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# HBsAg Reagent Kit
# Antibody to Hepatitis B Surface Antigen (Mouse Monoclonal IgG and IgM)

HBsAg
06P02
FDA_DRAFT_R05
B6P02E

**Revised June 2019.**

REF 06P0260

Instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from these instructions.

## NAME

Alinity s HBsAg Reagent Kit
Antibody to Hepatitis B Surface Antigen (Mouse Monoclonal IgG and IgM)

## INTENDED USE

The Alinity s HBsAg assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of hepatitis B surface antigen (HBsAg) in human serum and plasma specimens on the Alinity s System.

The Alinity s HBsAg assay is intended to screen individual human donors, including volunteer donors of whole blood and blood components, and other living donors for the presence of HBsAg. The assay is also intended for use in testing serum and plasma specimens to screen organ donors when specimens are obtained while the donor's heart is still beating, and in testing serum specimens to screen cadaveric (non-heart-beating) donors. It is not intended for use on cord blood specimens.

## SUMMARY AND EXPLANATION OF THE TEST

Hepatitis B virus (HBV) is the causative agent of hepatitis B. An estimated 257 million individuals are living with hepatitis B virus infection. More than 887 000 people die annually of HBV-related liver disease. Globally, chronic hepatitis B is a major cause of liver cirrhosis and hepatocellular carcinoma.[1, 2]

HBV belongs to the hepadnavirus family and is a partially double-stranded DNA virus. It consists of a central core nucleocapsid containing the viral DNA, DNA polymerase, and a surrounding envelope consisting of HBsAg, which is expressed during HBV infection. Additionally, HBV-infected cells produce spherical or long filamentous particles that consist of excess HBsAg.[3]

The virus is divided into multiple major serotypes (e.g., adr, adw, ayr, ayw) based on antigenic determinants present on the envelope proteins, and into at least 8 genotypes (A–H) according to overall nucleotide sequence variation of the genome. Differences among genotypes can affect the disease severity, course and likelihood of complications, response to treatment, and possibly vaccine protection.[2-5]

HBV, unlike other DNA viruses, replicates through a reverse transcription step. The reverse transcription process lacks proofreading capability; therefore, HBV is subject to a mutation rate more than 10 times higher than the mutation rate of other DNA viruses. Surface antigen gene mutations may cause changes in the antigenic structure of HBsAg, resulting in reduced recognition by some antibodies to HBsAg.[6-11]

HBV is transmitted through sexual, parenteral, and perinatal routes. Transmission may also occur through transfusion of HBV-contaminated blood and blood products. After infection with HBV, HBsAg is the first antigenic marker, appearing 1 to 12 weeks after exposure and 2 to 6 weeks before the onset of clinical symptoms. HBsAg persists during this acute phase and clears late in the convalescence period. Failure to clear HBsAg within 6 months indicates a chronic hepatitis B infection.[2, 3]

HBsAg assays are used to screen blood and blood products for the presence of HBsAg to prevent transmission of HBV infection to recipients of blood or blood products. HBsAg assays are also used to screen organ and tissue donors. In addition, HBsAg assays are used to identify persons infected with HBV and to monitor the status of infected individuals in combination with other hepatitis B serological markers. Testing for HBsAg as part of an antenatal screening program may identify HBV infected mothers and allow for appropriate immunoprophylaxis of the newborn.[12-18]

## BIOLOGICAL PRINCIPLES OF THE PROCEDURE

This assay is for the qualitative detection of HBsAg in human serum and plasma using chemiluminescent microparticle immunoassay (CMIA) technology.

Sample, anti-HBs coated paramagnetic microparticles, and anti-HBs acridinium-labeled conjugate are combined to create a reaction mixture and incubated. The HBsAg present in the sample binds to the anti-HBs coated microparticles and to the anti-HBs acridinium-labeled conjugate. The mixture is washed. Ancillary wash buffer is added and incubated. Following a wash cycle, Pre-Trigger and Trigger Solutions are added.

The resulting chemiluminescent reaction is measured as relative light units (RLU). There is a direct relationship between the amount of HBsAg in the sample and the RLU detected by the system optics. The presence or absence of HBsAg in the sample is determined by comparing the chemiluminescent RLU in the reaction to the cutoff RLU determined from an active calibration.

For additional information on system and assay technology, refer to the Alinity s System Operations Manual, Section 3.

## REAGENTS

### Kit Contents

Alinity s HBsAg Reagent Kit 06P02
Volumes (mL) listed in the table below indicate the volume per cartridge.

| REF | 06P0260 |
|---|---|
| Tests per cartridge | 500 |
| Number of cartridges per kit | 10 |
| Tests per kit | 5000 |
| MICROPARTICLES | 27.0 mL |
| CONJUGATE | 26.7 mL |
| ANCILLARY WASH BUFFER | 26.5 mL |

MICROPARTICLES Anti-HBs (mouse, monoclonal, IgM, IgG) coated microparticles in MES buffer with protein (bovine) stabilizer and surfactant. Minimum concentration: 0.08% solids. Preservatives: ProClin 300 and ProClin 950.

CONJUGATE Anti-HBs (mouse, monoclonal, IgG) and anti-HBs (goat IgG) acridinium-labeled conjugate in phosphate buffer with human plasma and protein (bovine, goat, mouse) stabilizers and surfactant. Minimum concentration: 0.35 µg/mL. Preservatives: ProClin 300, ProClin 950, and sodium azide.

ANCILLARY WASH BUFFER MES buffer and surfactant. Preservatives: ProClin 300 and ProClin 950.



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## Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use
- Performance characteristics of this product have not been established for laboratory diagnosis of HBV infection.

**Safety Precautions**

**CAUTION:** This product contains human-sourced and/or potentially infectious components. Refer to the **REAGENTS** section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. Therefore, all human-sourced materials should be considered potentially infectious. It is recommended that these reagents and human specimens be handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[19-22]

The human plasma used in the conjugate is nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HIV-1/HIV-2, anti-HCV, and anti-HBs.

