

# illumigene® Group B *Streptococcus* (GBS)

## DNA Amplification Assay for the Detection of Group B *Streptococcus* in Vaginal/Rectal Antepartum Specimens

REF 280350

IVD In vitro diagnostic medical device

### INTENDED USE

The *illumigene* Group B *Streptococcus* (GBS) assay, performed on the *illumipro-10*, is a qualitative in vitro diagnostic for the detection of *Streptococcus agalactiae* in enriched cultures obtained from vaginal/rectal swab specimens from antepartum women. Enriched cultures are obtained by 18-24 hour incubation of vaginal/rectal swab specimens in selective broth medium, either Lim Broth or TransVag Broth.

The *illumigene* GBS assay utilizes loop-mediated isothermal DNA amplification (LAMP),<sup>1, 2</sup> technology to detect *Streptococcus agalactiae* by targeting a segment of the *Streptococcus agalactiae* genome. Results from the *illumigene* GBS assay can be used as an aid in establishing the GBS colonization status of antepartum women. This assay does not diagnose or monitor treatment for GBS infections.

The *illumigene* GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

*illumigene* Group B *Streptococcus* is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

### SUMMARY AND EXPLANATION OF THE TEST

The *illumigene* Group B *Streptococcus* (GBS) molecular assay is based on loop-mediated amplification technology, which uses specifically designed primers to *Streptococcus agalactiae* to provide for specific and continuous isothermal DNA amplification. A by-product of this amplification is magnesium pyrophosphate, which forms a white precipitate leading to a turbid reaction solution. The absorbance characteristics of the sample mixture are monitored by the Meridian *illumipro-10* Incubator/Reader. Change in sample absorbance created by precipitation of magnesium pyrophosphate indicates the presence of Group B *Streptococcus* and is reported by the *illumipro-10* as 'Positive'. The absence of target DNA results in no detectable change in sample absorbance and is reported by the *illumipro-10* as 'Negative'.

The *illumigene* GBS assay specifically targets a highly conserved 213 base pair (bp) sequence of the *Streptococcus agalactiae* genome. The target DNA sequence is found in all eight GBS strains for which the *Streptococcus agalactiae* genome sequence information is available and is present in all eleven GBS Serotypes.

The *illumigene* GBS kit includes Control Reagent and Test Devices. The Control Reagent is a buffer solution containing *Staphylococcus aureus* DNA. The *illumigene* GBS Test Device contains one dry reagent lysosphere in each of two chambers: a TEST chamber with GBS-specific primers and a CONTROL chamber with *S. aureus*-specific primers. Together, the *S. aureus* DNA from the Control Reagent and the *S. aureus*-specific primers in the CONTROL chamber lysosphere function as the Internal Control for the assay. Each patient specimen is diluted with the Control Reagent during specimen preparation and prior to amplification. Addition of *S. aureus* DNA to the patient sample allows for parallel processing of target DNA and Control DNA through amplification and detection. The Internal Control monitors amplification inhibition, assay reagent performance and sample processing effectiveness. The Control *S. aureus* target must be amplified and detected in the final reaction or the test is considered invalid and patient results are not reported.

### BIOLOGICAL PRINCIPLES

Invasive Group B Streptococcal Disease emerged in the 1970s as the leading cause of infectious disease in infants.<sup>3</sup> Infants with early on-set infection (< 7 days of age) may show symptoms of respiratory distress, apnea or sepsis. Early on-set is most commonly associated with sepsis and pneumonia, however may lead to meningitis. The fatality rate for infants with early on-set Group B Streptococcal Disease is currently estimated at 4-6%.<sup>4</sup> Surviving infants may experience long-term disabilities including hearing loss, vision loss or mental retardation.<sup>5</sup> The primary risk factor for early-onset Group B Streptococcal Disease is maternal colonization in the genitourinary or gastrointestinal tracts.

Group B *Streptococcus* (*Streptococcus agalactiae* or GBS) is a gram positive bacteria commonly found in the gastrointestinal, genital and urinary tract of healthy adults. Approximately 10-30% of all pregnant women are colonized with GBS in the vagina or rectum. While Group B *Streptococcus* colonized mothers typically show no symptoms or health effects, the bacteria can be passed to their child during labor and delivery.

