

VITROS[®] Products
Immunodiagnostic



INSTRUCTIONS FOR USE

HbC M

VITROS Immunodiagnostic Products Anti-HBc IgM Reagent Pack Anti-HBc IgM

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

Intended Use

For the *in vitro* qualitative detection of IgM antibody to hepatitis B core antigen (anti-HBc IgM) in human adult and pediatric serum and plasma (heparin, EDTA and citrate) and neonate serum using the VITROS ECi Immunodiagnostic System.

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.

WARNING: **This assay has not been FDA cleared or approved for the screening of blood or plasma donors.**

Summary and Explanation of the Assay

IgM class antibodies against HBc are detected soon after infection and the presence of high concentrations of anti-HBc IgM has been shown to be an indicative marker of acute infection¹. The level of anti-HBc IgM decreases throughout the course of infection. However, low levels of anti-HBc IgM may persist for over a year after infection in some patients and are found occasionally in chronic carriers¹. The VITROS Anti-HBc IgM assay is designed to detect anti-HBc IgM at an appropriate level of sensitivity as an aid for the diagnosis of acute or chronic hepatitis B infection. The detection of anti-HBc IgM can be useful for the differential diagnosis of hepatitis B from other forms of viral hepatitis².

Principles of the Procedure

The VITROS Anti-HBc IgM assay is performed using the VITROS Anti-HBc IgM Reagent Pack and the VITROS Immunodiagnostic Products Anti-HBc IgM Calibrator on the VITROS ECi Immunodiagnostic System.

An antibody class capture technique is used³. This involves the dilution of the sample and the simultaneous reaction of IgM in the diluted sample with biotinylated mouse monoclonal anti-human IgM antibody. The immune complex is captured by streptavidin on the wells. Unbound materials are removed by washing. Horseradish peroxidase (HRP)-labeled mouse monoclonal anti-HBc IgM antibody, which has been complexed with recombinant HBc antigen (conjugate) is then captured by anti-HBc specific IgM bound to the wells. Unbound material is removed by washing.

The bound HRP conjugate is measured by a luminescent reaction⁴. A reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent, is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminol derivative, producing light. The electron transfer agent increases the level and duration of the light produced. The light signals are read by the VITROS ECi System. The amount of HRP conjugate bound is indicative of the concentration of anti-HBc IgM present in the sample.

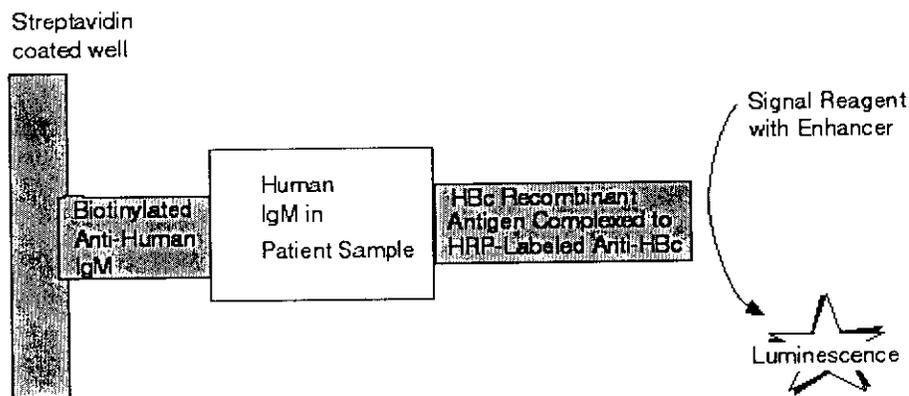
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Assay Type	Assay Time and Temperature
Immunometric (Antibody Class Capture)	Incubation time: 32 minutes Time to first result: 43 minutes Temperature: 37° C

Reaction Scheme



Warnings and Precautions

For in vitro diagnostic use only.

WARNING: Potentially Infectious Material

- Treat as if capable of transmitting infection.
- Handling of samples and assay components, their use, storage and solid and liquid waste disposal should be done at a biological safety level 2 and in accordance with the procedures defined by the appropriate national biohazard safety guideline or regulation (e.g. NCCLS Guideline M29)^{5,6}.

Human blood products provided as components of this pack, and of the VITROS Anti-HBc IgM Calibrator, have been obtained from donors who were tested individually and found to be negative for antibodies to human immunodeficiency virus (HIV 1+2) and hepatitis C virus (HCV) using FDA approved methods (enzyme immunoassays, EIA). The anti-HBc IgM positive plasma has been treated in order to reduce the titer of potentially infectious virus. However as no testing method can rule out the risk of potential infection, handle as if capable of transmitting infection.

Care should be taken when handling material of human origin. All samples should be considered potentially infectious. No test method can offer complete assurance that hepatitis B virus, HCV, HIV 1+2 or other infectious agents are absent.

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WARNING: ⁷ Contains Kathon

The biotinylated antibody reagent in the VITROS Anti-HBc IgM Reagent Pack contains Kathon (1.0% w/w).

The conjugate reagent in the VITROS Anti-HBc IgM Reagent Pack contains Kathon (2.0% w/w).

The VITROS Anti-HBc IgM Calibrator contains Kathon (2.0% w/w).

R36/38 – Irritating to eyes and skin.

R43 – May cause sensitization by skin contact.

R52/53 – Harmful to aquatic organisms. May cause long term adverse effects in the aquatic environment.

S24 – Avoid contact with skin.

S26 – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

S37/39 – Wear suitable gloves and eye/face protection.

Reagents

Reagent Pack Contents

One VITROS Anti-HBc IgM Reagent Pack, 52 tests (CAT No. 680 1425) contains:

- 52 coated wells (streptavidin, binds ≥ 3 ng biotin/well).
- 10.5 mL biotinylated antibody reagent (biotin-mouse monoclonal anti-human IgM, 0.75 $\mu\text{g}/\text{mL}$) in buffer with bovine serum albumin and anti-microbial agent (1.0% Kathon w/w).
- 7.6 mL conjugate reagent [HRP-mouse monoclonal anti-HBc, 57 ng/mL with recombinant HBc derived from bacteria (*E.coli*), 65 ng/mL] in buffer with bovine serum albumin and anti-microbial agent (2.0% Kathon w/w).

Reagent Pack Handling

- The reagent pack is supplied ready for use.
- Reagent packs do not need mixing.
- Avoid agitation, which may cause foaming or the formation of bubbles.

Reagent Pack Stability

When stored and handled as specified in the package labeling, the VITROS Anti-HBc IgM Reagent Pack is suitable for use until the expiration date printed on the outside of the carton.