The following warnings and precautions apply to: MICROPARTICLES

| | |
|---|---|
| **WARNING** | Contains methylisothiazolones. |
| H317 | May cause an allergic skin reaction. |
| **Prevention** | |
| P261 | Avoid breathing mist / vapors / spray. |
| P272 | Contaminated work clothing should not be allowed out of the workplace. |
| P280 | Wear protective gloves / protective clothing / eye protection. |
| **Response** | |
| P302+P352 | IF ON SKIN: Wash with plenty of water. |
| 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 in accordance with local regulations. |

The following warnings and precautions apply to: CONJUGATE

| | |
|---|---|
| **WARNING** | Contains methylisothiazolones and sodium azide |
| H317 | May cause an allergic skin reaction. |
| EUH032 | Contact with acids liberates very toxic gas. |
| **Prevention** | |
| P261 | Avoid breathing mist / vapors / spray. |
| P272 | Contaminated work clothing should not be allowed out of the workplace. |
| P280 | Wear protective gloves / protective clothing / eye protection. . |
| **Response** | |
| P302+P352 | IF ON SKIN: Wash with plenty of water. |
| 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 in accordance with local regulations. |

The following warnings and precautions apply to: ANCILLARY WASH BUFFER

| | |
|---|---|
| **WARNING** | Contains methylisothiazolones and dodecyltrimethylammonium bromide. |
| H317 | May cause an allergic skin reaction. |
| H412 | Harmful to aquatic life with long lasting |
| **Prevention** | |
| P261 | Avoid breathing mist / vapors / spray. |
| P272 | Contaminated work clothing should not be allowed out of the workplace. |
| P280 | Wear protective gloves / protective clothing / eye protection. |
| P273 | Avoid release to the environment. |
| **Response** | |
| P302+P352 | IF ON SKIN: Wash with plenty of water. |
| 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 in accordance with local regulations. |

Safety Data Sheets are available at www.transfusion.abbott or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the Alinity s System Operations Manual, Section 8.

**Reagent Handling**

- Do not invert reagent cartridges.
- Upon receipt, reagent cartridges can be used immediately or stored in an upright position.
- If a reagent cartridge is dropped, place in an upright position for 1 hour before use to allow bubbles that may have formed to dissipate.



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- Reagents are susceptible to the formation of foam and bubbles. Bubbles may interfere with the detection of the reagent level in the cartridge and cause insufficient reagent aspiration that may adversely affect results.

For a detailed discussion of reagent handling precautions during system operation, refer to the Alinity s System Operations Manual, Section 7.

### Reagent Storage

- Do not freeze.

| | Storage Temperature | Maximum Storage Time | Additional Storage Instructions |
|---|---|---|---|
| **Unopened** | 2 to 8°C | Until expiration date | Store in upright position. |
| **Opened** | 2 to 15°C | 15 days after opening* | Store in upright position.<br>Discard after 15 days.<br>If cartridge does not remain upright during storage off the system, discard the cartridge.<br>Do not reuse original reagent caps or replacement caps due to the risk of contamination and the potential to compromise reagent performance. |

*Includes time on board the system.

Reagents may be stored on or off the system. If removed from the system, store reagents with new replacement caps in an upright position at 2 to 15°C. For reagents stored off the system, it is recommended that they be stored in their original trays or boxes to ensure they remain upright.

For information on unloading reagents, refer to the Alinity s System Operations Manual, Section 5.

### Indications of Reagent Deterioration

Deterioration of the reagents may be indicated when a calibration error occurs or a control value is out of the specified range. Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary.

For troubleshooting information, refer to the Alinity s System Operations Manual, Section 10.

## INSTRUMENT PROCEDURE

The Alinity s HBsAg Assay File must be installed on the Alinity s System prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the Alinity s System Operations Manual, Section 2.

For information on printing assay parameters, refer to the Alinity s System Operations Manual, Section 5.

For a detailed description of system procedures, refer to the Alinity s System Operations Manual.

## SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

### Specimen Types

The specimen types listed below were verified for use with this assay. Other specimen types and anticoagulants have not been verified with this assay.

| Specimen Types | Anticoagulants |
|---|---|
| Serum (including serum separator tubes) | Not Applicable |
| Plasma | Dipotassium EDTA (including plasma preparation tubes)<br>Tripotassium EDTA<br>Lithium heparin (including plasma separator tubes)<br>Sodium citrate<br>Sodium heparin<br>ACD-A<br>ACD-B<br>CP2D<br>CPD<br>CPDA-1 |

- Liquid anticoagulants may have a dilution effect resulting in lower S/CO values for individual specimens.
- Performance has not been established for the use of umbilical cord blood or bodily fluids such as urine, saliva, semen, amniotic fluid, cerebrospinal fluid, or pleural fluid.
- Performance has been established for the use of cadaveric serum specimens (including specimens collected post-mortem, non-heart-beating) that have been collected up to 24 hours after death.[23] Follow general standards and/or regulations for collection, storage and handling.
- Performance has not been established for the use of cadaveric plasma specimens.
- Testing of cadaveric serum specimens from patients with plasma dilution due to transfusions of > 2000 mL of blood or colloids within 48 hours, or > 2000 mL of crystalloids within 1 hour (or any combination thereof) prior to collection of the specimens has not been verified.
- The system does not provide the capability to verify specimen types. It is the responsibility of the operator to verify that the correct specimen types are used with the assay.

