	0	0
Totals	Male	45	1	301	347
	Female	44	1	208	253
	All	89	2	509	600

The 750 remaining subjects were enrolled from populations considered at risk for viral hepatitis due to lifestyle or behavior. Of these, 449 were outpatients of a health screening clinic and 301 were hospitalized patients. Of the hospitalized and health screening clinic patients, 446 of the subjects were enrolled in Memphis, TN and 304 in Miami, FL. This collective group was African American (26%), Caucasian (19%), Hispanic (5%), Asian (<1%) or other (<1%) with 50% electing not to provide this information. The group was 49% male and 51% female ranging in age from 8 to 94 years. The following table summarizes the distribution of Elecsys Anti-HBs test results by age range and gender.

Anti-HBs

Antibody to hepatitis B surface antigen (anti-HBs)

Elecsys Anti-HBs Immunoassay					
Age	**Gender**	**Pos**	**Equiv**	**Neg**	**Total**
< 10	Male	0	0	1	1
	Female	0	0	0	0
10 - 19	Male	0	0	4	4
	Female	0	0	7	7
20 - 29	Male	58	0	48	106
	Female	42	0	32	74
30 - 39	Male	7	0	46	53
	Female	11	0	45	56
40 - 49	Male	8	0	48	56
	Female	13	0	53	66
50 - 59	Male	9	0	44	53
	Female	5	0	39	44
60 - 69	Male	1	1	36	38
	Female	8	1	46	55
70 - 79	Male	3	0	30	33
	Female	7	0	40	47
80 - 89	Male	4	0	8	12
	Female	4	0	15	19
90 - 99	Male	0	0	1	1
	Female	1	0	2	3
Unknown	Male	7	1	6	14
	Female	1	0	7	8
Totals	Not Given	0	0	0	0
	Male	97	2	272	371
	Female	92	1	286	379
	All	189	3	558	750

Limitations - interference[10]

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 interference was observed from rheumatoid factor up to 2100 U/ml. There is no high dose hook effect at anti-HBs concentrations up to 150,000 mIU/ml.

In rare cases interference due to extremely high titers of antibodies to streptavidin and ruthenium can occur. Elecsys Anti-HBs contains additives which minimize these effects.

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

This device is not intended for use in screening blood bank donors.

Assay performance characteristics have not been established for the use of the Elecsys Anti-HBs assay as an aid in determining susceptibility to HBV infection prior to or following vaccination in infants, children, or adolescents.

Individuals that have received blood component therapy, e.g., whole blood, plasma, immune globulin administration, during the previous 3 to 6 months may have a false reactive anti-HBs result due to passive transfer of anti-HBs.[11]

Results from immuno-suppressed individuals should be interpreted with caution.

Assay performance characteristics have not been established for any other specimen matrix than serum and plasma (EDTA-K_3).

Specific Performance Data of the Test[10]

Clinical Performance

A multi-center prospective study was conducted to characterize the performance of the Elecsys Anti-HBs Immunoassay 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 (44.5%), Memphis, TN (33.0%) and Miami, FL (22.3%).

Of the 1350 prospective subjects participating in the Elecsys Anti-HBs clinical study, 44.4% (n=600) were first time blood donors, asymptomatic for viral hepatitis and 750 subjects were at risk of HBV infection due to lifestyle or behavior. Of the 750 at risk subjects, 59.9% (n=449) were outpatients of a health screening clinic and 40.1% (n=301) were hospitalized patients.

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 (21%), Caucasian (19%), Hispanic (5%), Asian (< 1%) or other (<1%) with 55% 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 Anti-HBs immunoassay was analyzed relative to the reference anti-HBs reported results for all 1350 specimens. Complete testing using FDA approved methods for all six 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 348 of the subjects.

Results by Specimen Classification

HBV classification was 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 on the following table are the interpretations of HBV classifications made for each of the serological profiles observed.

HBV Classification	HBsAg	HBeAg	anti-HBc IgM	anti-HBc (total)	anti-HBe	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 Anti-HBs results with the reference results for the prospective studies with first time blood donors by HBV classification.

HBV Classification	Anti-HBs Result Reference EIA						Total
	-			+			
	Elecsys anti-HBs Result			Elecsys Anti-HBs Result			
	-	+	I*	-	+	I*	
Acute	0	0	0	0	0	0	0
Chronic	0	0	0	0	0	0	0
Early Recovery	0	0	0	0	1	0	1
Recovery	0	0	0	0	2	0	2
Recovered	0	0	0	0	1	0	1
Uninterpretable	0	0	0	0	0	0	0
HBV Vaccine Response	0	0	0	1	85	1	87
Not Previously Infected	30	0	1	0	0	0	31
Not Classified	477*	0	0	1	0	0	478
Total	507	0	1	2	89	1	600

* One specimen was indeterminate by the reference EIA.