Reagent Pack Storage and Preparation

- Store the unopened reagent pack refrigerated at 2°–8°C (36°–46°F). Do not freeze.
- Load reagent packs directly from refrigerated storage to minimize condensation.
- Use opened reagent packs within 8 weeks.
- Store opened reagent packs in the VITROS ECi System reagent supply, or refrigerated at 2°–8°C (36°–46°F) in a sealed reagent pack storage box that contains dry desiccant.

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Specimen Collection and Preparation

Patient Preparation

No special patient preparation is necessary.

Recommended Specimen Types

Serum, EDTA, heparin or citrated plasma.

Citrated plasma has been shown to lower the signal/cutoff (s/c) values in some anti-HBc IgM reactive samples. High negative results (0.80 – 0.99 s/c) obtained on samples collected with this anticoagulant should be interpreted accordingly. Additional testing may be required. Follow manufacturer's instructions for using plasma collection containers with anticoagulants.

Specimens Not Recommended

Turbidity in samples may affect results.

Special Precautions

Some sample collection devices have been reported to be detrimental to the integrity of certain analytes, and could interfere with some method technologies⁸. 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.

Specimen Collection and Preparation

- Collect specimens using standard procedures⁹.
- The VITROS Anti-HBc IgM assay uses 10 µL of sample for each determination.
- For details on minimum fill volume of sample cups or containers, refer to the VITROS Eci Immunodiagnostic System Operator's Guide.
- Mix samples, calibrator, and controls by inversion and bring to 15°–30°C (59°–86°F) before use.
- Samples should be thoroughly separated from all cellular material. Failure to do so may lead to an erroneous result.
- Do not use heat inactivated samples.

Handling and Storage Conditions

- Handle specimens in stoppered containers to avoid cross-contamination and evaporation. Use a separate disposable tip if samples are manually pipetted. Avoid splashing, forming an aerosol, or cross-contaminating sample tube stoppers.
- The amount of time samples are on board the system prior to analysis should be limited to avoid evaporation. This time should not exceed two hours. Refer to the VITROS Eci System Operator's Guide for further information.
- The National Committee for Clinical Laboratory Standards (NCCLS) provides the following recommendations for storing specimens:¹⁰
 - Store samples at 22°C (72°F) for no longer than 8 hours.
 - If the assay will not be completed within 8 hours, refrigerate samples at 2°–8°C (36°–46°F).
 - If the assay will not be completed within 48 hours, or for shipment, freeze samples at or below -20°C (-4°F).
- Samples are not to be repeatedly frozen and thawed because this can cause analyte deterioration. Samples are to be thawed only once.

Assay Procedure

Materials Required But Not Provided

The following items are required to perform the VITROS Anti-HBc IgM assay:

- VITROS ECi System
- VITROS Anti-HBc IgM Calibrator
- VITROS Immunodiagnostic Products High Sample Diluent B
- VITROS Immunodiagnostic Products Signal Reagent
- VITROS Immunodiagnostic Products Universal Wash Reagent
- Quality control materials, such as VITROS Immunodiagnostic Products Anti-HBc IgM Controls
- VITROS Immunodiagnostic Products Reagent Pack Storage Box (optional) with desiccant

Operating Instructions

Refer to the VITROS ECi System Operator's Guide for complete instructions on the operation of your VITROS ECi System.

Calibration

Required Calibrator

VITROS Anti-HBc IgM Calibrator

Calibrator Preparation, Handling, and Storage

Refer to the calibrator instructions for use for information on the use of the VITROS Anti-HBc IgM Calibrator.

Calibration Procedure

- Calibration must be performed using a calibrator of the same lot number as the reagent pack.
- Refer to the VITROS ECi System Operator's Guide for detailed instructions on how to calibrate.

When to Calibrate

- Calibrate when the lot of reagent pack and calibrator changes
- Calibrate every 28 days

The VITROS Anti-HBc IgM assay may also need to be recalibrated:

- After specified service procedures have been performed (see the VITROS ECi System Operator's Guide)
- If quality control results are consistently outside of your acceptable range.

For additional information on when to calibrate, refer to the VITROS ECi System Operator's Guide.

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Quality Control

Procedure Recommendations

- Choose control levels that check performance at clinically relevant points. The recommendation is to run a negative control and a positive control close to the anti-HBc IgM decision point [signal/cutoff (s/c) ≥ 1.00].
- To verify system performance, analyze control materials:
 - After calibration
 - At least once every 24 hours
 - After specified service procedures or maintenance to critical parts or subsystems that might influence performance of the assay (see the VITROS ECi System Operator's Guide)
- Analyze quality control materials in the same manner as patient specimens.
- If control results fall outside the stated range or outside your established acceptable range, patient results should not be reported. Investigate and determine the cause for the unacceptable control results. When the condition is corrected, retest the controls and confirm that results are within acceptable limits. It is advisable to repeat some or all patient specimens before reporting results for this run.
- For more detailed information on quality control procedures, refer to the VITROS ECi System Operator's Guide.
- Refer to *Internal Quality Control Testing: Principles and Definitions* or other published guidelines for general quality control recommendations¹¹.
- Additional controls may be tested according to guidelines or requirements of local, state, and/or federal regulations or accrediting organizations.

Quality Control Material Selection

Choose control material that has a composition similar to or identical with the patient sample matrix being analyzed.¹²

VITROS Anti-HBc IgM Controls are recommended for use with the VITROS ECi System. The performance of other commercial control fluids should be evaluated for compatibility with this assay before they are used for quality control.

Appropriate quality control value ranges must be established for all commercially available quality control materials used with the VITROS Anti-HBc IgM assay.

Quality Control Material Preparation and Storage

Refer to the manufacturer's product literature for preparation, storage, and stability information.

Interpretation of Results and Expected Values

Results are calculated as a normalized signal, relative to the cutoff value (signal/cutoff, s/c). During the calibration process, a lot-specific parameter, encoded on the lot calibration card, is used to determine a valid stored cutoff value for the VITROS ECI System.