Group B *Streptococcus* infection of neonates occurs most commonly when *Streptococcus agalactiae* ascends the vagina to amniotic fluid after membrane rupture. Transmission can also occur through intact membranes, by aspiration or by mucous membrane exposure during passage through the birth canal. Intrapartum transmission of Group B *Streptococcus* or early-onset infection can be prevented by administration of antibiotic prophylaxis prior to delivery.<sup>4</sup>

Screening for GBS colonization in antepartum women between 35 and 37 weeks' gestation, followed by intrapartum antibiotic treatment for women with positive colonization status has proven to be an effective mechanism for prevention of perinatal Group B Streptococcal disease. As colonization may be transient, intermittent or persistent throughout pregnancy, screening is most effective when performed when specimens are collected no more than five weeks (35 – 37 weeks gestation) prior to delivery and after enrichment with selective broth medium.

### REAGENTS/MATERIALS PROVIDED

The maximum number of tests obtained from this test kit is listed on the outer box.

- illumigene* Control Reagent:** Tris-buffered solution containing non-infectious Plasmid DNA (*S. aureus* insert) with sodium azide (0.09%) as a preservative.
- illumigene* Reaction Buffer:** Tris-buffered solution containing sodium azide (0.09%) as a preservative.
- illumigene* GBS Test Device:** Two separate chambers containing dry reagent lysospheres comprised of DNA polymerase, Deoxyribonucleoside Triphosphate Solution (dNTPs), and either GBS-specific primers (TEST Chamber) or *S. aureus* primers (CONTROL Chamber).
- illumigene* Heat Treatment Tubes**

### MATERIALS PROVIDED SEPARATELY

*illumigene* GBS External Control Kit, Catalog Number: 279900

### MATERIALS NOT PROVIDED

- Disposable latex gloves, powder free
- DNase/RNase-free, aerosol resistant pipette tips
- Vaginal/Rectal Swabs: Rayon, Cotton, Dacron/polyester, Flocked nylon, Foam, Liquid Amies Swab, Modified Stuarts Swab. Use of alternate swab material has not been validated with the *illumigene* GBS Assay.
- Enrichment broth:
  - Lim Broth [Todd Hewitt Broth supplemented with colistin (10 µg/mL) and nalidixic acid (15 µg/mL)] OR
  - TransVag Broth [Todd Hewitt Broth supplemented with gentamicin (8 µg/mL) and nalidixic acid (15 µg/mL)]

### EQUIPMENT NOT PROVIDED

- Dry-bath with 12 mm heat block capable of 95 C
- Digital thermometer with Max/Min Temperature Memory (eg, Traceable® Lollipop™ Waterproof/Shockproof Thermometer)
- Vortex mixer
- Interval timer
- Micropipette capable of dispensing 50 µL
- Micropipette capable of dispensing 200 µL
- illumipro-10*™, Meridian Bioscience, Inc. Catalog Number: 610172

### PRECAUTIONS

- All reagents are for in vitro diagnostic use only.
- Do not interchange Control Reagents or Test Devices between lots. Reaction Buffer and Heat Treatment Tubes are interchangeable provided they are within assigned expiration dates when used.
- Follow Biosafety Level 2 and Good Laboratory practices during testing.<sup>6</sup> Treat all specimens and used Test Devices as capable of transmitting infectious agents. Do not eat, drink or smoke in areas where specimens or kit reagents are handled.
- Wear disposable gloves while handling specimens and thoroughly wash hands afterwards.
- Quality Control Programs for Molecular Testing Laboratories should be employed.<sup>7</sup>
- The *illumigene* GBS Test Device contains lyophilized reagents. The protective pouch should not be opened until ready to perform the assay.
- The *illumigene* GBS Test Device includes a latch feature that is designed to prevent contamination of the test area with amplification product. Do NOT use Test Devices with broken latches.
- Dispose of used *illumigene* Test Devices immediately after processing, leaving the device latch securely in place. Do NOT open the Test Device after processing. Opening the device after amplification may result in contamination of the test area with amplification product.

### SHELF LIFE AND STORAGE

The expiration date is indicated on the kit label. Store the kit at 2-27 C.