### Specimen Conditions

- Do not use:
  - heat-inactivated specimens
  - pooled specimens
  - grossly hemolyzed specimens
  - specimens with obvious microbial contamination
  - specimens with fungal growth
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

### Preparation for Analysis

**Failure to follow the specified centrifugation procedure may give erroneous or inconsistent test results.**

- Clear, nonhemolyzed specimens should be used when possible. Specimens containing visible particulate matter may give erroneous or inconsistent test results.
- Specimens should be free of bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

- Prior to centrifugation, previously frozen specimens (including previously frozen plasmapheresis specimens) must be mixed gently and thoroughly after thawing.
- Specimens collected by plasmapheresis, which have not been frozen, do not require centrifugation. All other specimens (including previously frozen plasmapheresis specimens) must be centrifuged between 30 000 - 75 000 g-minutes.
- All specimens must be tested or retested within 48 hours of initial centrifugation. After 48 hours, these specimens need to be recentrifuged between 30 000 - 75 000 g-minutes.

The acceptable time and force ranges that meet this criterion are listed in the table below.

| Centrifugation Time (Minutes) | RCF (x g) | g-Minutes |
|---|---|---|
| 10 | 3000 | 30 000 |
| 15 | 2000 – 3000 | 30 000 – 45 000 |
| 20 | 1500 – 3000 | 30 000 – 60 000 |
| 25 | 1300 – 3000 | 32 500 – 75 000 |

Convert rpm to RCF as follows: $RCF = 1.12 \times r_{max} (rpm/1000)^2$

Convert RCF to rpm as follows:

$$rpm = 1000 \times \sqrt{\frac{RCF}{1.12 \times r_{max}}}$$

| | |
|---|---|
| RCF- | The relative centrifugal force generated during centrifugation. |
| rpm - | The revolutions per minute of the rotor on which the specimens are being spun (usually the digital readout on the centrifuge will indicate the rpm). |
| Centrifugation Time - | The time should be measured from the time the rotor reaches the required RCF or rpm to the time it begins decelerating. |
| rmax - | Radius of the rotor in millimeters. The radius measured is dependent on whether the rotor is a fixed angle rotor or a swinging bucket rotor. This value is typically provided with the rotor by the manufacturer. For the fixed angle rotor, $r_{max}$ is the measure of the distance from the rotor axis (center) to the bottom of the specimen tube in the rotor or rotor adapter. For the swinging bucket rotor, $r_{max}$ is the measure of the distance from the rotor axis (center) to the bottom of the specimen tube in the rotor adapter or bucket at full extension.<br>**NOTE:** If custom tube adapters (i.e., adapters not defined by the centrifuge manufacturer) are used, then the radius ($r_{max}$) should be manually measured in millimeters and the RCF calculated. |
| g- minutes - | The unit of measure for the product of RCF (× g) and centrifugation time (minutes). |

### Specimen Storage

| Specimen Type | Temperature | Maximum Storage Time | Special Instructions |
|---|---|---|---|
| Living Donor Serum/ Plasma | Room temperature (15 to 30°C) | 7 days | Specimens may be stored on or off the clot, red blood cells, or separator gel. |
| | 2 to 8°C | 14 days | Specimens may be stored on or off the clot, red blood cells, or separator gel. |
| | -20°C or colder | 3 months | Remove serum or plasma from the clot, red blood cells, or separator gel. |

- Living donor specimens stored at -20°C or colder for greater than 3 months may be used for informational purposes (*e.g.*, lookback testing, discordant sample testing, clinical and validation testing).
- Storage at a combination of 15 to 30°C and 2 to 8°C may not exceed 14 days (inclusive of shipping time) and cannot exceed the maximum durations listed in the table above.
- Performance has not been established for living donor specimens that have undergone more than 6 freeze/thaw cycles.

| Specimen Type | Temperature | Maximum Storage Time | Special Instructions |
|---|---|---|---|
| Cadaveric Serum | Room temperature (15 to 30°C) | 3 days | If specimens are not processed directly after initial centrifugation, it is recommended to remove the supernatant from the clot, red blood cells, or separator gel until further processing. |
| | 2 to 8°C | 14 days | If specimens are not processed directly after initial centrifugation, it is recommended to remove the supernatant from the clot, red blood cells, or separator gel until further processing. |
| | -20°C or Colder | 3 months | If specimens are not processed directly after initial centrifugation, it is recommended to remove the supernatant from the clot, red blood cells, or separator gel until further processing. |

- Performance has not been established using cadaveric specimens stored at -20°C or colder for greater than 3 months.
- Storage at a combination of 15 to 30°C and 2 to 8°C may not exceed 14 days (inclusive of shipping time) and cannot exceed the maximum durations listed in the table above.
- Performance has not been established for cadaveric specimens that have undergone more than 6 freeze/thaw cycles.

### Specimen Shipping

Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.

## ■PROCEDURE

### Materials Provided

06P02 Alinity s HBsAg Reagent Kit

### Materials Required but not Provided

- Alinity s HBsAg Assay File
- 06P0204 Alinity s HBsAg Calibrator Kit
- 06P0213 Alinity s HBsAg Assay Control Kit
- 06P0215 Alinity s HBsAg Release Control Kit
- Alinity Trigger Solution
- Alinity Pre-Trigger Solution
- Alinity s Concentrated Wash Buffer

For information on materials required for operation of the system, refer to the Alinity s System Operations Manual, Section 1.

For information on materials required for maintenance procedures, refer to the Alinity s System Operations Manual, Section 9.

### Assay Procedure

For a detailed description of how to run an assay, refer to the Alinity s System Operations Manual, Section 5.

- Primary tubes may be on board the system for up to 10 hours.
- If using primary or aliquot tubes, refer to the Alinity s System Operations Manual, Section 4 to ensure sufficient specimen is present.
- To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.
- Maximum number of replicates sampled from the same sample cup: 10
  - ≤ 3 hours on the reagent and sample manager:
    - Sample volume for first test: 275 µL
    - Sample volume for each additional test from same sample cup: 75 µL
  - > 3 hours on the reagent and sample manager:
    - Replace with a fresh aliquot of sample.
- Refer to the Alinity s HBsAg Calibrator Kit, Assay Control Kit, and/or Release Control Kit package inserts for preparation and usage.
- For general operating procedures, refer to the Alinity s System Operations Manual, Section 5.
- For optimal performance, it is important to perform routine maintenance as described in the Alinity s System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

### Calibration

For instructions on performing a calibration, refer to the Alinity s System Operations Manual, Section 5.