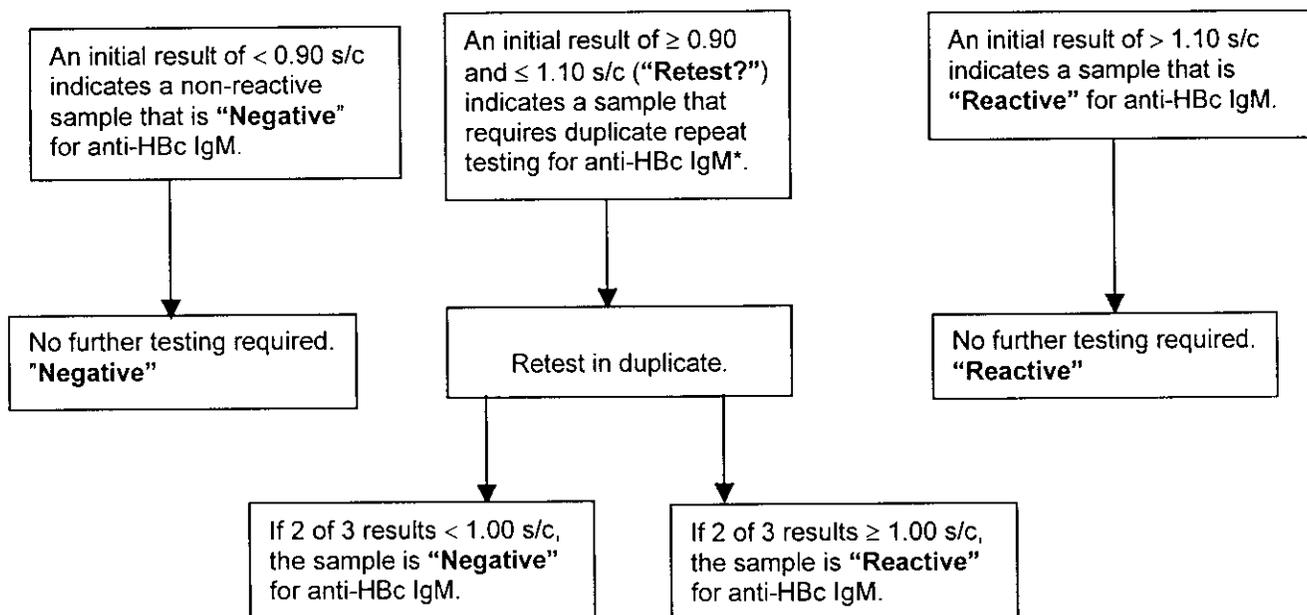
$$\text{Result} = \frac{\text{Signal for test sample}}{\text{Cutoff value}}$$

Patient sample results will be displayed with a “**Negative**”, “**Retest?**” or “**Reactive**” label. An initial result labeled with “**Retest?**” indicates a sample that requires duplicate repeat testing for anti-HBc IgM.

Result (s/c)	< 0.90	≥ 0.90 and ≤ 1.10	> 1.10
Result Text	Negative	Retest?	Reactive

Final results should be manually interpreted using the algorithm below.

Testing Algorithm



* See Interpretation of Results for neonate samples

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Interpretation of Results

The following table summarizes the interpretation of results obtained with the VITROS Anti-HBc IgM assay upon completion of all testing steps required in the testing algorithm.

VITROS Anti-HBc IgM Assay Result (s/c)	Conclusion from Testing Algorithm	Interpretation
< 0.90	Negative	Specimen is negative for anti-HBc IgM.
≥ 0.90 and ≤ 1.10	Retest in duplicate	Specimen is negative for anti-HBc IgM if 2 of 3 results are < 1.00. Specimen is presumed to be reactive for anti-HBc IgM if 2 of 3 results are ≥ 1.00 .
> 1.10	Reactive	Specimen is presumed to be reactive for anti-HBc IgM.

- Results obtained with the VITROS Anti-HBc IgM assay may not be used interchangeably with values obtained with different manufacturers' assay methods.
- The magnitude of a VITROS Anti-HBc IgM assay result cannot be correlated to an endpoint titer.
- Citrated plasma has been shown to lower the signal/cutoff (s/c) values in some anti-HBc IgM reactive samples. High negative results (0.80 – 0.99 s/c) obtained on samples collected with this anticoagulant should be interpreted accordingly. Additional testing may be required. Follow manufacturer's instructions for using plasma collection containers with anticoagulants.
- Neonate samples with results ≥ 0.90 and ≤ 1.10 s/c should not be retested in duplicate. Obtain a new sample and retest.
- During the assessment of clinical performance for the VITROS Anti-HBc IgM assay, it was determined that all samples that were VITROS Anti-HBc IgM reactive were also reactive when tested using the VITROS Immunodiagnostic Products Anti-HBc Reagent Pack and Calibrator.

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Expected Results

Approximately 65.7% (1111/1691) of the prospective subjects in Population I reported no recent or current signs or symptoms of hepatitis. Of these 1111 asymptomatic individuals, 25.3% were enrolled in Miami, FL, 36.5% were enrolled in Dallas, TX, and 38.2% were enrolled in Chicago, IL. The group was Caucasian (27.7%), African American (44.8%), Hispanic (18.7%), and Asian (4.8%) with the remaining 4% represented by other ethnic groups. The group was 51.6% male and 48.4% female and ranged in age from 5 to 89 years. All were at risk for viral hepatitis due to lifestyle, behavior, occupation or known exposure event. The VITROS Anti-HBc IgM assay was reactive in 0.7% of the individuals in this group. The percent VITROS Anti-HBc IgM reactive results observed in the asymptomatic population at each site was 0.27% at Miami, FL, 0.18% at Dallas, TX, and 0.27% at Chicago, IL.

The table below summarizes the distribution of VITROS Anti-HBc IgM reactive and negative results among the study subjects without signs or symptoms of hepatitis, by age and gender.

Expected Results for the VITROS Anti-HBc IgM Assay in Study Subjects Without Signs or Symptoms of Hepatitis - Population I (N=1111)						
Age Range	Gender	VITROS Anti-HBc IgM Result				Total
		Reactive		Negative		
		N	Percent	N	Percent	
0-9	Female	0	0	0	0	0
	Male	0	0	1	100	1
10-19	Female	1	9.1	10	90.9	11
	Male	0	0	11	100	11
20-29	Female	0	0	96	100	96
	Male	0	0	84	100	84
30-39	Female	1	0.9	116	99.1	117
	Male	4	2.5	157	97.5	161
40-49	Female	0	0	129	100	129
	Male	1	0.6	179	99.4	180
50-59	Female	0	0	93	100	93
	Male	1	1.4	69	98.6	70
60-69	Female	0	0	63	100	63
	Male	0	0	40	100	40
70-79	Female	0	0	22	100	22
	Male	0	0	23	100	23
80-89	Female	0	0	5	100	5
	Male	0	0	2	100	2
90-100	Female	0	0	0	0	0
	Male	0	0	0	0	0
Total		8	0.7	1100	99.3	1108*

* Age was not reported for 3 subjects.

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Expected results for the VITROS Anti-HBc IgM assay were also determined using unlinked samples from a population of pediatric and adolescent subjects in Utah at low risk for viral hepatitis (N=100). The group was 57% male and 43% female, and the subjects' ages ranged from two to 19 years.

All 100 samples were negative with the VITROS Anti-HBc IgM assay.

