

# LABORATORY PROCEDURE

## Directigen™ Meningitis Combo Test

**For the detection of *Haemophilus influenzae* type b, *Streptococcus pneumoniae*, *Escherichia coli* K1, group B *Streptococcus* and *Neisseria meningitidis* groups A, B, C, Y and W135.**

### I. INTENDED USE

The **Directigen™** Meningitis Combo Test is a presumptive latex agglutination test for the direct qualitative detection of antigens to *H. influenzae* type b, *S. pneumoniae*, *N. meningitidis* groups A, B, C, Y or W135 and *Escherichia coli* K1 in cerebrospinal fluid (CSF), serum or urine. The test can also be used for the direct qualitative detection of antigens to group B *Streptococcus* in CSF and serum. In addition, the test kit provides confirmation and serogrouping capabilities from suspected colonies of *H. influenzae* type b, *S. pneumoniae*, group B *Streptococcus*, and *N. meningitidis* groups A / Y, B or C / W135. Visible agglutination occurs when a sample containing any of these bacterial antigens is reacted with its respective antibody-coated latex beads.

### II. SUMMARY AND EXPLANATION

The diagnosis of bacteremia and meningitis, especially in young children, can be difficult. As many as 55% of children are seen by a physician and started on antibiotics before meningitis is detected.<sup>1</sup> Detection of microbial antigens in the CSF is a rapid and helpful method for diagnostic microbiology. It may be the single most important test in cases of partially treated meningitis since Gram stain and culture may be negative. Detection of a specific antigen is a clinically significant finding and a valuable aid when choosing antimicrobial therapy.<sup>2</sup>

*Haemophilus influenzae* type b, *Neisseria meningitidis*, and *Streptococcus pneumoniae* have been reported to be the three causative agents responsible for approximately 84% of cases of bacterial meningitis.<sup>3</sup>

Group B *Streptococcus* and *Escherichia coli* K1 are major bacterial pathogens in the newborn.<sup>4-7</sup> Strains of group B streptococci and *E. coli* K1 frequently colonize in the vagina and/or rectum and may be associated with maternal septicemia and neonatal septicemia, pneumonia and meningitis.<sup>8</sup> The *E. coli* K1 polysaccharide antigen has been shown to be structurally and immunologically similar to *Neisseria meningitidis* group B antigen.<sup>9,10</sup> The **Directigen** *Neisseria meningitidis* group B Latex Reagent does not differentiate the two antigens, but can be useful in the diagnosis of neonatal *E. coli* K1 meningitis. The high morbidity and mortality associated with Group B streptococci and *E. coli* K1 in newborns make rapid, accurate identification of these organisms extremely important.<sup>4</sup>

Immunological methods for detecting characteristic exoantigens of pathogenic microorganisms in patient fluids (CSF, serum, urine) are typically faster than traditional methods such as culture. These techniques include counterimmunoelectrophoresis (CIE) and latex agglutination.<sup>11-14</sup> The latex

agglutination procedure has been found to be more rapid and sensitive than CIE in the detection of purified antigen.<sup>15-17</sup>

### III. PRINCIPLES OF THE PROCEDURE

Specific antibodies are bound to the surface of latex beads. Latex particle aggregation becomes large enough to allow rapid visualization of positive agglutination in the presence of specific antigens. These specific soluble polysaccharide antigens accumulate in CSF, serum or urine as a result of infection by *H. influenzae* type b, *S. pneumoniae*, and *N. meningitidis* groups A, B, C, Y or W135 and *Escherichia coli* K1; and in CSF and/or serum, as a result of infection by group B *Streptococcus*. All of these antigens can be detected with the **Directigen** Meningitis Combo Test Kit.