Three replicates of Alinity s HBsAg Calibrator 1 and Calibrator 2 are automatically tested by the system. The calibrators must be priority loaded.

Each assay control must be tested to evaluate the assay calibration. Once a calibration is accepted and stored, it may be used for 14 days. During this time, all subsequent samples may be tested without further calibration unless:

- A reagent kit with a new lot number is used.
- Daily quality control results are outside of quality control limits used to monitor and control system performance.

This assay may require recalibration after maintenance to critical parts or subsystems or after service procedures have been performed.

### Quality Control Procedures

#### Assay Controls

The Alinity s HBsAg Assay Controls must be tested once every 24 hours when the system is being used.

Assay control values must be within the ranges specified in the Alinity s HBsAg Assay Control Kit package insert. When the assay control values are within range, sample results are generated, and a valid release control result is required to release test results. If an assay control value is not within range, sample results are not generated for in-process or scheduled samples. For troubleshooting information, refer to the Alinity s System Operations Manual, Section 10.

#### Release Controls

The Alinity s HBsAg Release Control must be tested in order to release test results.

The release control is tested at user-defined intervals. For configuring the release control, refer to the Alinity s System Operations Manual, Section 2. For manually ordering the release control, refer to the Alinity s System Operations Manual, Section 5.

The release control must meet specifications defined in the Alinity s HBsAg Release Control Kit package insert in order to validate the system functionality and release test results. If the release control does not meet specifications, refer to the Alinity s System Operations Manual, Section 10, for additional information.

#### Other Controls

Additional controls may be tested at operator's discretion in accordance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy. For additional information on configuring customer controls, refer to the Alinity s System Operations Manual, Section 2.

**Invalidate controls:** Additional controls may be tested anywhere within a run as an invalidate control. Specifications may be assigned to invalidating controls. If an invalidate control fails to meet assigned specifications, no sample results are calculated or provided by the system. When an invalidate control meets assigned specifications, sample processing continues, and a valid release control result is required to release test results.

**Non-validating controls:** Additional controls may be tested anywhere within a run as a non-validating control. Specifications may be assigned to non-validating controls. A valid release control result is required to release test results. If the user-assigned specifications for the non-validating control(s) are not met and the release control specifications are met, there will be no effect on sample processing. In this case, reactive sample results must not be considered invalid.

#### Quality Control Guidance

Refer to "Basic QC Practices" by James O Westgard, Ph.D. for guidance on laboratory quality control practices.[24]

## RESULTS

### Calculation

The Alinity s System calculates results for the Alinity s HBsAg assay using the ratio of the sample RLU to the cutoff RLU (S/CO) for each specimen and control.

Cutoff RLU = (Calibrator 1 mean RLU x 0.0575) + (Calibrator 2 mean RLU × 0.8)

The cutoff RLU is stored for each reagent lot calibration.

S/CO = Sample RLU/Cutoff RLU

### Interpretation of Results

The cutoff is 1.00 S/CO.

**Initial Results**

| Initial Result (S/CO) | Interpretation | Retest Procedure |
|---|---|---|
| < 1.00 | Nonreactive | No retest required. Specimen considered negative for HBsAg. |
| ≥ 1.00 | Reactive | Retest in duplicate. |

**Final Interpretation**

| Retest Result (S/CO) | Final Results | Final Interpretation |
|---|---|---|
| Both results < 1.00 | Nonreactive | Specimen considered negative for HBsAg. |
| One or both results ≥ 1.00 | Repeatedly Reactive | Specimen must be further tested by the Alinity s HBsAg Confirmatory assay. |

Only specimens that are confirmed by specific neutralization with anti-HBs using the Alinity s System are considered positive for HBsAg.

### Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the Alinity s System Operations Manual, Section 5.

## LIMITATIONS OF THE PROCEDURE

- Potential interference has not been evaluated for substances other than those described in the **SPECIFIC PERFORMANCE CHARACTERISTICS - Interference** section of this package insert.
- False reactive results can be expected with any test kit. Falsely elevated results have been observed due to non-specific interactions (refer to the **SPECIFIC PERFORMANCE CHARACTERISTICS** section of this package insert).



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- Although the association of infectivity and the presence of HBsAg is strong, it is recognized that presently available methods for HBsAg detection are not sensitive enough to detect all potentially infectious units of blood or possible cases of HBV infection. A nonreactive test result does not exclude infection.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[25] Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous results may be observed.
- Vaccination with a recombinant HBsAg Hepatitis B vaccine may cause transient positive results caused by a passive transfer of antigen by vaccination.

Refer to the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert for specimen limitations.

## ■SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

### Reproducibility

A study was performed based on guidance from CLSI EP15-A2.[26] Testing was conducted using 3 lots of the Alinity s HBsAg Reagent Kit, Calibrator Kit, Assay Control Kit, and Release Control Kit. Panel members and controls were tested twice a day for 5 days in replicates of 4 at 3 sites.

| | | | Within-Run | | Between-Run | | Between-Day | | Within-Laboratory[a] | | Between-Site | | Between-Lot | | Reproducibility[b] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sample | N | Mean S/CO | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Low HBsAg | 360 | 1.70 | 0.080 | 4.7 | 0.000 | 0.0 | 0.010 | 0.6 | 0.081 | 4.8 | 0.000 | 0.0 | 0.032 | 1.9 | 0.091 | 5.4 |
| High HBsAg | 360 | 8.43 | 0.356 | 4.2 | 0.000 | 0.0 | 0.078 | 0.9 | 0.364 | 4.3 | 0.000 | 0.0 | 0.115 | 1.4 | 0.406 | 4.8 |
| Positive Control | 360 | 2.50 | 0.096 | 3.8 | 0.000 | 0.0 | 0.030 | 1.2 | 0.100 | 4.0 | 0.000 | 0.0 | 0.000 | 0.0 | 0.114 | 4.6 |
| Negative Control | 360 | 0.18 | 0.023 | NA | 0.019 | NA | 0.004 | NA | 0.030 | NA | 0.003 | NA | 0.000 | NA | 0.031 | NA |

%CV = coefficient of variation expressed as a percentage; N = number of replicates; NA = Not applicable: %CVs are not meaningful when S/CO approaches zero; SD = standard deviation

[a] Includes within-run, between-run, and between-day variability.