Expected Results for the VITROS Anti-HBc IgM Assay in Pediatric and Adolescent Subjects At Low Risk for Viral Hepatitis (N=100)						
Age Range	Gender	VITROS Anti-HBc IgM Result				Total
		Reactive		Negative		
		N	Percent	N	Percent	
2-4	Female	0	0	9	100	9
	Male	0	0	16	100	16
5-9	Female	0	0	13	100	13
	Male	0	0	12	100	12
10-14	Female	0	0	8	100	8
	Male	0	0	17	100	17
15-19	Female	0	0	13	100	13
	Male	0	0	12	100	12
Total		0	0	100	100	100

Limitations of the Procedure

- The results from this or any other diagnostic kit should be used and interpreted only in the context of the overall clinical picture. A negative test result does not exclude the possibility of exposure to hepatitis B virus. Levels of anti-HBc IgM may be undetectable both in early infection and late after infection.
- Heterophilic antibodies in serum or plasma samples may cause interference with immunoassay¹³. These antibodies may be present in blood samples from individuals regularly exposed to animals or who have been treated with animal serum products. Results, which are inconsistent with clinical observations indicate the need for additional testing.

Performance Characteristics

Clinical Performance

A multi-center prospective study was conducted to evaluate the clinical performance of the VITROS Anti-HBc IgM assay among individuals with signs or symptoms or biochemical manifestations (elevated liver function tests) of hepatitis and those at high risk of hepatitis infection due to lifestyle, behavior, occupation, or known exposure events. Specimens were obtained from 1691 subjects prospectively enrolled at three geographically separated collection sites within the United States (Population I) located in Miami, FL (37.0%), Dallas, TX (28.1%) and Chicago, IL (34.9%). Specimens were also obtained from 315 subjects prospectively enrolled in an area in India with a high prevalence of viral hepatitis (Population II). Statistical testing performed to evaluate the homogeneity of the distribution of VITROS Anti-HBc IgM s/c values across the four collection sites indicated that the data from Population I and Population II could not be pooled for statistical analysis.

The HBV disease classification for each subject was determined by a single point serological assessment using a hepatitis marker profile consisting of reference assays (previously licensed or approved by the FDA) for the detection of HBsAg, HBeAg, anti-HBc, anti-HBc IgM, anti-HBe, and anti-HBs (quantitative). The reference assays' procedures were adhered to during the clinical laboratory study.

The subjects in Population I were Caucasian (24.9%), African American (44.1%), Hispanic (22.4%) and Asian (3.7%), with the remaining 4.9% represented by other ethnic groups. The group was 52.4% male and 47.6% female, and ranged in age from 5 to 89 years. Testing of these specimens with the VITROS Anti-HBc IgM assay occurred at diagnostic laboratories located in Miami, FL (37.0%), Port Jefferson, NY (34.9%) and Minneapolis MN, (28.1%). Agreement of the VITROS Anti-HBc IgM assay was assessed relative to the reference anti-HBc IgM assay and HBV disease classification using serum samples from the 1691 subjects in Population I.

The subjects in Population II were Indian (100.0%). The group was 73.0% male and 27.0% female, and ranged in age from 18 to 90 years. Testing of these specimens with the VITROS Anti-HBc IgM assay occurred at diagnostic laboratories located in Miami, FL (33.0%), Minneapolis MN, (32.4%) and Los Angeles, CA (34.6%). Agreement of the VITROS Anti-HBc IgM assay was assessed relative to the reference anti-HBc IgM assay and HBV disease classification using serum samples from the 315 subjects in Population II.

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Results by Specimen Classification

The data were analyzed following the assignment of HBV disease classifications based upon the positive (+) / negative (-) patterns for the six HBV serological reference markers. The table below summarizes how these classifications were derived. There were 28 unique reference marker profiles observed among the subjects in Populations I and II (24 unique patterns in Population I and 18 unique patterns in Population II) during the VITROS Anti-HBc IgM clinical study.

HBV Reference Marker Profiles and HBV Disease Classification						
Reference HbsAg**	Reference HBeAg	Reference IgM aHBc	Reference Total aHBc	Reference aHBe	Reference aHBs ≥10 mIU/mL	HBV Disease Classification
+	+	+	+	+	-	Acute
+	+	+	+	-	-	Acute
+	-	+	+	+	+	Acute
+	-	+	+	+	-	Acute
+	-	+	+	-	-	Acute
+	-	-	-	-	-	Acute
+	+	-	+	+	-	Chronic
+	+	-	+	-	+	Chronic
+	+	-	+	-	-	Chronic
+	-	-	+	+	+	Chronic
+	-	-	+	+	-	Chronic
+	-	-	+	-	-	Chronic
-	-	+	+	+	+	Early Recovery
-	-	+	+	+	-	Early Recovery
-	-	+	+	-	+	Early Recovery
-	-	+	+	-	-	Early Recovery
-	-	-	+	+	-	Early Recovery
-	-	-	+	+	+	Recovery
-	-	-	+	-	+	Recovered
-	-	-	+	-	-	Recovered
-	-	-	-	-	+	HBV Vaccine Response
-	-	-	-	-	-	Not Previously Infected with HBV
+	+	-	-	+	+	Uninterpretable
+	-	-	-	-	+	Uninterpretable
-	+	-	+	-	-	Uninterpretable
-	+	-	-	-	+	Uninterpretable
-	+	-	-	-	-	Uninterpretable
-	-	+	-	-	-	Uninterpretable

* Positive = Reference HBsAg assay reactive and confirmed by neutralization.

** Negative = Reference HBsAg assay negative or not confirmed by neutralization.

Comparison of Results

The table below compares the VITROS Anti-HBc IgM results with the reference anti-HBc IgM results by specimen classification for the subjects in Population I.

Comparison of VITROS Anti-HBc IgM Results with Reference Anti-HBc IgM Results by HBV Disease Classification - Population I (N=1691)					
HBV Disease Classification	Reference Anti-HBc IgM Result				Total
	Reactive		Negative		
	VITROS Anti-HBc IgM Result		VITROS Anti-HBc IgM Result		
	Reactive	Negative *	Reactive **	Negative	
Acute	8	0	0	9	17
Chronic	0	0	2	41	43
Early Recovery	4	6	1	36	47
Recovery	0	0	0	138	138
Recovered	0	0	1	195	196
HBV Vaccine Response	0	0	0	169	169
Not Previously Infected with HBV	0	0	0	1074	1074
Uninterpretable	0	1	0	6	7
Overall	12	7	4	1668	1691

* These samples were tested with a second FDA approved anti-HBc IgM assay with the following results:

Early recovery: 2/6 negative
 Uninterpretable: 1/1 negative
 Overall: 3/7 (42.9%) negative

** These samples were tested with a second FDA approved anti-HBc IgM assay with the following results:

Chronic: 2/2 positive
 Early Recovery: 1/1 positive
 Recovered: 1/1 positive
 Overall: 4/4 (100%) positive

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The table below compares the VITROS Anti-HBc IgM results with the reference anti-HBc IgM results by specimen classification for the subjects in Population II.