Anti-HBs

Antibody to hepatitis B surface antigen (anti-HBs)

The following table compares the Elecsys Anti-HBs 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	Anti-HBs Result Reference EIA						Total
	-			+			
	Elecsys Anti-HBs Result			Elecsys Anti-HBs Result			
	-	+	I*	-	+	I*	
Acute	1	0	0	0	0	0	1
Chronic	1	0	0	0	0	0	1
Early Recovery	0	0	0	0	0	0	0
Recovery	0	0	0	1	23	0	24
Recovered	2	2	1	3	20	0	28
Uninterpretable	2*	1*	0	0	2	0	5
HBV Vaccine Response	0	0	0	11	122	1	134
Not Previously Infected	30	3	0	0	0	0	33
Not Classified	505	2	0	2	14	1	524
Total	541	8	1	17	181	2	750

*These samples were indeterminate by the reference EIA.

Percent Agreement

The table below summarizes the percent agreement between the Elecsys Anti-HBs Immunoassay and the anti-HBs reference assay with first time blood donors by specimen classification exclusive of the one specimen with equivocal results by the reference assay. 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	100 (1/1)	2.5 - 100.0	NA	NA
Recovery	100 (2/2)	15.9 - 100.0	NA	NA
Recovered	100 (1/1)	2.5 - 100.0	NA	NA
Uninterpretable	NA	NA	NA	NA
HBV Vaccine Response	97.7 (85/87)	91.9 - 99.7	NA	NA
Not Previously Infected	NA	NA	96.8 (30/31)	83.3 - 99.9
Not Classified	0 (0/1)	NA	100 (476/476)	99.2 - 100.0
Overall	96.7 (89/92)	90.8 - 99.3	99.8 (506/507)	98.9 - 100.0

The table below summarizes the percent agreement between the Elecsys Anti-HBs Immunoassay and the anti-HBs reference assay with subjects at risk for HBV infection due to lifestyle or behavior by specimen classification exclusive of the three specimens with equivocal results by the reference assay. 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	100 (1/1)	2.5 - 100
Chronic	NA	NA	100 (1/1)	2.5 - 100
Early Recovery	NA	NA	NA	NA
Recovery	91.7 (22/24)	73.0 - 99	NA	NA
Recovered	87.0 (20/23)	66.4 - 97.2	40.0 (2/5)	5.3 - 85.3
Uninterpretable	100 (2/2)	15.8 - 100	NA	NA
HBV Vaccine Response	91.0 (122/134)	84.9 - 95.3	NA	NA
Not Previously Infected	NA	NA	90.9 (30/33)	75.7 - 98.1
Not Classified Infected	82.4 (14/17)	56.6 - 96.2	99.6 (505/507)	98.6 - 100
Overall	90.0 (180/200)	85.0 - 93.8	98.5 (539/547)	97.1 - 99.4

Results for the Elecsys Anti-HBs Immunoassay for Subjects at Various Discrete Stages of HBV Infection or Recovery

The performance of the Elecsys Anti-HBs Immunoassay was studied with archived specimens representing various discrete stages of HBV infection or recovery. The following table compares the Elecsys Anti-HBs immunoassay with the anti-HBs reference assay results by specimen classification.

HBV Classification	Anti-HBs Result Reference EIA						Total
	-			+			
	Elecsys Anti-HBs Result			Elecsys Anti-HBs Result			
	-	+	I*	-	+	I*	
Acute	152	0	1	0	0	0	153
Chronic	179*	2	0	5	9	1	196
Early Recovery	1	0	0	0	3	0	4
Recovery	0	0	1	0	35	0	36
Recovered	4	0	0	1	17	0	22
Uninterpretable	3	0	0	1	1	0	5
HBV Vaccine Response	0	0	0	0	6	0	6
Not Previously Infected	10	0	0	0	0	0	10
Not Classified	1	0	0	0	0	0	1
Total	350	2	2	7	71	1	433

* Two samples were indeterminate by the reference EIA.

Anti-HBs

Antibody to hepatitis B surface antigen (anti-HBs)

Percent Agreement

The following table summarizes the percent agreement between the Elecsys Anti-HBs Immunoassay and the anti-HBs reference assay by specimen classificaiton exclusive of the two specimens with equivocal results by the reference assay. The following table also provides the upper adn lower 95% exact confidence bounds.