### SPECIMEN COLLECTION AND PREPARATION

**Sample type:** Vaginal/rectal swabs taken from antepartum women.

**Sample Collection:** Vaginal and rectal sample collection should be performed in accordance with published guidelines for collection of clinical specimens for culture of Group B *Streptococcus*.<sup>4</sup> Vaginal and rectal specimens may be collected using the same swab or two different swabs. Cervical, perianal, perirectal or perineal specimens are not acceptable sample types. A speculum should not be used for sample collection.

Place swab(s) in a non-nutritive transport medium (eg, Stuart's or Amies without charcoal) and transported to the laboratory. In the event that two different swabs are used for sample collection, a single transport device may be used.

**Sample Enrichment:** Remove vaginal/rectal swab(s) from transport device and place in culture enrichment broth (Lim Broth or TransVag Broth). Incubate sample(s) in culture enrichment broth at 37 ± 2 C for 18-24 hours.

Enriched samples should be tested as soon as possible. Enriched samples may be held at room temperature for up to six hours prior to testing. When testing will not be initiated within this time, the enriched sample may be stored at 2-8 C for up to seven days. Long-term storage of enriched samples may yield invalid results.

## REAGENT PREPARATION

Ensure kit reagents are at room temperature (21-27 C) before use. Incorrect results may be obtained if reagents are not brought to room temperature prior to use.

## SPECIMEN PREPARATION

**NOTE:** Ensure that the *illumipro-10* is powered on and required performance verifications have been completed prior to initiation of SPECIMEN PREPARATION. Refer to the *illumipro-10* Operator's Manual for further information regarding instrument set-up and operation.

1. Label 1 Heat Treatment Tube for each sample to be tested.
2. Add 200 µL of the *illumigene* Control Reagent to each heat treatment tube.
3. Mix each enriched broth culture thoroughly.
4. Add 50 µL of the mixed, enriched broth liquid to the *illumigene* Control Reagent. Specimens diluted in *illumigene* Control Reagent may be held at room temperature (21-27 C) for up to 15 minutes prior to proceeding. Incorrect results may be obtained if diluted specimens are held longer than 15 minutes before heat treatment.
5. Vortex each Sample/Control mixture for a minimum of 10 seconds.
6. Heat each Sample/Control mixture in a dry-bath/heat block at 95 ± 5 C for 10 ± 2 minutes. Monitor heat-treatment step with digital thermometer and interval timer.
7. Remove each Heat Treatment Tube from the dry-bath/heat block and vortex for approximately 10 seconds. Heat-treated samples may be held at 19-29 C for up to 45 minutes prior to addition to Reaction Buffer. Heat-treated samples may not be frozen.

## TEST PROCEDURE

**NOTE:** A maximum of 10 samples can be processed in a single *illumipro-10* run.

1. Transfer 50 µL of heat-treated sample to an appropriately labeled *illumigene* Reaction Buffer tube.
2. Vortex the Reaction Buffer tube containing heat-treated sample for approximately 10 seconds.
3. Repeat steps 1 and 2 for all the samples to be analyzed before proceeding.
4. Remove 1 *illumigene* GBS Test Device from its protective pouch per sample. Carefully open the device, holding the chambers such that the lyophilized reagent will not fall out upon opening. Place device on a flat surface or in a rack that can accommodate the device.
5. Using a new pipette tip, transfer 50 µL from the Reaction Buffer tube containing heat-treated sample to the TEST chamber (White Bead) of the *illumigene* Test Device. Do not introduce air bubbles. Using a new pipette tip, transfer 50 µL from the Reaction Buffer tube containing heat-treated sample to the CONTROL chamber (Yellow Bead) of the *illumigene* Test Device. Do not introduce air bubbles. Close the *illumigene* Test Device and fasten the latch securely.
6. Tap device on the bench top or mix to remove air bubbles. Carefully examine the test device to ensure that there are no air bubbles left in the tube and no liquid remaining in the top of the device.
7. Insert the *illumigene* Test Device into the *illumipro-10* and initiate amplification reaction and detection. Results will be displayed at the conclusion of the run.