### IV. REAGENTS

**Directigen** Meningitis Combo Kit:

<b>Reagent 1</b>	(1.0 mL), Anti- <i>H. influenzae</i> type b, Rabbit Polyclonal Antibody-Coated Latex Suspension,
<b>Reagent 2</b>	(1.0 mL), Anti- <i>S. pneumoniae</i> , Rabbit Polyclonal Antibody-Coated Latex Suspension,
<b>Reagent 3</b>	(1.0 mL), Anti-group B <i>Streptococcus</i> , Rabbit Polyclonal Antibody-Coated Latex Suspension,
<b>Reagent 4</b>	(1.0 mL), Anti- <i>N. meningitidis</i> groups C and W135, Rabbit Polyclonal Antibody-Coated Latex Suspension,
<b>Reagent 5</b>	(1.0 mL), Anti- <i>N. meningitidis</i> groups A and Y, Rabbit Polyclonal Antibody-Coated Latex Suspension,
<b>Reagent 6</b>	(1.0 mL), Anti- <i>N. meningitidis</i> group B / <i>E. coli</i> K1, Mouse Monoclonal Antibody-Coated Latex Suspension,
<b>Reagent A</b>	(0.5 mL), Control Latex, Rabbit Immunoglobulin-Coated Latex Suspension,
<b>Reagent B</b>	(0.5 mL), Control Latex, Mouse Immunoglobulin-Coated Latex Suspension, each of the above with 0.2% sodium azide and 0.01% thimerosol (preservatives),
<b>Control +</b>	(9.0 mL), Polyvalent Positive Antigen Control, <i>H. influenzae</i> type b, <i>S. pneumoniae</i> , group B <i>Streptococcus</i> and <i>N. meningitidis</i> groups A, B, C, Y and W135 antigens,
<b>Control -</b>	(9.0 mL), Negative Antigen Control, glycine buffered saline, each of the above with 0.2% sodium azide (preservative),
<b>Specimen Buffer</b>	(8.0 mL), Specimen Buffer Solution, containing EDTA.

**PRECAUTIONS:** For *in vitro* Diagnostic Use.

**WARNING:** Pathogenic microorganisms, including hepatitis virus and Human Immunodeficiency Virus, may be present in clinical specimens. “Standard Precautions”<sup>18-21</sup> and institutional guidelines should be followed in handling all items contaminated with blood and other body fluids. Prior to discarding, sterilize specimen containers and other contaminated materials by autoclaving.

**Reagents:** Do not use beyond the expiration date. Upon removal from refrigeration, allow reagents to warm to room temperature (15 - 30°C) before use.

To assure proper drop delivery, reagent-dispensing bottle must be held vertically, dispensing one free-falling drop at a time.

**Warning:** Reagents contain sodium azide, which is very toxic by inhalation, in contact with skin, and if swallowed. Contact with acids liberates very toxic gas. After contact with skin, wash immediately with plenty of water. Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal, flush with a large volume of water to prevent azide build-up.

**Controls:** Do not use the kit if Control + and Control - do not yield appropriate results.

**Test Cards:** Cards must be flat for proper reactions. If necessary, flatten cards by bowing back in a direction opposite to that of the curl. Care should be taken not to finger-mark the test areas, since this may result in an oily deposit and improper test results. Use each card once and discard. Store cards in original package in a dry area at room temperature. When spreading within confines of test areas, avoid scratching card surface with the plastic stirrer. If the specimen does not spread to outer perimeter of test area, use another test area of the card.

**Test Slide (Glass):** If the glass slide is used, disinfect the slide after each use, and wash before reuse. A phenolic disinfectant is suggested. Be sure all detergent and/or disinfectants are thoroughly rinsed from the slide before reuse.

**Rotation:** The recommended speed for mechanical rotation is  $100 \pm 2$  rpm, but rotation between 95 and 110 rpm does not significantly affect the results obtained. The rotator should circumscribe a circle approximately 2 cm in diameter in the horizontal plane. A moistened humidifying cover should be used to prevent drying of test specimens during rotation.

**Storage of Reagents:** Upon receipt, remove carton containing reagents and refrigerate at 2 - 8°C. DO NOT FREEZE. Reagents should be recapped and returned to refrigeration when not in use, taking care not to mix color-coded caps.

## V. SPECIMEN COLLECTION AND HANDLING

Refer to appropriate texts for details of specimen collection and handling procedures. Specimens should be tested as soon as possible; however, if the sample cannot be tested immediately, it should be stored at 2 - 8°C (for up to 48 h), or at -20°C.