Comparison of VITROS Anti-HBc IgM Results with Reference Anti-HBc IgM Results by HBV Disease Classification - Population II (N=315)					
HBV Disease Classification	Reference Anti-HBc IgM Result				Total
	Reactive		Negative		
	VITROS Anti-HBc IgM Result		VITROS Anti-HBc IgM Result		
	Reactive	Negative *	Reactive	Negative	
Acute	69	19	0	16	104
Chronic	0	0	0	185	185
Early Recovery	1	0	0	0	1
Recovery	0	0	0	0	0
Recovered	0	0	0	3	3
HBV Vaccine Response	0	0	0	3	3
Not Previously Infected with HBV	0	0	0	17	17
Uninterpretable	0	0	0	2	2
Overall	70	19	0	226	315

* These samples were tested with a second FDA approved anti-HBc IgM assay with the following results:

Acute: 8/19 negative; 3/19 indeterminate
 Overall: 11/19 (57.9%) negative or indeterminate

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Anti-HBc IgM

Percent Agreement

Positive and negative percent agreement between the VITROS Anti-HBc IgM assay and the reference anti-HBc IgM assay were calculated for subjects in Population I (N=1691) with various HBV disease classifications, and for the overall study population. The table below summarizes these calculations and provides the upper and lower 95% exact confidence intervals.

Positive and Negative Percent Agreement between the Vitros Anti-HBc IgM and Reference Anti-HBc IgM Assays in Population I				
HBV Disease Classification	Positive Percent Agreement (%)	95% Exact Confidence Interval	Negative Percent Agreement (%)	95% Exact Confidence Interval
Overall	12/19 (63.16%)	38.36 - 83.71	1668/1672 (99.76%)	99.39 - 99.93
Acute	8/8 (100%)	63.06 - 100	9/9 (100%)	66.37 - 100
Chronic	0/0 (N/A)	N/A	41/43 (95.35%)	84.19 - 99.43
Early Recovery	4/10 (40%)	12.16 - 73.76	36/37 (97.3%)	85.84 - 99.93
Recovery	0/0 (N/A)	N/A	138/138 (100%)	97.36 - 100
Recovered	0/0 (N/A)	N/A	195/196 (99.49%)	97.19 - 99.99
HBV Vaccine Response	0/0 (N/A)	N/A	169/169 (100%)	97.84 - 100
Not Previously Infected with HBV	0/0 (N/A)	N/A	1074/1074 (100%)	99.66 - 100
Uninterpretable	0/1 (0%)	N/A	6/6 (100%)	54.07 - 100

The positive percent agreement with the reference anti-HBc IgM assay was determined by dividing the number of reactive VITROS Anti-HBc IgM results by the total number of subjects reactive with the reference anti-HBc IgM assay. As a result of this study, the overall positive percent agreement of the VITROS Anti-HBc IgM assay with the reference anti-HBc IgM assay in Population I was estimated to be 63.16% (12/19, with a 95% exact confidence interval of 38.36% to 83.71%).

The negative percent agreement with the reference anti-HBc IgM assay was determined by dividing the number of negative VITROS Anti-HBc IgM results by the total number of subjects negative with the reference anti-HBc IgM assay. As a result of this study, the overall negative percent agreement of the VITROS Anti-HBc IgM assay with the reference anti-HBc IgM assay in Population I was estimated to be 99.76% (1668/1672, with a 95% exact confidence interval of 99.39% to 99.93%).

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Positive and negative percent agreement between the VITROS Anti-HBc IgM assay and the reference anti-HBc IgM assay were also calculated for subjects in Population II (N=315) with various HBV disease classifications, and for the overall study population. The table below summarizes these calculations and provides the upper and lower 95% exact confidence intervals.

Positive and Negative Percent Agreement between the VITROS Anti-HBc IgM and Reference Anti-HBc IgM Assays in Population II				
HBV Disease Classification	Positive Percent Agreement (%)	95% Exact Confidence Interval	Negative Percent Agreement (%)	95% Exact Confidence Interval
Overall	70/89 (78.65%)	68.69 - 86.63	226/226 (100%)	98.38 - 100
Acute	69/88 (78.41%)	68.35 - 86.47	16/16 (100%)	79.41 - 100
Chronic	0/0 (N/A)	N/A	185/185 (100%)	98.03 - 100
Early Recovery	1/1 (100%)	2.5 - 100	0/0 (N/A)	N/A
Recovered	0/0 (N/A)	N/A	3/3 (100%)	29.24 - 100
HBV Vaccine Response	0/0 (N/A)	N/A	3/3 (100%)	29.24 - 100
Not Previously Infected with HBV	0/0 (N/A)	N/A	17/17 (100%)	80.49 - 100
Uninterpretable	0/0 (N/A)	N/A	2/2 (100%)	15.81 - 100

The positive percent agreement with the reference anti-HBc IgM assay was determined by dividing the number of reactive VITROS Anti-HBc IgM results by the total number of subjects reactive with the reference anti-HBc IgM assay. As a result of this study, the overall positive percent agreement of the VITROS Anti-HBc IgM assay with the reference anti-HBc IgM assay in Population II was estimated to be 78.65% (70/89, with a 95% exact confidence interval of 68.69% to 86.63%).

The negative percent agreement with the reference anti-HBc IgM assay was determined by dividing the number of negative VITROS Anti-HBc IgM results by the total number of subjects negative with the reference anti-HBc IgM assay. As a result of this study, the overall negative percent agreement of the VITROS Anti-HBc IgM assay with the reference anti-HBc IgM assay in Population II was estimated to be 100.0% (226/226, with a 95% exact confidence interval of 98.38% to 100.0%).

INSTRUCTIONS FOR USE
HbC M

Anti-HBc IgM

The performance of the VITROS Anti-HBc IgM assay was further evaluated among archived serum samples from subjects with clinical and laboratory documentation of acute or chronic (HBsAg present for ≥ 6 months) HBV infection. The table below summarizes the performance of the VITROS Anti-HBc IgM assay in samples from subjects with documented acute or chronic HBV infection.