## INTERPRETATION OF RESULTS

Sample ID	Reported Result	Interpretation
Patient Specimen	POSITIVE	Sample contains <i>Streptococcus agalactiae</i> target DNA.
	NEGATIVE	No <i>Streptococcus agalactiae</i> DNA detected.
	INVALID	<b>No reportable result. Repeat the test using the original enriched broth sample.</b> Inhibitory patient specimen, improper sample preparation, reagent failure, instrument failure or internal control failure.
Positive Control	POSITIVE	Valid positive control result. Reagents active at time of use, <i>illumipro-10</i> performing correctly.
	NEGATIVE	<b>Incorrect control result.</b> Repeat control testing as the first step in determining the root cause of the failure. If control failures are repeated please contact Meridian's Technical Services at 1-800-343-3858 (US) or your local distributor.
	INVALID	<b>No reportable result. Repeat entire assay run using original samples.</b> Improper sample preparation, reagent failure, instrument failure or internal control failure.
Negative Control	POSITIVE	<b>Incorrect control result.</b> Repeat control testing as the first step in determining the root cause of the failure. If control failures are repeated please contact Meridian's Technical Services at 1-800-343-3858 (US) or your local distributor.
	NEGATIVE	Valid negative control result. Reagents active at time of use, <i>illumipro-10</i> performing correctly.
	INVALID	<b>No reportable result. Repeat entire assay run using original samples.</b> Improper sample preparation, reagent failure, instrument failure or internal control failure.
EMPTY WELL	NONE	No <i>illumigene</i> Test Device in the <i>illumipro-10</i> Well. <b>OR</b> The <i>illumigene</i> Test Device present is compromised due to sample preparation failure, dirty device or improperly seated device. <b>Repeat the test using original sample.</b>

## QUALITY CONTROL

**This test should be performed per applicable local, state, or federal regulations or accrediting agencies.**

1. Each device contains an internal control chamber that controls for amplification inhibition, assay reagents and sample processing effectiveness.

2. The heat-treatment step is monitored with an external thermometer and interval timer. Use the max/min temperature memory of the thermometer to ensure that a temperature of 95 ± 5 C is maintained. Use the interval timer to ensure that heat-treatment duration is 10 ± 2 minutes.
3. Good laboratory practice recommends the use of control materials. Users should follow the appropriate federal, state and local guidelines concerning the running of external quality controls.
4. *illumigene* GBS External Control Reagents are supplied separately (Catalog 279900). It is recommended that the reactivity of each new lot and each new shipment of *illumigene* GBS be verified on receipt and before use. External control tests should be performed thereafter in accordance with appropriate federal, state and local guidelines. The *illumigene* GBS test kit should not be used in patient testing if the external controls do not produce the correct results.
5. A separate device must be used for each external control reagent.
6. Heat-treatment of GBS External Positive or Negative Control samples is not required.

## EXPECTED VALUES

Approximately 10-30% of antepartum women are colonized with Group B *Streptococcus* in the vagina or rectum.<sup>4</sup> The overall incidence of GBS colonization in antepartum women tested during this study was 24.3% (201 of 826). Incidence of GBS colonization for enrichment performed using Lim Broth was found to be 25.1% (101 of 403); while incidence for specimens enriched by TransVag Broth was found to be 23.6% (100 of 423).

## LIMITATIONS OF THE PROCEDURE

1. The *illumigene* GBS assay does not distinguish between viable and non-viable organisms.
2. The *illumigene* GBS assay is for use with vaginal/rectal swab specimens collected in accordance with established guidelines for collection of Group B *Streptococcus* culture specimens. Cervical, perianal, perirectal or perineal specimens are not acceptable sample types. A speculum should not be used for sample collection.
3. The *illumigene* GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.
4. GBS colonization during pregnancy can be intermittent, persistent or transient. The clinical utility of GBS screening decreases when testing is performed more than five weeks prior to delivery.
5. Evaluation of non-hemolytic colonies was not performed as part of Clinical Site testing.
6. Crossreactivity with *Enterococcus dispar* was observed during performance characteristic testing. Negative Lim Broth specimens inoculated with *Enterococcus dispar* at a final concentration of 1.2 x 10<sup>8</sup> CFU/mL produced positive results for one of seven replicates tested.

## SPECIFIC PERFORMANCE CHARACTERISTICS

*illumigene* GBS was evaluated in 2011 by four independent clinical test sites located in the Midwestern and Southern regions of the United States. Overall performance information is shown in Table 1.