Serum must be separated from whole blood prior to testing or storage.

### Specimen Pretreatment

The use of covered glass test tubes (borosilicate) in a 100°C (boiling) water bath is the most effective means of specimen treatment. Although glass test tubes in a heat block may be used, greater variation in the thorough heating of a sample may be noted as a result of variations in tube size and sample volume.

**Specimen Preparation (CSF):**

1. Heat specimens for 3 min at 100°C (e.g., water bath or heat block) and allow to cool to room temperature before use. For optimal sensitivity, *N. meningitidis* group B and *E. coli* K1 testing should be performed on unheated specimens (see "Limitations of the Procedure").
2. For CSF specimens showing turbidity, centrifuge after heating for 10 min at 1400 x g prior to testing. The supernatant fluid is to be used as the test specimen.
3. Test specimens as described in "Procedures."

**Specimen Preparation (Serum):**

1. Dilute serum specimens of at least 0.6 mL 1:1 with **Directigen** Specimen Buffer and mix.
2. Heat specimens for 5 min at 100°C (e.g., water bath or heat block) and allow to cool to room temperature before use.
3. Using a wooden applicator stick, break up the protein "clot" formed, and vortex vigorously (approximately 5 sec).
4. Centrifuge at a minimum of 1400 x g for 15 min.
5. Test supernatant fluid as described in "Procedures."

**Specimen Preparation (Unconcentrated Urine):**

1. Dilute urine specimens of at least 0.4 mL 1:1 with **Directigen** Specimen Buffer and mix.
2. Heat specimens for 5 min at 100°C (e.g., water bath or heat block) and allow to cool to room temperature before use.
3. Centrifuge at a minimum of 1400 x g for 10 min.
4. Test supernatant as described in "Procedures."

**Specimen Preparation (Concentrated Urine):**

1. Urine samples that are turbid or have particulate material should be centrifuged at 1400 x g for 10 min before concentrating.
2. Urine samples may be concentrated 25-fold with a Minicon B-15 concentrator (Amicon Corporation, Danvers, Massachusetts).
3. Dilute at least 200 µL of urine concentrate 1:1 with **Directigen** Specimen Buffer and mix.
4. Heat specimens for 5 min at 100°C (e.g., water bath or heat block) and allow to cool at room temperature before use.
5. Centrifuge at a minimum of 1400 x g for 10 min.
6. Test supernatant fluid as described in "Procedures."

**Preparation for Confirmation of Colonies from Culture:**

1. Locate suspected colonies on the agar surface from 18 - 24 h cultures that meet morphological and Gram stain characteristics of organisms that are appropriate for testing with **Directigen** Meningitis latex reagents. **Note:** A Gram stain should be performed prior to testing to ensure that organisms are appropriate for testing with the **Directigen** Meningitis latex reagents.
2. Pipette 0.5 mL (approximately 10 drops) of Control - reagent into a small glass test tube (10 x 75 mm or equivalent).
3. Select several (2 - 3) isolated colonies of similar morphology from the original or subculture plate using a sterile loop and suspend into the above tube to achieve a suspension equal to a McFarland #1 turbidity standard. **Note:** Over inoculating will yield an excessively heavy suspension, which may cause erroneous results.
4. Heat the suspension for 3 min. at 100°C (e.g., boiling water bath or heat block) and allow to cool

to room temperature before testing.

5. Centrifuge at a minimum of 1400 x g for 10 min.
6. Test supernatant as described under "Procedures." **Note:** If atypical agglutination patterns are observed, refer to "Limitations of the Procedure."

## VI. PROCEDURES

The testing area, reagents, test specimens and test components should be at room temperature (15-30°C) when used.

**Materials Provided:** All materials as listed under "Reagents," work station, disposable test cards and accessories.

**Materials Required but Not Provided:** **Directigen** Meningitis Test slide (glass), rotator, humidifying cover, micropipettor (50 µL delivery) and pipette tips (see "Availability").

Also required are the necessary equipment and labware used for preparation, storage and handling of CSF, serum and urine specimens.