[b] Includes within-run, between-run, between-day, between-site, between-lot and the site-lot interaction variability.

### Specificity

A total of 7347 fresh serum specimens and 6511 fresh plasma specimens from volunteer whole blood donors were collected at 3 distinct blood centers. A total of 3135 specimens from plasmapheresis donors were collected at one additional blood center. The initial and repeat reactive rates for the serum specimens were 0.10% (7/7347) and 0.07% (5/7347), respectively. The initial and repeat reactive rates for the plasma specimens were 0.05% (3/6511) and 0.05% (3/6511), respectively. The initial and repeat reactive rates for the plasmapheresis donor specimens were 0.00% (0/3135) and 0.00% (0/3135), respectively. Repeatedly reactive specimens were further tested using the Alinity s HBsAg Confirmatory assay; 2 specimens were confirmed positive and 6 specimens were not confirmed. The 2 confirmed positive specimens were positive by HBV Qualitative DNA.

Specificity based on assumed zero prevalence of HBsAg in whole blood and plasmapheresis donors was estimated in this study to be 99.96% (16 985/16 991) with a 95% confidence interval of 99.92% to 99.99%.

| Specimen Category | Number Tested | IR (% of Total) (95% CI) | RR (% of Total) (95% CI) | Number Confirmed Positive (% of RR) | Specificity (%)[a] (95% CI) |
|---|---|---|---|---|---|
| Volunteer Blood Donors- Serum | 7347 | 7 (0.10) (0.04 – 0.20) | 5 (0.07) (0.02 – 0.16) | 2 (40.00) | 99.96 (7342 / 7345) (99.88 – 99.99) |
| Volunteer Blood Donors- Plasma | 6511 | 3 (0.05) (0.01 – 0.13) | 3 (0.05) (0.01 – 0.13) | 0 (0.00) | 99.95 (6508 / 6511) (99.87 – 99.99) |
| **Total Volunteer Blood Donors** | **13 858** | **10 (0.07) (0.03 – 0.13)** | **8 (0.06) (0.02 – 0.11)** | **2 (25.00)** | **99.96 (13 850 / 13 856) (99.91 – 99.98)** |
| Plasmapheresis Donors | 3135 | 0 (0.00) (0.00 – 0.12) | 0 (0.00) (0.00 – 0.12) | NA | 100.00 (3135 / 3135) (99.88 – 100.00) |
| **Total Donors** | **16 993** | **10 (0.06) (0.03 – 0.11)** | **8 (0.05) (0.02 – 0.09)** | **2 (25.00)** | **99.96 (16 985 / 16 991) (99.92 – 99.99)** |

IR = Initially Reactive; RR = Repeatedly Reactive; CI = Confidence Interval

[a] Specimens confirmed positive were excluded from specificity calculations

For total donors, the IR rate not reactive on retest was estimated to be 0.01% (2/16 985) with a 95% confidence interval of 0.00% to 0.04%.

IR Rate Not Reactive on Retest = 100% x (Number of IR – Number of RR) / (Number Tested – Number of RR)

### Sensitivity

A total of 886 specimens from the categories shown in the table below were tested using the Alinity s HBsAg assay at 3 clinical sites. All repeatedly reactive specimens were tested using the Alinity s HBsAg Confirmatory assay.

Sensitivity was estimated to be 100.00% (432/432) with a 95% confidence interval of 99.15% to 100.00% for preselected positive specimens.

| Specimen Category | Number Tested | Number RR (% of Total) | Number Confirmed Positive (% of RR) | Sensitivity (%) (95% CI) |
|---|---|---|---|---|
| Preselected HBsAg Positive[a] | 167 | 167 (100.00) | 167 (100.00) | 100.00 (167/167) [97.82 – 100.00] |
| Preselected HBsAg Positive - Acute HBV Infection[a] | 70 | 70 (100.00) | 70 (100.00) | 100.00 (70/70) [94.87 – 100.00] |
| Preselected HBsAg Positive - Chronic HBV Infection[a] | 195 | 195 (100.00) | 195 (100.00) | 100.00 (195/195) [98.13 – 100.00] |
| **Subtotal** | **432** | **432 (100.00)** | **432 (100.00)** | **100.00 (432/432) [99.15 – 100.00]** |
| Increased Risk of HBV Infection[b] | 403 | 3 (0.74) | 3 (100.00) | NA[d] |
| Recovered HBV Infection[c] | 51 | 0 (0.00) | NA | NA |
| **Total** | **886** | **435 (49.10)** | **435 (100.00)** | **100.00 (435/435) [99.16 – 100.00]** |

NA = not applicable; RR = Repeatedly Reactive

[a] Preselected HBsAg positive specimens were previously confirmed positive by specific antibody neutralization using FDA approved assays. Acute and chronic HBV classifications were determined using four HBV reference markers (HBsAg, anti-HBc IgM, anti-HBc, and anti-HBs) or by medical diagnosis.

[b] The following risk factors were included: current or past residence in a Hepatitis B endemic region, diagnosed or treated for a sexually transmitted disease, hemodialysis patient, heterosexual contact with a high-risk individual or an infected individual, history of incarceration, household contact with HBV infected individual, intravenous drug user, men who have sex with men, and multiple sex partners.

[c] Specimens were classified as recovered using four HBV reference markers (HBsAg, anti-HBc IgM, anti-HBc, and anti-HBs). Recovered HBV infection specimens were assumed HBsAg negative and were not included in the sensitivity analysis.