**Table 1. Overall performance data**

Group B <i>Streptococcus</i> Culture	<i>illumigene</i> Group B <i>Streptococcus</i> (GBS)		
	Positive	Negative	Total
<b>Positive</b>	150	4	154
<b>Negative</b>	51	610	661
<b>Total</b>	201	614	815
			<b>95% CI</b>
<b>Sensitivity</b>	150/154	97.4%	91.9 – 99.0%
<b>Specificity</b>	610/661	92.3%	90.0 – 94.1%
<b>Correlation</b>	760/815	93.3%	91.3 – 94.8%

Forty-eight of the 51 false positive results were positive by another molecular method. Invalid results were obtained for 11/826 samples tested or 1.3%. Two of the 11 samples remained invalid after repeat testing of the original sample.

A total of 826 qualified patient samples were evaluated. Samples were obtained according to established guidelines for collection of clinical specimens for culture of Group B *Streptococcus* and enriched for 18-24 hours in either Lim Broth or TransVag Broth. A total 403 (48.8%) Lim Broth enriched specimens were tested by Clinical Site 2 (210) and Clinical Site 4 (193). A total of 423 (51.2%) TransVag Broth enriched specimens were tested by Clinical Site 1 (234) and Clinical Site 3 (189). The age groups of patients tested ranged from 15 years of age to 44 years of age, with age unknown for 3 (0.4%) of the patient population. No differences in test performance were observed based on enrichment medium or patient age. Table 2 shows assay performance by enrichment medium; Table 3 summarizes assay performance by Clinical Site.

**Table 2. Performance characteristics by enrichment method**

	Positive Samples			Negative Samples		
	<i>illumigene</i> / GBS Culture	Sensitivity %	95% CI	<i>illumigene</i> / GBS Culture	Specificity %	95% CI
<b>Total</b>	150/154	97.4%	91.9 – 99.0%	610/661	92.3%	90.0 – 94.1%
Lim Broth	82/84	97.6%	91.7 – 99.3%	296/315	94.0%	90.8 – 96.1%
TransVag Broth	68/70	97.1%	90.2 – 99.2%	314/346	90.8%	87.2 – 93.4%

**Table 3. Performance characteristics by clinical site**

Site	Positive Samples			Negative Samples		
	<i>illumigene</i> / GBS Culture	Sensitivity %	95% CI	<i>illumigene</i> / GBS Culture	Specificity %	95% CI
Total	150/154	97.4%	91.9 – 99.0%	610/661	92.3%	90.0 – 94.1%
Site 1	32/33	97.0%	84.7 – 99.5%	197/199	99.0%	96.4 – 99.7%
Site 2	38/39	97.4%	86.8 – 99.5%	162/168	96.4%	92.4 – 98.4%
Site 3	36/37	97.3%	86.2 – 99.5%	117/147	79.6%	72.4 – 85.3%
Site 4	44/45	97.8%	88.4 – 99.6%	134/147	97.8%	85.5 – 94.8%

**ANALYTICAL SENSITIVITY**

The analytical sensitivity or Limit of Detect for the *illumigene* Group B *Streptococcus* (GBS) assay was determined for all common *S. agalactiae* strains and serotypes.

Limit of Detect was determined following Lim Broth enrichment, using a minimum of 20 replicates for each measurand and a stated probability (eg. 95% where 19/20 replicates are positive) of obtaining positive responses. Analytical sensitivity testing is summarized below:

Serotype	<i>Streptococcus agalactiae</i> Strain Description	CFU/Test
Ia	NCTC 11248	60
Ib	ATCC 12401	80
Ic	NCTC 11253	640
II	II/2	320
III	ATCC 12403	160
V	ATCC BAA-611	1280

**ASSAY REACTIVITY**

The following *S. agalactiae* strains were tested and produced positive reactions at 1280 CFU/test with *illumigene* GBS: NCTC 11930 (Serotype IV), NCTC 08188 (Serotype VIa), VII/2 (Serotype VII), VIII/2 (Serotype VIII), NCTC 11249 (Serotype X); ATCC 13813 and ATCC 12386.