Overall Clinical Performance of the VITROS Anti-HBc IgM Assay in Samples from Subjects with Clinically Documented Acute or Chronic HBV Infection			
HBV Infection	Number of Samples	Number (%) of VITROS Anti-HBc IgM Reactive Samples	Number (%) of Reference Anti-HBc IgM Reactive Samples
Acute	8	8 (100.0)	8 (100.0)
Chronic	76	11 (14.5)	30 (39.5)

Seroconversion Panels

Six commercially available seroconversion panels were tested. The VITROS and reference anti-HBc IgM assay results are summarized below. The table lists the first bleed of each panel that tested reactive with the VITROS and the reference assays as well as the difference between the two assays in identifying the first reactive panel member by number of days.

Anti-HBc IgM Seroconversion Panel Study - Summary Results					
Panel ID	Days to Reactive Anti-HBc IgM Result				Difference in Days to Anti-HBc IgM Reactive Result Reference - VITROS
	Reference Anti-HBc IgM Assay		VITROS Anti-HBc IgM Assay		
	-*	+**	-*	+**	
6278	33	37	37	41	-4
6281	41	43	41	43	0
PHM935A	50	66	66	68	-2
RP009	36	43	36	43	0
RP016	56	59	56	59	0
RP017	76	78	76	78	0

* Post bleed day of last nonreactive result, usually denotes previous bleed from first reactive.

** Post bleed day of first reactive result.

HbC M

INSTRUCTIONS FOR USE

Anti-HBc IgM

Potentially Cross-Reacting Subgroups

Samples with evidence of hepatitis A virus infection (HAV) or hepatitis C virus infection (HCV) were identified in a population of 1691 samples prospectively collected from subjects in the U.S with signs or symptoms of, or at risk for, viral hepatitis (Population I). The tables below compare VITROS Anti-HBc IgM results with reference anti-HBc IgM results according to the HBV disease classifications assigned to the study subjects.

HBV Disease Classification	Reference Anti-HBc IgM Result				Total
	Reactive		Negative		
	VITROS Anti-HBc IgM Result		VITROS Anti-HBc IgM Result		
	Reactive	Negative	Reactive	Negative	
Acute	0	0	0	0	0
Chronic	0	0	0	0	0
Early Recovery	0	0	0	0	0
Recovery	0	0	0	0	0
Recovered	0	0	0	2	2
HBV Vaccine Response	0	0	0	0	0
Not Previously Infected with HBV	0	0	0	5	5
Uninterpretable	0	0	0	0	0
Overall	0	0	0	7	7

HBV Disease Classification	Reference Anti-HBc IgM Result				Total
	Reactive		Negative		
	VITROS Anti-HBc IgM Result		VITROS Anti-HBc IgM Result		
	Reactive	Negative	Reactive	Negative	
Acute	1	0	0	3	4
Chronic	0	0	0	9	9
Early Recovery	1	3	0	21	25
Recovery	0	0	0	43	43
Recovered	0	0	1	99	100
HBV Vaccine Response	0	0	0	22	22
Not Previously Infected with HBV	0	0	0	148	148
Uninterpretable	0	0	0	2	2
Overall	2	3	1	347	353

INSTRUCTIONS FOR USE

HbC M

Anti-HBc IgM

Samples with evidence of hepatitis A virus infection (HAV) or hepatitis C virus infection (HCV) were identified in a population of 315 samples prospectively collected from subjects in an area in India with a high prevalence of viral hepatitis (Population II). The tables below compare VITROS Anti-HBc IgM results with reference anti-HBc IgM results according to the HBV disease classifications assigned to the study subjects.

HBV Disease Classification	Reference Anti-HBc IgM Result				Total
	Reactive		Negative		
	VITROS Anti-HBc IgM Result		VITROS Anti-HBc IgM Result		
	Reactive	Negative	Reactive	Negative	
Acute	3	8	0	7	18
Chronic	0	0	0	1	1
Early Recovery	0	0	0	0	0
Recovery	0	0	0	0	0
Recovered	0	0	0	0	0
HBV Vaccine Response	0	0	0	3	3
Not Previously Infected with HBV	0	0	0	6	6
Uninterpretable	0	0	0	1	1
Overall	3	8	0	18	29

HBV Disease Classification	Reference Anti-HBc IgM Result				Total
	Reactive		Negative		
	VITROS Anti-HBc IgM Result		VITROS Anti-HBc IgM Result		
	Reactive	Negative	Reactive	Negative	
Acute	45	13	0	0	58
Chronic	0	0	0	32	32
Early Recovery	0	0	0	0	0
Recovery	0	0	0	0	0
Recovered	0	0	0	0	0
HBV Vaccine Response	0	0	0	0	0
Not Previously Infected with HBV	0	0	0	0	0
Uninterpretable	0	0	0	0	0
Overall	45	13	0	32	90

HbC M

INSTRUCTIONS FOR USE

Anti-HBc IgM

The specificity of the VITROS Anti-HBc IgM assay was evaluated by testing 244 samples from 16 potentially cross-reacting sub-groups. Patient samples from the following sub-groups were tested: HAV, HEV, non-viral liver disease, autoimmune disease (rheumatoid arthritis and systemic lupus erythematosus), CMV, EBV, HSV, parvovirus B19 infection, rubella, syphilis, toxoplasmosis, HIV 1/2 antibody positive, HTLV 1/2 antibody positive, and heterophilic antibodies and anti-HBc positive/ anti-HBc IgM negative.

Of the 244 samples tested, 244 were observed to be negative.

Summary of Specificity Data from Cross-Reacting Sub-Groups				
Sample Category	No. Samples Tested	VITROS	VITROS	VITROS
		Negative	Initial Reactive	Repeat Reactive
Hepatitis A Infection	20	20	0	0
HEV Infection	10	10	0	0
Nonviral Liver Disease	50	50	0	0
Autoimmune Diseases (Rheumatoid arthritis)	50	50	0	0
Autoimmune Diseases (Lupus Erythematosus)	10	10	0	0
CMV IgM Positive	10	10	0	0
EBV IgG Positive	10	10	0	0
HSV IgM Positive	9	9	0	0
Parvovirus B19 Infection	10	10	0	0
Rubella Infection	10	10	0	0
Syphilis Infection	10	10	0	0
Toxoplasmosis Infection	10	10	0	0
HIV ½ Ab Positive	10	10	0	0
HTLV ½ Ab Positive	10	10	0	0
Heterophilic Antibodies	5	5	0	0
anti-HBc Positive/anti-HBc IgM negative	10	10	0	0

A total of 20 cord blood patient samples were tested in the VITROS Anti-HBc IgM assay.

In testing the cord blood samples, 0 out of 20 samples were found to give a repeatedly reactive result in the VITROS Anti-HBc IgM assay.