### **Test Procedure (CSF, serum, urine, concentrated urine and colony confirmation):**

Remove reagents from refrigerated storage, and place reagents and card (or glass test slide) in designated wells of Work Station Tray.

*Use only the test card or glass slide recommended for this kit.* Before use of the glass slide, thoroughly clean with a lint-free tissue.

1. Dispense one drop of **Control +** onto circles 1 through 6 of row "+". Place one drop of **Control -** onto circles 1 through 6 of row "-."
2. Micropipette 50 µl of test sample onto circles 1 through 6, row **S** (Sample) and in circles labeled "A" and "B." Rows "+" (Positive) and "-" (Negative) are used for controls. Subsequent sample testing can be done using rows +, - and **S** of new (or cleaned) test cards (slides).
3. Holding the dispensing bottle by the cap, vigorously swing (without inverting) to thoroughly mix **Reagents 1 - 6** and **Reagents A** and **B**. Before uncapping each bottle, gently tap base on counter top to assure no latex reagent remains in the tip.
4. Dispense one drop of **Reagent A** (Control Latex Suspension) onto the "A" circle. Repeat the procedure dispensing one drop of **Reagent B** (Control Latex Suspension) onto the "B" circle.
5. Dispense one drop of Latex Suspension **Reagent 1** onto the circles in column 1, rows "+" (Positive), "-" (Negative) and "**S**" (Sample). Repeat the procedure for the remaining Latex Suspensions (**Reagents 2 - 6**) in rows "+", "-", and "**S**", columns 2 through 6.
6. Mix the samples and Latex reagents in each circle with a plastic stirrer, alternately using first one end, and then the opposite end for the next circle. Discard the stirrer.
7. Place the card or glass slide on a mechanical rotator and rotate at a speed of  $100 \pm 2$  rpm for *10 min*. Use a moistened humidifying cover to prevent evaporation.
8. Immediately at the end of 10 min, read the test results macroscopically under a high intensity

incandescent light.

Note: *For testing a specimen (CSF, serum, urine, concentrated urine or colony confirmation) with one individual **Reagent 1 - 5, Reagent A** must be used. For testing with one individual **Reagent 6, Reagent B** must be used. Use the above procedure.*

## VII. INTERPRETATION OF TEST RESULTS

Record Control + and Control - test results first: The Control + should yield strong agglutination in circles of row "+" within 10 min. The Control - should show no agglutination in circles of row "-". Agglutination in any of the circles containing Control - renders the reaction uninterpretable.

Record sample test results:

**Positive Test** - Should show agglutination. Any degree of agglutination present in one of the latex reagents indicates the presence of the corresponding antigen. *Agglutination in two or more latex reagents or the corresponding **Reagent A (Reagents 1-5) or Reagent B (Reagent 6)** renders the reaction uninterpretable.*

**Negative Test** - Should show no agglutination.

## VIII. USER QUALITY CONTROL

Include Control + and Control - testing with each batch of specimens tested as described in step 1, "Test Procedure."

Quality control requirements must be performed in accordance with applicable local, state and/or federal regulations or accreditation requirements and your laboratory's standard Quality Control procedures. It is recommended that the user refer to pertinent NCCLS guidance and CLIA regulations for appropriate Quality Control practices.

## IX. LIMITATIONS OF THE PROCEDURE

These latex agglutination tests are not intended as a substitute for bacterial culture. Confirmatory diagnosis of bacterial meningitis infection is only possible with appropriate culture procedures.

Samples with extremely low levels of antigen, for instance early in the course of infection, may yield false negative results. Furthermore, samples with exceedingly high antigen concentrations may exhibit prozone effects producing inappropriately negative results. Although not extensively studied, prozone phenomena have only been observed in specimens seeded with extremely high antigen levels, and not in clinical specimens.

This assay is for the qualitative detection of antigens to *H. influenzae* type b, *S. pneumoniae*, *N. meningitidis* groups A, B, C, Y or W135 and *E. coli* K1 in CSF, serum or urine; and to group B

*Streptococcus* in CSF and serum. In addition, the test kit can also be used with suspected colonies of *H. influenzae* type b, *S. pneumoniae*, group B *Streptococcus* and *N. meningitidis* groups A, B, C, Y or W135. Performance with other specimen types has not been assessed.