**REPRODUCIBILITY**

Blind coded panels of 10 samples were supplied to three independent laboratories for reproducibility studies. Samples were randomly sorted within each panel to mask sample identities. The panels included contrived samples manufactured as low positive samples (ie. near the assay limit of detection, n = 3) and high negative samples, (n = 3). The panels also included contrived positive (n = 3) samples and natural negative samples (n = 1). Testing was performed by different operators at each site on the same day (intra-assay variability) for five days (inter-assay variability). Three lots of *illumigene* GBS and five *illumipro-10* instruments were used in this study. Positive and Negative Controls were tested each day of testing. The results are given in the table below:

Sample Type	Clinical Site 1		Clinical Site 2		Clinical Site 4		Total	
	Percent agreement	Percent agreement	Percent agreement	Percent agreement	Percent agreement	Percent agreement	Percent agreement	Percent agreement
Negative	10/10	100%	10/10	100%	10/10	100%	10/10	100%
High Negative	30/30	100%	30/30	100%	30/30	100%	30/30	100%
Low Positive	30/30	100%	30/30	100%	30/30	100%	30/30	100%
Positive	30/30	100%	30/30	100%	30/30	100%	30/30	100%
Negative Control	10/10	100%	10/10	100%	10/10	100%	10/10	100%
Positive Control	10/10	100%	10/10	100%	10/10	100%	10/10	100%

**CROSSREACTIVITY STUDIES**

Crossreactivity studies were performed with positive and negative Lim Broth specimens inoculated with bacterial or fungal organisms to a final concentration of 1.2 x 10<sup>8</sup> CFU/mL or virus at a minimum of 1 x 10<sup>5</sup> TCID<sub>50</sub>/mL. Crossreactivity with *Enterococcus dispar* was observed in one of seven replicates tested. None of the following organisms reacted with *illumigene* GBS:

*Aeromonas hydrophila*, *Alcaligenes faecalis*, *Bacillus cereus*, *Bacillus subtilis*, *Bacteroides fragilis*, *Campylobacter coli*, *Campylobacter fetus*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida parapsilosis*, *Candida tropicalis*, *Citrobacter freundii*, *Clostridium bifermentans*, *Clostridium butyricum*, *Clostridium difficile*, *Clostridium histolyticum*, *Clostridium novyi*, *Clostridium perfringens*, *Clostridium septicum*, *Clostridium sordellii*, *Clostridium sporogenes*, *Clostridium tetani*, *Corynebacterium genitalium*, *Corynebacterium urealyticum*, *Corynebacterium xerosis*, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Enterococcus avium*, *Enterococcus durans*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Escherichia coli* O157:H7, *Escherichia fergusonii*, *Escherichia hermannii*, *Gardnerella vaginalis*, *Haemophilus ducreyi*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Lactobacillus acidophilus*, *Lactobacillus brevis*, *Lactobacillus casei*, *Lactobacillus delbruekii* subspecies *lactis*, *Lactobacillus jensenii*, *Lactococcus lactis*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella osloensis*, *Morganella morganii*, *Neisseria gonorrhoeae*, *Peptostreptococcus anaerobius*, *Plesiomonas shigelloides*, *Porphyromonas asaccharolytica*, *Prevotella melaninogenica*, *Propionibacterium acnes*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Salmonella* Group B, *Salmonella* Group C, *Salmonella* Group D, *Salmonella* Group E, *Serratia liquefaciens*, *Serratia marcescens*, *Shigella boydii*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus aureus* (Cowan), *Staphylococcus epidermidis*, *Staphylococcus saprophyticus*, *Streptococcus anginosus*, *Streptococcus bovis*, *Streptococcus dysgalactiae* equisimilis, *Streptococcus intermedius*, *Streptococcus mitis*, *Streptococcus oralis*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus salivarius*, *Streptococcus sanguinis*, *Vibrio parahaemolyticus*, *Yersinia enterocolitica*, Adenovirus 40, Adenovirus 41, BK virus, Coxsackievirus, Echovirus, Epstein Barr virus, Herpes simplex virus-1, Herpes simplex virus-2, Rotavirus.

*Mycoplasma genitalium*, *Mycoplasma hominis* and *Ureaplasma urealyticum* were tested at final concentrations ranging between 1.6 x 10<sup>5</sup> and 9.9 x 10<sup>6</sup> CFU/mL with no reaction with the *illumigene* GBS assay.

**TESTS FOR INTERFERING SUBSTANCES**

The following substances, at the specified saturated solvent/diluent concentrations, do not interfere with test results: Amniotic fluid (10% v/v), Human DNA (100 ng/Test), Urine (30% v/v), Whole Blood (2.5% v/v). Whole Blood at concentrations greater than 2.5% v/v interferes with the *illumigene* GBS assay.