[d] The sensitivity calculation and confidence interval are not meaningful due to the small number of specimens.

### Genotype Detection

A total of 16 preselected HBsAg positive specimens of known genotype (genotypes A–H) obtained from commercial vendors were tested using the Alinity s HBsAg assay. The results were compared to a commercially available HBsAg assay. All specimens were repeatedly reactive by both the Alinity s HBsAg assay and the commercially available HBsAg assay.

### HBsAg Mutant Detection

A total of 52 preselected HBsAg positive mutant specimens (14 native mutant specimens and 38 recombinant mutant specimens) obtained from commercial vendors were tested using the Alinity s HBsAg assay. The results were compared to a commercially available HBsAg assay.

| Mutant | Alinity s HBsAg Interpretation | Commercially Available HBsAg Assay Interpretation |
|---|---|---|
| **Native Mutant Specimens** | | |
| Ser-143-Leu+Pro-211-His | **RR** | **RR** |
| Gly-145-Ala+Thr-189-Ile | **RR** | **RR** |
| Thr-27-Lys+Tyr-100-Cys+Gln-129-Arg+Leu-175-Ser+Trp-199-Leu | **RR** | **RR** |
| Leu-49-Arg+Gln-101-His+Thr-126-Ile+Glu-164-Gly | **RR** | **RR** |
| Gly-145-Ala | **RR** | **RR** |
| Cys-76-Trp+Pro-120-Ser+Ser-132-Phe | **RR** | **RR** |
| Asp-144-Glu+Ser-204-Asn+Ser-207-Asn | **RR** | **RR** |
| Pro-127-Leu+Gln-129-His | **RR** | **RR** |
| Ser-143-Leu+Thr-189-Ile | **RR** | **RR** |
| Gly-145-Ala+Thr-189-Ile+Phe-212-Tyr | **RR** | **RR** |
| Ser-143-Leu | **RR** | **RR** |
| Thr-118-Lys+ Thr-140-Ile+Cys-149-Tyr | **RR** | **RR** |
| Pro-135-Leu+ Cys-139-Tyr+ Asp-144-Ala+ Gly-145-Arg+Ser-171-Tyr+ Val-180-Ala | **RR** | **RR** |
| Phe-93-Cys+ Met-103-Ile+ Gly-145-Arg+ Ser-174-Asn | **RR** | **RR** |
| **Recombinant Mutant Specimens** | | |
| Cys-137-Tyr | **RR** | **RR** |
| Cys-147-Ser | **RR** | **RR** |
| Cys-124-Arg | **RR** | Nonreactive |
| 122-Asp-Thr | **RR** | Nonreactive |
| Pro-120-Ser+Thr-125-Met+Pro-127-Tyr+Ser-143-Leu | **RR** | **RR** |
| Cys-121-Tyr+Lys-122-Leu+Thr-123-Asn+Gly-130-Glu+Met-133-Ile+Asp-144-Gly+Gly-145-Arg | **RR** | Nonreactive |
| Gln-129-His | **RR** | **RR** |
| Met-133-Leu | **RR** | **RR** |
| Asp-144-Ala | **RR** | **RR** |
| Gly-145-Arg | **RR** | **RR** |
| Pro-142-Leu+Gly-145-Arg | **RR** | **RR** |
| Pro-142-Ser+Gly-145-Arg | **RR** | **RR** |
| Thr-123-Ala | **RR** | Nonreactive |
| 122-Asn-Thr | **RR** | Nonreactive |
| 122-Arg-Ala | **RR** | Nonreactive |
| Thr-123-Asn | **RR** | Nonreactive |
| Gly-145-Lys | **RR** | **RR** |
| Thr-143-Leu | **RR** | **RR** |
| Thr-123-Ser | **RR** | Nonreactive |
| 123-Arg-Gly-Ala | **RR** | Nonreactive |
| Thr-123-Ala+Gly-145-Arg | **RR** | Nonreactive |
| Gly-145-Glu | **RR** | **RR** |
| Met-133-Leu+Gly-145-Arg | **RR** | **RR** |
| Thr-126-Ser | **RR** | **RR** |
| Met-133-Thr | **RR** | **RR** |
| Gly-145-Ala | **RR** | **RR** |
| Pro-120-Ser+Asp-144-Glu+Gly-145-Arg+Thr-189-Ile | **RR** | **RR** |
| Phe-134-His+Pro-142-Leu+Asp-144-Glu+Gly-145-Arg | **RR** | **RR** |
| Thr-126-Ile | **RR** | **RR** |
| Thr-123-Asn+Thr-143-Ser | **RR** | Nonreactive |
| Thr-126-Ala+Met-133-Ile | **RR** | **RR** |
| Pro-127-Thr+Gly-145-Arg | **RR** | **RR** |
| Asp-144-Glu+Gly-145-Arg | **RR** | **RR** |
| Thr-126-Ile+Phe-134-His+Pro-142-Leu+Gly-145-Arg | **RR** | **RR** |
| Thr-143-Leu+Val-190-Ala+Tyr-200-Cys+Tyr-206-Arg | **RR** | **RR** |
| Leu-109-Ile+Gly-112-Lys+Ser-113-Ala+Pro-120-Thr+Phe-134-Ser | **RR** | **RR** |
| Ile-110-Arg+Lys-122-Tyr+Phe-134-Ser+Pro-142-Leu+Asp-144-Ala | **RR** | **RR** |
| Thr-125-Met+Thr-126-Asn+Pro-127-Thr | **RR** | **RR** |

RR = repeatedly reactive

### Analytical Sensitivity

Analytical sensitivity was evaluated using dilutions of the WHO 3rd International Standard for hepatitis B surface antigen (HBsAg) (subtypes ayw1/adw2, genotype B4, NIBSC Code 12/226). The dilutions ranged from 0.005 to 0.100 IU/mL (0.03 to 0.56 ng/mL). The dilutions were tested across 3 lots of the Alinity s HBsAg Reagent Kit on 1 Alinity s System. The analytical sensitivity of the Alinity s HBsAg assay was 0.013 IU/mL for all 3 reagent lots. For the ng/mL unit, the analytical sensitivity of the Alinity s HBsAg assay ranged from 0.07 to 0.08 ng/mL.