The **Directigen** Meningitis Combo Test cannot be used with blood culture media.

A positive or negative Group B streptococcal result is only indicative of the presence or absence of Group B streptococcal antigen and is not diagnostic for the presence or absence of group B streptococcal disease.

This device should not be used as a substitute for bacterial culture in the diagnosis of group B streptococcal septicemia and/or meningitis.

A positive or negative result is a presumptive result for group B streptococcal antigen. The result must be confirmed by culture.

The only *infant* specimens recommended for the direct qualitative detection of group B streptococcal antigen are serum and cerebrospinal fluid. Testing infant urine with devices for direct qualitative detection of group B streptococcal antigen cannot be recommended at this time; currently there is insufficient performance data supporting the use of this test on urine as a reliable predictor of group B streptococcal disease.

Pneumococcal and *Haemophilus influenzae* type b strains not possessing a capsular antigen may not be detected by immunological techniques.

Cross-reactions of *H. influenzae* reagent are known to occur in the presence of *Escherichia coli* K100. *N. meningitidis* groups C and W135 reagent is known to cross react in the presence of *Escherichia coli* K92. Other cross-reactions, uninterpretable and false positives may occur which are reduced or eliminated by proper specimen preparation (see "Specimen Pretreatment" and "Specimen Preparation").

Studies with CSF specimens seeded with *N. meningitidis* group B and *E. coli* K1 antigen have suggested that some loss in sensitivity may result after heating as compared to unheated samples.

Untreated serum and urines may yield uninterpretable results with the latex reagents and should be treated as in "Specimen Preparation." CSF specimens showing turbidity should be centrifuged for 10 min at 1400 x g or after heating, and prior to testing. The supernatant fluid is to be used as the test specimen.

Urine specimens (see "Specimen Preparation") that yield uninterpretable or suspected false positive results may be filtered using a MILLIPORE™ Millex-HA 0.45 µm filter (#SLHA-0250S) and retested with the reactive test latex(es) and the corresponding control latex(es).

Colony confirmation samples that yield uninterpretable or atypical agglutination reactions may require a 1:10 dilution of the supernatant with Control - reagent. Care should be taken to avoid bacterial suspensions greater than a McFarland #1 turbidity standard.

Latex agglutination tests of urine have potential usefulness in providing supportive evidence for the presence of a pathogenic organisms in infants presently with fever with localizing signs.<sup>22</sup> However, the excretion of urinary antigen may persist in infants for 3 - 14 days, or up to 30 days, following the administration of *Haemophilus influenzae* type b (Hib) vaccines. Frequency and duration of antigenuria depends on the patient and the type of vaccine given. Patient vaccination history is important for the correct interpretation of positive urinary Hib antigen results in vaccinated infants.<sup>22-24</sup>

Cross-reactions have been produced by some strains of the viridans streptococci group (i.e., *S. mitis*, *S. sanguis* II, *S. salivarius*)<sup>25</sup> with the **Directigen** *S. pneumoniae* latex reagent. Additional tests may be needed to differentiate the viridans streptococci group from *S. pneumoniae*.

A Gram stain should be performed prior to use with the colony confirmation procedure. Certain bacterial isolates obtained from blood culture plates, which are morphologically similar to, but Gram stain inconsistent with the suspect colony, may exhibit non-specific agglutination and/or false positive reactions (i.e., beta-hemolytic nonpathogenic *Neisseria* species) with the group B Strep latex.