Additional testing was performed by coating cotton swabs with potentially interfering substances. Coated swabs were combined with Lim Broth sample and processed through the *illumigene* GBS assay. The following substances do not interfere with test results: Meconium, Stool, Hemorrhoidal cream (30.65 mg/100 mg), Miconazole (fungicide), Mucin (0.5-1.5%), Spermicidal gel (nonoxynol 9) (4 mg/100 mg). Lubricating gel produced False Negative Results in one of 11 replicates tested. Body Powder produced False Negative Results in one of 10 replicates tested.

**REFERENCES**

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## INTERNATIONAL SYMBOL USAGE

You may see one or more of these symbols on the labeling/packaging of this product:

**Key guide to symbols (Guida ai simboli, Guide des symbols, Guia de simbolos, Erläuterung der gaphischen symbole)**

	Use By / Utilizzare entro / Utiliser jusque / Fecha de caducidad / Verwenden bis	<b>CONTROL +</b>	Positive control / Controllo positivo / Contrôle positif / Control positivo / Positive Kontrolle
<b>LOT</b>	Batch Code / Codice del lotto / Code du lot / Código de lote / Chargenbezeichnung	<b>CONTROL -</b>	Negative control / Controllo negativo / Contrôle négatif / Control negativo / Negative Kontrolle
<b>IVD</b>	In vitro diagnostic medical device / Dispositivo medico-diagnostico in vitro / Dispositif médical de diagnostic in vitro / Dispositivo médico para diagnóstico in vitro / In-Vitro-Diagnostikum	<b>EC REP</b>	Authorized Representative in the European Community / Rappresentante Autorizzato nella Comunità Europea / Mandataire dans la Communauté européenne / Representante autorizado en la Comunidad Europea / Bevollmächtigter in der Europäischen Gemeinschaft
	This product fulfills the requirements of Directive 98/79/EC on in vitro diagnostic medical devices / Questo prodotto soddisfa i requisiti della Direttiva 98/79/CE sui dispositivi medico-diagnostici in vitro / Ce produit répond aux exigences de la Directive 98/79 CE relative aux dispositifs médicaux de diagnostic in vitro / Este producto cumple con las exigencias de la Directiva 98/79/CE sobre los productos sanitarios para diagnóstico in vitro / Dieses Produkt entspricht den Anforderungen der Richtlinie über In Vitro Diagnostica 98/79/EG.	<b>SMP PREP DIL SPE</b>	Sample Preparation Apparatus containing Sample Diluent / Dispositivo per la preparazione del campione contenente il diluente del campione / Système pour la préparation de l'échantillon, diluant inclus / Aparato para Preparación de Muestra con Diluyente de Muestra / System zur Probenvorbereitung, in dem sich Probenverdünnungspuffer befindet
<b>REF</b>	Catalogue number / Numero di catalogo / Référence du catalogue / Número de catálogo / Bestellnummer		Do not freeze / Non congelare / Ne pas congeler / No congelar / Nicht Einfrieren
	Consult Instructions for Use / Consultare le istruzioni per l'uso / Consulter les instructions d'utilisation / Consulte las instrucciones de uso / Gebrauchsanweisung beachten	<b>RoHS</b>	Restriction of Hazardous Substances / Restrizione all'uso di sostanze pericolose / Limitation de substances dangereuses / Restricción de Substancias Peligrosas / Beschränkung der Verwendung bestimmter gefährlicher Stoffe
	Manufacturer / Fabricante / Fabricant / Fabricante / Hersteller		Caution, consult accompanying documents / Attenzione, vedere le istruzioni per l'uso / Attention voir notice d'instructions / Atención, ver instrucciones de uso / Achtung, Begleitdokumente beachten
	Contains sufficient for <n> tests / Contenuto sufficiente per "n" saggi / Contenu suffisant pour "n" tests / Contenido suficiente para <n> ensayos / Inhalt ausreichend für <n> Prüfungen	<b>BUF RXN</b>	Reaction Buffer / Tampone di reazione / Solution de réaction tamponnée / Tampón de Reacción / Reaktionspuffer