### Seroconversion Sensitivity

To determine the seroconversion sensitivity, 20 seroconversion panels obtained from commercial vendors were tested on the Alinity s System using the Alinity s HBsAg assay. The results were compared to a commercially available HBsAg assay and representative data from 5 panels are summarized in the following table.

| Panel ID | Days Since 1st Bleed | Alinity s HBsAg Reactive ≥ 1.00 S/CO | Commercially-Available HBsAg Assay Reactive ≥ 1.00 S/CO |
|---|---|---|---|
| **HBV6272**[a] | 72 | 0.41 | 0.71 |
| | 74 | 0.44 | 0.71 |
| | 94 | **1.24** | **1.81** |
| | 97 | **1.90** | **2.75** |
| | 101 | **2.77** | **3.82** |
| | 104 | **3.73** | **4.54** |
| | 108 | **6.20** | **7.58** |
| | 111 | **12.53** | **11.09** |
| | 115 | **21.39** | **15.89** |
| **HBV6277** | 0 | 0.16 | 0.41 |
| | 4 | 0.16 | 0.45 |
| | 21 | 0.21 | 0.53 |
| | 26 | 0.36 | 0.65 |
| | 28 | 0.49 | 0.59 |
| | 33 | **1.24** | **1.38** |
| | 35 | **1.94** | **1.83** |
| | 40 | **4.89** | **4.73** |
| | 42 | **6.35** | **7.65** |
| | 47 | **26.54** | **28.93** |
| | 49 | **45.06** | **44.42** |

| | | | |
|---|---|---|---|
| **HBV11002** | 0 | 0.35 | 0.57 |
| | 2 | 0.51 | 0.61 |
| | 7 | **1.57** | **1.60** |
| | 9 | **2.14** | **1.97** |
| | 35 | **1563.84** | **327.21** |
| | 39 | **480.36** | **186.51** |
| **HBV11013**[b] | 232 | 0.24 | 0.42 |
| | 239 | 0.39 | 0.49 |
| | 244 | **1.06** | **1.27** |
| | 246 | **1.41** | **1.73** |
| | 251 | **3.51** | **2.44** |
| | 253 | **5.21** | **3.97** |
| | 258 | **7.31** | **5.43** |
| | 260 | **11.85** | **9.68** |
| | 265 | **28.53** | **21.70** |
| | 267 | **80.06** | **36.41** |
| **HBV11027** | 0 | 0.19 | 0.44 |
| | 5 | 0.16 | 0.40 |
| | 12 | 0.17 | 0.39 |
| | 14 | 0.15 | 0.43 |
| | 19 | 0.26 | 0.38 |
| | 21 | 0.20 | 0.39 |
| | 26 | 0.28 | 0.47 |
| | 29 | 0.47 | 0.52 |
| | 33 | **1.14** | 0.88 |
| | 37 | **2.82** | **1.95** |
| | 40 | **5.77** | **3.88** |
| | 64 | **6538.18** | **473.16** |

[a] Sixteen early bleeds are not shown as they are all nonreactive.
[b] Twenty-five early bleeds are not shown as they are all nonreactive.

### Other Specimen Conditions or Disease States

A total of 191 specimens from individuals with other specimen conditions or disease states unrelated to HBV infection were evaluated. Of the 191 specimens, 9 were repeatedly reactive using the Alinity s HBsAg assay and a commercially available HBsAg assay, and all 9 specimens were confirmed positive by both the Alinity s HBsAg Confirmatory assay and a commercially available HBsAg confirmatory assay; therefore, supplemental testing was not required.

| Specimen Category | Number Tested | IR (% of Total) | RR (% of Total) | Number Final Status Positive[a] (% of Repeatedly Reactive) |
|---|---|---|---|---|
| Other Specimen Conditions or Disease States[b] | 191 | 9 (4.71) | 9 (4.71) | 9[c] (100.00) |

IR = Initially Reactive; RR = Repeatedly Reactive

[a] Final status positive is defined as concordant with another HBsAg and HBsAg confirmatory assay.
[b] The specimens included the following: Anti-HIV-1/HIV-2 Positive (10), Anti-HTLV I/II Positive (10), Anti-HCV Positive (10), Anti-HAV Positive (10), Anti-HDV Positive (9), Co-infected CMV/EBV/HSV (10), Anti-*T pallidum* Positive (10), Non-viral Hepatitis (10), Rheumatoid Factor Positive (10), Anti-ds DNA Positive (10), Pregnant Females (14), p8replacMultiparous Females (10), Hyper IgG/IgM (10), Influenza Vaccine Recipient (10), Hemodialysis Patients (10), HAMA Positive (10), *E coli* Infection (9), Heterophilic Antibody Positive (9), and Fungal (Yeast) Infection (10).
[c] One anti-HIV-1/HIV-2 Positive and 8 anti-HDV Positive specimens were confirmed positive.

### Interference

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07-A2.[27]

No interference was observed using the Alinity s HBsAg assay from potentially interfering substances at the levels shown below.

| Potentially Interfering Substance | Interferent Level |
|---|---|
| Conjugated Bilirubin | ≤ 20 mg/dL |
| Unconjugated Bilirubin | ≤ 20 mg/dL |
| Hemoglobin | ≤ 500 mg/dL |
| Triglycerides | ≤ 3000 mg/dL |
| Total Protein | ≤ 12 g/dL |

In addition, a negative and positive control were spiked with biotin to a concentration of 4250 ng/mL. No interference was observed using the Alinity s HBsAg assay.