Summary of VITROS Anti-HBc IgM Specificity Data from Cross-Reacting Sub-Groups				
Sample Category	No. Samples Tested	No. Negative	No. Initially Reactive	No. Repeatedly Reactive
	Cord Blood	20	20	0

Substances that do not Interfere

The potentially interfering effects of hemoglobin, bilirubin and triolein were evaluated using samples from 10 blood donors. The results (mean of test results at each level of interferent) demonstrate that hemoglobin (up to 500 mg/dL), bilirubin (up to 20 mg/dL) and triolein (up to 3000 mg/dL), cause no misclassification of results. Anti-HBc IgM spiked samples were tested near the cut-off (cut-off s/c ≥ 1.00), and were observed to remain reactive at all levels tested with each potential interferent. Similarly no interference was observed in samples not spiked with anti-HBc IgM (Negative), with anti-HBc IgM values remaining < 1.00 s/c.

Test Substance	Maximum Level Tested	Mean Result at 0 Interferent Level		Mean Result at Maximum Interferent Level	
		s/c	Classification	s/c	Classification
Hemoglobin					
anti-HBc IgM Spiked Specimen	500 mg/dL	1.40	Reactive	1.39	Reactive
anti-HBc IgM Negative Specimen	500 mg/dL	0.03	Negative	0.03	Negative
Bilirubin					
anti-HBc IgM Spiked Specimen	20 mg/dL	1.58	Reactive	1.58	Reactive
anti-HBc IgM Negative Specimen	20 mg/dL	0.03	Negative	0.02	Negative
Triolein					
anti-HBc IgM Spiked Specimen	3000 mg/dL	1.55	Reactive	1.58	Reactive
anti-HBc IgM Negative Specimen	3000 mg/dL	0.02	Negative	0.02	Negative

HBc M

INSTRUCTIONS FOR USE

Anti-HBc IgM

Precision

Precision was evaluated on a different VITROS ECI Immunodiagnostic System at three external sites, using one reagent pack and calibrator kit lot. At least two replicates each of a three member panel were assayed on a single occasion per day on 20 different days. The data shown in the table were rounded following all calculations.

Clinical Site	Mean VITROS aHBc IgM S/C (Ratio)	Within day *		Between day**		Total †		No. Obs.	No. Days
		SD	CV (%)	SD	CV (%)	SD	CV (%)		
Site 1	0.01	0.001	11.0	0.001	10.5	0.001	15.2	40	20
	1.95	0.021	1.1	0.033	1.7	0.039	2.0	40	20
	0.98	0.021	2.2	0.012	1.3	0.025	2.5	40	20
Site 2	0.01	0.001	16.1	0.000	0.0	0.001	16.1	40	20
	1.89	0.023	1.2	0.047	2.5	0.052	2.8	40	20
	0.96	0.014	1.4	0.025	2.6	0.028	2.9	40	20
Site 3	0.01	0.001	8.6	0.000	6.0	0.001	10.5	40	20
	1.95	0.021	1.1	0.032	1.6	0.038	2.0	40	20
	0.97	0.015	1.6	0.017	1.8	0.023	2.4	40	20

* Within Day: Variability of the assay performance from replicate to replicate.

** Between Day: Variability of the assay performance from day to day.

† Total: Variability of the assay performance combining the effects of within day and between day

Precision was further evaluated incorporating between site and between lot variation. The study was performed at three external sites using three reagent lots. At least three replicates each of a four member panel were assayed on a single occasion per day on six different days. The between site, between lot, and total precision estimates (CV (%)) were derived from a variance component analysis. The data shown in the table were rounded following all calculations.

Mean VITROS Anti-HBc IgM S/C (Ratio)	Between Site *		Between Lot**		Total †		No. Obs.
	SD	CV (%)	SD	CV (%)	SD	CV (%)	
2.49	0.076	3.0	0.097	3.9	0.135	5.4	162
1.06	0.031	3.0	0.025	2.3	0.047	4.5	162
0.97	0.027	2.8	0.016	1.7	0.040	4.1	162
0.23	0.008	3.4	0.008	3.8	0.013	5.7	162

* Between site: Variability of the assay performance from site to site.

** Between lot: Variability of the assay performance from lot to lot, calculated using data across all sites.

† Total: Variability of the assay incorporating factors of site, lot and day.

Warning: Assay reproducibility has not been established when using a plasma matrix. It is recommended when using other matrices, the user establish reproducibility by performing the appropriate reproducibility studies.

INSTRUCTIONS FOR USE**HbC M**

Anti-HbC IgM

References

1. Gerlich WH et al. Cutoff Levels of Immunoglobulin M Antibody Against Viral Core Antigen for Differentiation of Acute, Chronic, and Past Hepatitis B Virus Infections. *J Clin Micro.* 24: 288-293 (1986).
2. Lemon S. What is the Role of Testing for IgM Antibody to Core Antigen of the Hepatitis B Virus. *Mayo Clinic Proceedings* 63: 201-204 (1988).
3. Gerlich WH & Luer W. Selective Detection of IgM Antibody Against Core Antigen of the Hepatitis B Virus by a Modified Enzyme Immune Assay. *J Med Virol* 4: 227-238 (1979).
4. Summers M et al. Luminogenic Reagent Using 3-Chloro 4-Hydroxy Acetanilide to Enhance Peroxidase/Luminol Chemiluminescence. *Clin Chem.* 41:S73; 1995.
5. CDC-NIH. *Biosafety in Microbiological and Biomedical Laboratories – 3rd Edition.* HHS Publication No (CDC) 93–8395. US Government Printing Office, Washington D.C., 1993.
6. NCCLS. *Protection of Laboratory Workers from Instrument Biohazards and Infectious Disease Transmitted by Blood, Body Fluids, and Tissue: Approved Guideline.* NCCLS document M29-A (ISBN 1-56238-339-6). NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087, 1997.
7. European 'Dangerous Preparations Directive (1999/45/EC)'.
8. Calam RR. Specimen Processing Separator Gels: An Update. *J Clin Immunoassay.* 11:86–90; 1988.
9. NCCLS. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture – Third Edition; Approved Standard.* NCCLS document H3-A3 (ISBN 1-56238-108-3). NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087, 1991.
10. 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, 1999
11. NCCLS. *Internal Quality Control: Principles and Definitions; Approved Guideline.* NCCLS document C24-A (ISBN 1-56238-112-1). NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087, 1991.
12. NCCLS. *Internal Quality Control Testing for Quantitative Measurements: Principles and Definitions: Approved Guidelines-Second Edition.* NCCLS document C24-A2 (ISBN 1-56238-371-X), NCCLS, 940 West Valley Road, Suite 1400. Wayne, Pennsylvania 19087, 1999.
13. Levinson SS. The Nature of Heterophilic Antibodies and Their Role in Immunoassay Interference, *J Clin Immunoassay* 15: 108-115 (1992).