## X. EXPECTED VALUES & PERFORMANCE CHARACTERISTICS

*Haemophilus influenzae* type b, *Neisseria meningitidis* and *Streptococcus pneumoniae* have been reported to be the three causative agents responsible for approximately 84% of cases of bacterial meningitis.<sup>3</sup>

Group B *Streptococcus* and *Escherichia coli* K1 are major bacterial pathogens in the newborn.<sup>4-7</sup> Strains of group B streptococci and *E. coli* K1 frequently colonize in the vagina and/or rectum and may be associated with maternal septicemia and neonatal septicemia, pneumonia and meningitis.<sup>8</sup>

**Sensitivity:** In a series of retrospective clinical evaluations, cerebrospinal fluids (heated and unheated), serum and urine specimens were tested by the **Directigen** Meningitis latex reagents. The specimens tested were originally derived from patients with culture, CIE or commercial latex reagent positive confirmed cases of either *Haemophilus influenzae* type b, *Streptococcus pneumoniae*, *Neisseria meningitidis* groups A, B, C, W135 or group B streptococcal infection. The latex results were also compared to counterimmunoelectrophoresis (CIE) but, not all samples were tested with CIE (**Table 1**). The **Directigen** Meningitis latex reagents were equal to, or more sensitive than CIE in detecting antigen in CSF, serum and urine specimens.

*E. coli* K1 sensitivity was determined by using whole cell *E. coli* K1 seeded into body fluids and compared to commercially available latex agglutination reagent. The **Directigen** *N. meningitidis* group B Latex Reagent could detect *E. coli* K1 in CSF (4/4), serum (4/4), urine (3/4) and concentrated urine (4/4). The endpoint sensitivities were equal to or better than those observed with a similar commercially available latex reagent.<sup>15</sup>

Each **Directigen** latex reagent was also compared with CIE for its ability to detect partially purified antigen seeded in CSF, serum, urine and concentrated urine. Commercial antiserum specific for each antigen was used in the CIE test. The **Directigen** latex reagents were more sensitive than CIE.<sup>15</sup>

TABLE 1

### Comparison of Directigen and CIE in Stored Samples

Specimen	Antigen Present	Methods	No. Positive	No. Negative
CSF	<i>H. influenzae</i> type b	<b>Directigen</b>	83	14
		CIE	66	31
	<i>S. pneumoniae</i>	<b>Directigen</b>	36	9
		CIE	33	12
	group B <i>Streptococcus</i>	<b>Directigen</b>	18	6
		CIE	2	4
<i>N. meningitidis</i> group A	<b>Directigen</b>	22	3	
	CIE	Not Tested	Not Tested	
Serum	<i>H. influenzae</i> type b	<b>Directigen</b>	7	2
		CIE	5	4
	<i>S. pneumoniae</i>	<b>Directigen</b>	17	5
CIE		17	5	
<i>N. meningitidis</i> group A, B, C or W135	<b>Directigen</b>	12	9	
	CIE	7	13	
Urine	<i>H. influenzae</i> type b	<b>Directigen</b>	12	4
		CIE	2	14
	<i>S. pneumoniae</i>	<b>Directigen</b>	7	12
		CIE	1	18
group B <i>Streptococcus</i>	<b>Directigen</b>	41	16	
	CIE	2	3	
<i>N. meningitidis</i> group A or C	<b>Directigen</b>	5	2	
	CIE	1	4	

**Specificity:** The specificity of the **Directigen** Meningitis reagents was determined by testing retrospective and prospective CSF, serum, urine and concentrated urine specimens in multiple clinical studies (**Table 2**). Both culture negative and nonindexed culture positive specimens were tested. The data indicates specificity ranges of 97-100% depending on the latex and specimen tested.