HBV Classification	Positive Percent Agreement	95% Exact Confidence Interval	Negative Percent Agreement	95% Exact Confidence Interval
Acute	NA	NA	100 (153/153)	97.6 - 100
Chronic	60 (9/15)	34.9 - 90.1	98.9 (177/179)	96.0 - 99.9
Early Recovery	100 (3/3)	29.5-100	100 (1/1)	2.5 - 100
Recovery	100 (35/35)	90.0 - 100	0 (0/1)	0.0 - 97.5
Recovered	94.4 (17/18)	72.7 - 99.9	100 (4/4)	40.0 - 100
Uninterpretable	50 (1/2)	1.3 - 98.7	100 (3/3)	29.5 - 100
HBV Vaccine Response	100 (6/6)	54.3-100	NA	NA
Not Previously Infected	NA	NA	100 (10/10)	69.3 - 100
Not Classified	NA	NA	100 (1/1)	2.5 - 100
Overall	89.9 (71/79)	83.6 - 97.1	99.1 (349/352)	97.5 - 99.8

Clinical Performance with Individuals Having Received Hepatitis B Vaccine

A retrospective study was conducted to evaluate specimens from 55 subjects who had received a full series of at least three HBV vaccinations. Each sample was studied using the Elecsys Anti-HBs immunoassay and the qualitative methodology of the reference anti-HBs EIA. At the time of final testng, the specimen was required to be free of all HBV markers (except anti-HBs) to substantiate that the reactivity was a consquence of vaccination and not natural infection. The following table presents the results of the Elecsys Anti-HBs test results compared to the reference anti-HBs EIA test results. The agreement between the Elecsys and the reference assay was 98.2%, with 54 concordant positives and one specimen positive by the reference assay but equivocal by Elecsys.

		Reference anti-HBs Immunoassay		
		Pos	Equivocal	Neg
Elecsys anti-HBs Immunoassay	Pos	54	0	0
	Equivocal	1	0	0
	Neg	0	0	0

	% (N)	95% Exact Confidence Interval
Positive Percent Agreement with the Reference Method	98.2 (54/55)	90.3 - 100
Negative Percent Agreement with the Reference Method	NA	NA

Clinical Performance with Matched Pre- and Post-Vaccination Samples

The performance of the Elecsys Anti-HBs immunoassay was assessed in subjects undergoing HBV vaccination (Smithkline Engerix). Paired samples from 40 subjects purported to never have been vaccinated or previously exposed to HBV were perspectively evaluated at the University of Miami site. The inclusion criteria required no history of HBV vaccination in the pre-vaccination specimen and negative serology for HBV markers in both the pre- and post-vaccination specimens. The following table presents the results of the final Elecsys Anti-HBs test results compared to the reference anti-HBs EIA test results. The agreement between Elecsys and the reference assay was 100%, with 38 concordant positives and 42 concordant negatives.

Pre-Vaccination Panel

		Reference anti-HBs Immunoassay		
		Pos	Equivocal	Neg
Elecsys anti-HBs Immunoassay	Pos	0	0	0
	Equivocal	0	0	0
	Neg	0	0	40

Post-Vaccination Panel

		Reference anti-HBs Immunoassay		
		Pos	Equivocal	Neg
Elecsys anti-HBs Immunoassay	Pos	38	0	0
	Equivocal	0	0	0
	Neg	0	0	2

Combined Pre- and Post-Vaccination Panels

		Reference anti-HBs Immunoassay		
		Pos	Equivocal	Neg
Elecsys anti-HBs Immunoassay	Pos	38	0	0
	Equivocal	0	0	0
	Neg	0	0	42

	% (N)	95% Exact Confidence Interval
Positive Percent Agreement with the Reference Method	100.0 (38/38)	90.8 - 100.0
Negative Percent Agreement with the Reference Method	100.0 (42/42)	91.6 - 100.0

Anti-HBs

Antibody to hepatitis B surface antigen (anti-HBs)

Analytical Specificity

For all analytical specificity categories tested, 98.9% agreement was observed between Elecsys Anti-HBs Immunoassay final results and the reference anti-HBs test results (260/263). Perfect correlation between the reference and Elecsys immunoassays was observed for patients having HEV (7/7), HCV (8/8), EBV (10/10), CMV (10/10), HIV (10/10), HSV (16/16), Rubella (16/16), Toxoplasmosis (2/2), syphilis (9/9), non-viral liver disease (20/20), alcoholic hepatitis (4/4), rheumatoid factor (17/17), high titer immunoglobulin (37/37), received influenza vaccination (5/5), and for pregnant women (49/49). Although there were isolated occasions of discrepancy between the reference and Elecsys test results noted in the HAV (1/10), chronic dialysis (1/10) and IV drug user (1/10) panels, there was no indication that any difference was due to cross-reactivity.