HbC M

INSTRUCTIONS FOR USE

Anti-HbC IgM

Revision History

Date of Revision:	Version:	Description:
2004-02-06	1.0	Initial version of Instructions for Use

When this Instructions For Use is replaced, sign and date below and retain as specified by local regulations or laboratory policies, as appropriate.

Signature

Obsolete Date

Glossary of Symbols

	Use by Expiration date (Year-Month-Day)		Authorized representative
	Lot number		Contains sufficient tests for "n" tests
	Serial Number	$\Sigma = 'n' \text{ tests}$	
	Catalog number		<i>In Vitro</i> diagnostic medical device
	Attention: see instructions for use.		Temperature limitation/ Store between
	Manufacturer		Consult instructions for use
			Irritant
			Manufacturer follows packaging management procedures

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**Anti-HBc IgM
Calibrator**



PIGEMC216/100.0

Vitros Immunodiagnostic Products
Anti-HBc IgM Calibrator



PIGEMC216/100.0

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

Intended Use

For use in the calibration of the Vitros ECI Immunodiagnostic System when used for the *in vitro* qualitative detection of IgM antibody to hepatitis B virus core antigen (anti-HBc IgM) in human adult and pediatric serum and plasma (EDTA, heparin or citrate) and neonate serum using Vitros Anti-HBc IgM Reagent Packs.

The Vitros Anti-HBc IgM Calibrator has been validated for use only on the Vitros System with the Vitros Immunodiagnostic Products Anti-HBc IgM Reagent Packs. Refer to the Vitros Anti-HBc IgM Reagent Pack instructions for use for further details.

Principles of Procedure

Calibration is lot specific; reagent packs and calibrators are linked by lot number. A Master Calibration is established for each new reagent lot by performing multiple assays. This is the process by which a lot-specific parameter (a) which links the cut-off value to the calibrator signal is determined.

Cut-off value = (a x Signal of CAL1)

The lot-specific parameter, the expected calibrator signal and the data which enables a System to calculate the cut-off value, are encoded on the lot calibration card.

Scanning the lot calibration card loads the encoded data onto the System. When the calibrator is processed the validity of the calibration is assessed against a quality parameter which compares the actual signal of the calibrator with the expected signal. If the calibration is acceptable the cut-off value is calculated and stored for use with any reagent pack of that lot. The quality of calibration cannot be completely described by a single parameter. The calibration report should be used in conjunction with control values to determine the validity of the calibration. Recalibration is required after a pre-determined calibration interval (refer to the *Vitros Anti-HBc IgM Reagent Pack* calibration instructions), or when a different reagent lot is loaded.

Warnings and Precautions

For *In Vitro* Diagnostic Use Only

Warning - Potentially Infectious Material

- Treat as if capable of transmitting infection.
- Handling of samples and assay components, their use, storage, and solid and liquid waste disposal should be done at a biological safety level 2 and be in accordance with the procedures defined by the appropriate national biohazard safety guideline or regulation (e.g. NCCLS Guideline M29¹²).

The *Vitros* Anti-HBc IgM Calibrator contains human anti-HBc IgM positive plasma from donors who were tested individually and found to be negative for antibodies to human immunodeficiency virus (HIV 1+2) and hepatitis C virus (HCV) using FDA approved methods (enzyme immunoassays, EIA). The anti-HBc IgM positive plasma has been treated in order to reduce the titer of potentially infectious virus. However, as no testing method can rule out the risk of potential infection, handle as if capable of transmitting infection.

Care should be taken when handling material of human origin. All samples should be considered potentially infectious. No test method can offer complete assurance that hepatitis B virus, HCV, HIV 1+2 or other infectious agents are absent.

Warning - Contains Kathon

The *Vitros* Anti-HBc IgM Calibrator contains Kathon. R43: May cause sensitisation by skin contact. R52/53: Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment. S24: Avoid contact with skin. S37: Wear suitable gloves.

Materials Provided

- 1 *Vitros* Anti-HBc IgM calibrator (0.8 mL, anti-HBc IgM positive human plasma; 54.0 ± 21.6 PEI Units*/mL) in buffer with antimicrobial agent, kathon 2.0%.
- Lot calibration card.
- Protocol card.
- 8 calibrator bar code labels.

Note: Contains bovine serum albumin.

*Paul-Ehrlich-Institute Anti-HBc IgM reference preparation.

Reagent Preparation and Storage

The *Vitros* Anti-HBc IgM Calibrator is supplied ready for use. Store unopened at 2-8 °C (36-46 °F). Do not use beyond the expiration date. After opening store for up to 13 weeks at 2-8 °C (36-46 °F) or 13 weeks at -20 °C (-4 °F) (with no more than 1 freeze-thaw cycle).

Quality Control and Procedural Notes

- Use only with reagent packs of the same lot number. Mix thoroughly by inversion and bring to 15-30 °C (59-86 °F) before use. Each pack contains sufficient volume for a minimum of 6 calibration events.
- The *Vitros* Anti-HBc IgM Calibrator is automatically processed in duplicate.
- Handle calibrators in stoppered containers to avoid contamination and evaporation. To avoid evaporation, limit the amount of time calibrators are on board the *Vitros* System. Refer to the *Vitros* System Operator's Guide for further information. Return to 2-8 °C (36-46 °F) as soon as possible after use, or load only sufficient amounts for a single use. The calibrator may be aliquoted into alternative containers, which may be bar coded with the labels provided.

Procedure

For further information refer to the *Vitros* Anti-HBc IgM Reagent Pack instructions for use. For detailed instructions on calibration refer to the *Vitros* Immunodiagnostic System Operator's Guide, Chapter 5, Performing Calibration.

References

1. CDC-NIH. *Biosafety in Microbiological and Biomedical Laboratories-3rd Edition*, HHS Publication No. CDO93-8395. U.S. Government Printing Office, Washington, D.C. 1993.
2. NCCLS. *Protection of Laboratory Workers from Instrument Biohazards and Infectious Disease Transmitted by Blood, Body Fluids, and Tissue; Approve Guideline*. NCCLS Document M29-A (ISBN1-56238-339-6). NCCLS 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087, 1997.

Symbols used



Use by/Expiration date (Year-Month-Day)

LOT

Lot Number

SN

Serial number

REF

Catalogue number



Attention, see instructions for use



Manufacturer

EC REP

Authorized representative



Contains sufficient tests for 'n' tests

$\Sigma = 'n'$ tests



In vitro diagnostic medical device



Temperature limitation/Store between



Consult instructions for use



Irritant



Manufacturer follows packaging management procedures

Manufacturer:
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62 The Broadway, Amersham, Bucks., UK

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