	Temperature limitation / Limiti di temperatura / Limites de température / Limite de temperatura / Temperaturbegrenzung		ETL Registered Mark Certified / Marchio di certificazione registrato a livello nazionale / Certifié Conforme ETL / Marca de Certificación Registrada Nacional / ETL Konform begluebt
<b>SN</b>	Serial number / Numero di serie / Numéro de série / Número de serie / Seriennummer		Recycle - do not dispose of as general waste / Riciclare - non eliminare come rifiuto generico / Recycler - ne pas jeter dans une poubelle / Recycle - no desecho como basura general / Recycle - dieses Produkt nicht über den Hausmüll entsorgen
<b>TEST</b>	Test Device / Dispositivo test / Dispositif de test / Dispositivo de Prueba / Testgerät	<b>HT TUBE</b>	Heat Treatment Tube / Provetta per il trattamento termico / Tube pour le traitement thermique / Tubo de tratamiento de calor / Röhren zur Hitzebearbeitung
	Date of manufacture / Data di fabbricazione / Date de fabrication / Fecha de fabricación / Herstellungsdatum		For IVD Performance Evaluation Only / Solamente per valutazione delle prestazioni / Réservez IVD reserves à l'évaluation des performances / Sólo para evaluación del funcionamiento / Nur zur IVD Leistungsbewertung
	LASER RADIATION: Avoid Exposure to Beam / RADIACIONE LASER: Evitare l'esposizione al raggio / RAYONNEMENT LASER: Eviter toute exposition au faisceau / Radiación Laser: Evite Exposición a los Rayos / LASERSTRABUNG: Direkten Kontakt mit dem Strahl vermeiden		HOT SURFACE: Keep hands Away from Hot Surfaces / Superficie calda: tenere le mani lontane dalle superfici calde / SURFACES CHAUDES: Ne pas toucher les surfaces chaudes / Superficie Caliente: Mantenga las manos alejadas de la superficie caliente / Heiße Oberfläche: Kontakt mit heißen Oberflächen vermeiden
	CAUTION: Laser Radiation / ATTENZIONE: Radiazione Laser / AVERTISSEMENT: Rayonnement Laser / Precaución: Radiación Laser / WARNUNG: Laserstrahlung	<b>IPX-0</b>	CAUTION: Protect from water / ATTENZIONE: Proteggere dall'acqua / AVERTISSEMENT: Protéger de l'humidité / Precaución: Proteja del agua / WARNUNG: Vor Feuchtigkeit schützen
	CAUTION: Risk of Danger / ATTENZIONE: Pericolo / AVERTISSEMENT: Risques de danger / Precaución: Peligroso / WARNUNG: Risikogefahr	<b>CONTROL</b>	Assay Control / Controllo del test / Test de contrôle / Control de Ensayo / Kontrolltest
<b>BUF</b>	Buffer / Soluzione tampone / Solution tamponnée / Tampón / Puffer	<b>REAG</b>	Reagent / Reagente / Réactif / Reactivos / Reagenzien
<b>CONJ</b>	Conjugate / Coniugato / Conjugué / Conjugado / Konjugat	<b>BUF WASH</b>	Wash Buffer / Soluzione di lavaggio / Solution de lavage / Tampón de lavado / Waschpuffer
<b>SUBS</b>	Substrate / Substrato / Substrat / Substrato / Substrat		Warning / Avvertenze / Mise En Garde / Advertencia / Warnhinweise
<b>SOLN STOP</b>	Stopping Solution / Soluzione di Stop / Solution d'arrêt / Solución de parada / Stopplösung	<b>DIL SPE</b>	Specimen Diluent (or Sample Diluent) / Diluente del Campione / Diluant échantillons / Diluyente de muestra / Probenverdünnungspuffer
<b>CONJ ENZ</b>	Enzyme Conjugate / Coniugato enzimatico / Conjugué enzymatique / Conjugado enzimático / Enzymkonjugat	<b>BUF WASH 20X</b>	Wash Buffer Concentration: 20X / Soluzione di lavaggio 20X / Solution de lavage concentrée 20X / Solución tampón de lavado 20X / 20fach konzentriertes Waschkonzentrat

For technical assistance, call Technical Support Services at 800-343-3858 between the hours of 8AM and 6PM, USA Eastern Standard Time. To place an order, call Customer Service Department at 800-543-1980.