**TABLE 2**  
**Specificity Testing of Culture Negative and Culture Positive Clinical Specimens**

Specimen	Latex Reagent	No. Tested	No. Negative	Specificity %
CSF	<i>H. influenzae</i> type b	146	146	100
	<i>S. pneumoniae</i>	146	146	100
	group B <i>Streptococcus</i>	127	127	100
	<i>N. meningitidis</i>	236	232	98.3
	groups C / W135			
	<i>N. meningitidis</i>	75	74	98.7
	groups A / Y			
Serum	<i>N. meningitidis</i> group B / <i>E. coli</i> K1	148	148	100
	<i>H. influenzae</i> type b	124	124	100
	<i>S. pneumoniae</i>	125	125	100
	Group B <i>Streptococcus</i>	64	64	100
	<i>N. meningitidis</i>	143	143	100
	groups C / W 135			
	<i>N. meningitidis</i>	36	35	97.2
Urine	groups A / Y			
	<i>N. meningitidis</i> group B / <i>E. coli</i> K1	126	126	100
	<i>H. influenzae</i> type b	120	119	99
	<i>S. pneumoniae</i>	120	119	99
	group B <i>Streptococcus</i>	82	81	98.7
	<i>N. meningitidis</i>	147	147	100
	groups C / W135			
Urine (conc)	<i>N. meningitidis</i>	51	50	98
	groups A / Y			
	<i>N. meningitidis</i> group B / <i>E. coli</i> K1	120	120	100
	<i>H. influenzae</i> type b	30	30	100
	<i>S. pneumoniae</i>	30	29	97
	group B <i>Streptococcus</i>	41	40	97.5
	<i>N. meningitidis</i>	53	52	98.1
groups C / W135				
Urine (conc)	<i>N. meningitidis</i>	37	37	100
	groups A / Y			
	<i>N. meningitides</i> group B / <i>E. coli</i> K1	30	30	100

**Colony Confirmation:** Latex reagents were tested using suspensions of isolated colonies that met morphological characteristics of the organisms. Performance characteristics are listed in **Table 3**.

**TABLE 3**  
**Colony Confirmation Performance Characteristics**  
**Directigen Meningitis vs. Biochemical Identification**

Suspected Organism	No. Tested	Relative Sensitivity (95% Confidence Interval)	Relative Specificity (95% Confidence Interval)	% Uninterpretable Initial Testing
<i>H. influenzae</i> type b	112	100% (92-100)	98.5% (92-100) <sup>2</sup>	3.6%
<i>S. pneumoniae</i>	124	93% (84-98)	79.0% (66-88) <sup>1</sup>	0%
group B <i>Streptococcus</i>	129	100% (95-100)	90.5% (80-96) <sup>1</sup>	0%
<i>Neisseria meningitidis</i> group A / Y	106	100% (83-100)	100% (96-100) <sup>2</sup>	10.4%
<i>Neisseria meningitidis</i> group C / W135	94	96% (82-100)	98.5% (92-100) <sup>2</sup>	11.7%
<i>Neisseria meningitidis</i> group B	106	85% (55-98)	100% (96-100) <sup>2</sup>	4.7%

1 Refer to "Limitations of the Procedure".

2 Results after repeat testing with 1:10 dilution.

## XI. AVAILABILITY

### Cat. No. Description

#### Directigen™ Kits:

252360	Meningitis Combo Test, (30 patient tests, 60 controls).
255460	Group B <i>Streptococcus</i> Test, (30 patient tests, 60 controls).
252260	<i>H. influenzae</i> type b Test, (30 patient tests, 60 controls).
255560	<i>N. meningitidis</i> group B / <i>E. coli</i> K1 Test, (30 patient tests, 60 controls).
250160	<i>N. meningitidis</i> groups A, C, Y and W135 Test, (30 patient tests, 60 controls).
251960	<i>S. pneumoniae</i> Test, (30 patient tests, 60 controls).

#### Directigen™ Cards (single-use):

252480	Meningitis Combo, 20 test circles, Box 30
250780	Meningitis, generic, 12 test circles, Box 30.
250180	<i>N. meningitidis</i> groups A, C, Y and W135, 10 test circles, Box 30.

#### Directigen™ Slides (glass):

252460	Meningitis Combo, 20 test circles, Pkg. one
250779	Meningitis, generic, 12 test circles, Pkg. one.

## Additional Supplies

256391	<b>Directigen™</b> Specimen Buffer, 8 mL.
252350	<b>Directigen™</b> Meningitis Negative Control Reagent, 9 mL, Box 4.
273310	Pipette Tips, Box 1000.

## XII. REFERENCES

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### **XIII. TECHNICAL INFORMATION**

In the United States, telephone BD Diagnostics Technical Services, toll free (800) 638-8663, Prompt 2.

Approved By: \_\_\_\_\_

Date Effective: \_\_\_\_\_

Supervisor: \_\_\_\_\_ Date: \_\_\_\_\_

Director: \_\_\_\_\_ Date: \_\_\_\_\_

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