The table below summarizes the Elecsys Anti-HBs Immunoassay final test results compared to the reference anti-HBs test results for all sites combined.

Elecsys Anti-HBs Immunoassay	Neg	Neg	Pos	Pos	Total
Reference anti-HBs Immunoassay	Neg	Pos	Neg	Pos	
Other Viral Hepatitis Infections	17	0	1	7	25
Other Infectious Diseases	53	0	0	20	73
Non-Viral Liver Diseases	20	0	0	4	24
Autoimmune Diseases	17	0	0	0	17
High Risk Populations	15	1	1	16	33
Post Influenza Vaccination	0	0	0	5	5
High Titer Immunoglobulin	35	0	0	2	37
Pregnancy	49	0	0	0	49
Total	206	1	2	54	263

Precision[†10]

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 Elecsys 2010 analyzers at three centers had within run precision ranging from 1.8 to 7.7% CV. Between day precision, which also included within run and between run, ranged from 2.9 to 14.7% CV; between lot precison ranged from 2.9 to 5.3% CV; between site ranged from 2.3 to 11.2%, and total precision, which included all precision components, ranged from 7.5 to 21.4% CV.

Panel Member	Mean	Within Run		Between Day*		Between Lot		Between Site		Total**	
	(mIU/ml)	SD	CV	SD	CV	SD	CV	SD	CV	SD	CD
1	< 10.0	0.45	7.7	0.86	14.7	0.26	4.4	0.66	11.2	1.26	21.4
2	21.99	0.75	3.4	1.21	5.5	0.63	2.9	0.50	2.3	1.74	7.9
3	42.27	0.95	2.3	3.54	4.1	1.99	4.7	1.61	3.8	3.35	7.9
4	87.45	1.64	1.9	2.56	2.9	4.42	5.1	2.96	3.4	6.69	7.7
5	154.3	3.44	2.2	5.98	3.9	7.64	5.0	5.16	3.3	11.64	7.6
6	447.3	7.90	1.8	16.35	3.7	23.74	5.3	14.46	3.2	33.53	7.5

* Include between run and between day components.
** Includes run, between run, between day, between site/lot interaction, between lot and between site components.

References

1 Lander JJ, Holland PV, Alter HJ, Chanock RM, Purcell RH. Antibody to hepatitis-associated antigen. Frequency and patterns of response as detected by radioimmunoprecipitation. J Am Med Assoc 1972:220:1079-1082.

2 Gold JW, Alter HJ, Holland PV, Berin JF, Purcell RH. Passive hemagglutination assay for antibody to subtypes of hepatitis B antigen. J Immunol 1974; 112;110-1106.

3 Jilg W, Schmidt M, Deinhardt F. Immune Response to Hepatitis B Revaccination. J Med Virol 1988;24:377-384.

4 STIKO-Recommendations, Bundesgesundhbl 1996;1/96:32-42.

5 Hoofnagle JH Di Bisceglie AM. Serologic Diagnosis of Acute and Chronic Viral Hepatitis, Seminars in Liver Disease 1991; 11/2; 73-83.

6 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.

7 Council Directive (90/679/EEC). Official Journal of the European Communities No. L374 from Dec. 31, 1990.

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

9 NCCLS. Procedures for the Handling and Processing of Blood Specimens; Approved Guideline-Second Edition. NCCLS document H18-A2 (ISBN 1-56238-388-4). NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087, 1991.

10 Data on file at Roche.

11 Bornhak H, Jilg W, Hüdig H, Kaufmann J. Quantitation of anti-HBs in solid phase immunoassays. What influences the results? From: Virushepatitis A bis E. Diagnose, Therapie Prophylaxe. Kilian Verlag, ISBN: 3-9803688-1-5 1994;212-221.

11 Frösner G. Moderne Hepatitisdiagnostik. Kilian Verlag,Marburg 1996.

† For more detailed information consult the operators' manual for the Elecsys 2010, and the package inserts for the system reagents, Elecsys Anti-HBs Precicontrol and Diluent Universal.

054581800
2002 - 02

Roche Diagnostics GmbH, D-68298 Mannheim

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

Roche