The effect of potentially interfering substances has only been evaluated for those listed in this package insert.

## PERFORMANCE CHARACTERISTICS OF CADAVERIC SPECIMEN TESTING

### Reproducibility

Twenty-four cadaveric donor serum specimens and 24 living donor serum specimens were spiked with human serum or plasma reactive for HBsAg to create low level reactive specimens.

Each specimen was tested once per day for 6 days using each of 3 lots of the Alinity s HBsAg Reagent Kit. Total %CV values were determined.

| | | | Total[a] | |
|---|---|---|---|---|
| **Specimen Category** | **Number of Replicates** | **Mean S/CO** | **SD** | **%CV** |
| Cadaveric[b] | 432 | 2.77 | 0.103 | 3.7 |
| Living Donor | 432 | 2.82 | 0.150 | 5.3 |

[a] Total variability contains within-specimen, between-lot and lot-specimen interaction variance components.

[b] Cadaveric serum specimens were collected up to 13.7 hours after death.

### Specificity

Specificity was determined by testing 55 cadaveric serum specimens and 55 living donor serum specimens. Each specimen was tested once using each of 3 lots of the Alinity s HBsAg Reagent Kit.

| Specimen Category | Lot | Nonreactive | Repeatedly Reactive | Specificity (%) (95% CI) |
|---|---|---|---|---|
| Cadaveric[a] | Lot 1 | 55 | 0 | 100.00 (93.51 – 100.00) |
| | Lot 2 | 55 | 0 | 100.00 (93.51 – 100.00) |
| | Lot 3 | 55 | 0 | 100.00 (93.51 – 100.00) |
| Living Donor | Lot 1 | 55 | 0 | 100.00 (93.51 – 100.00) |
| | Lot 2 | 55 | 0 | 100.00 (93.51 – 100.00) |
| | Lot 3 | 55 | 0 | 100.00 (93.51 – 100.00) |

[a] Cadaveric serum specimens were collected up to 23.7 hours after death.

### Analytical Sensitivity

Cadaveric serum specimens and living donor serum specimens were spiked with human serum or plasma reactive for HBsAg to create low-level reactive specimens. Each specimen was tested once, within 24 hours of spiking, using each of 3 lots of the Alinity s HBsAg Reagent Kit. All specimens were reactive on all 3 reagent lots.

| Specimen Category | Lot | Number of Specimens | Mean S/CO | Sensitivity (%) (95% CI) |
|---|---|---|---|---|
| Cadaveric[a] | Lot 1 | 55 | 2.92 | 100.00 (93.51 – 100.00) |
| | Lot 2 | 55 | 2.98 | 100.00 (93.51 – 100.00) |
| | Lot 3 | 55 | 3.02 | 100.00 (93.51 – 100.00) |
| Living Donor | Lot 1 | 54 | 3.00 | 100.00 (93.40 – 100.00) |
| | Lot 2 | 54 | 2.99 | 100.00 (93.40 – 100.00) |
| | Lot 3 | 54 | 2.98 | 100.00 (93.40 – 100.00) |

[a] Cadaveric serum specimens were collected up to 23.7 hours after death.

### Cadaveric Specimen Storage

Cadaveric specimen storage was determined by testing a minimum of 12 low-level reactive specimens, prepared by spiking nonreactive cadaveric serum specimens to a target S/CO value near the cutoff with human plasma reactive for HBsAg, and a minimum of 12 nonreactive cadaveric serum specimens. Each specimen was tested at Day 0, and then subjected to either 2 to 8°C storage for 14 days, room temperature (15 to 30°C) storage for 3 days, −20°C or colder storage for 3 months, or 6 freeze/thaw cycles. Nonreactive specimens were evaluated by calculating the differences between the mean S/CO of Day 0 and the mean S/CO of each storage condition and related timepoint. Reactive specimens were evaluated by calculating the percent differences between the mean S/CO of Day 0 and the mean S/CO of each storage condition and related timepoint. There were no changes to the interpretation; the data demonstrate that cadaveric serum specimens can be stored at the following conditions when tested with the Alinity s HBsAg assay.

| | | Nonreactive Specimens | Reactive Specimens |
|---|---|---|---|
| Storage Condition | Timepoint | Upper Limit of 2-sided 95% CI of Differences | Lower Limit of 2-sided 95% CI of % Differences |
| Room Temperature (15 to 30°C)[a] | 3 days | 0.00 S/CO | -8.7 % |
| 2 to 8°C[a] | 14 days | -0.03 S/CO | -14.9 % |
| -20°C or colder[b] | 3 months | 0.03 S/CO | -3.0 % |
| Freeze/Thaw[a] | 6 cycles | -0.01 S/CO | -14.8 % |

Abbreviations: CI = confidence interval; S/CO = sample to cutoff ratio

[a] Cadaveric serum specimens were collected up to 22.9 hours after death.

[b] Cadaveric serum specimens were collected up to 17.3 hours after death.

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Note for number formatting:

- A space is used as thousands separator (example: 10 000 specimens).
- A period is used to separate the integer part from the fractional part of a number written in decimal form (example: 3.12%).

## ■Key to Symbols

| | |
|---|---|
|  | Caution |
|  | Consult instructions for use |
|  | Manufacturer |
|  | Sufficient for |
|  | Temperature limitation |
|  | Use by/Expiration date |
| ANCILLARY WASH BUFFER | Ancillary Wash Buffer |
| CONJUGATE | Conjugate |
| CONTAINS: AZIDE | Contains Sodium Azide. Contact with acids liberates very toxic gas. |
| DISTRIBUTED IN THE USA BY | Distributed in the USA by |
| INFORMATION FOR USA ONLY | Information needed for United States of America Only |
| IVD | *In Vitro* Diagnostic Medical Device |
| LOT | Lot Number |
| MICROPARTICLES | Microparticles |
| PRODUCT OF IRELAND | Product of Ireland |
| REF | List Number |
| SN | Serial Number |




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