Key Code TSMX7712B

www.oxoid.com/ifu

Europe +800 135 79 135 US 1 855 2360 190

CA 1 855 805 8539 ROW +31 20 794 7071

Wellcogen™ N. meningitidis B/ E. coli K1.

REF ZL24/R30859502 .....30 Tests **EN**

1 INTENDED USE

Wellcogen™ N. meningitidis B/E. coli K1 is a rapid latex test for use in the qualitative detection of antigen from Neisseria meningitidis (meningococcus) group B and Escherichia coli K1, present in body fluids as a consequence of infection. The latex can also be used for the detection of specific antigen in blood culture supernatants and for the identification of meningococcus group B or E. coli K1 cultures. Meningococcus group B antigen and E. coli K1 antigen are immunologically indistinguishable from each other.

NOTE: Tests performed directly on clinical specimens are intended for screening purposes and should augment, not replace, culture procedures. Results must be used in conjunction with other data; eg symptoms, results of other tests, clinical impressions etc.

2 SUMMARY

Cerebrospinal meningitis and meningococcaemia are common manifestations of meningococcal disease, which is endemic in many areas and occurs epidemically throughout the world[6,10]. Early diagnosis is of great importance[12] to assist the selection of appropriate therapy. The infecting organisms carry group-specific polysaccharide surface antigens, a quantity of which is released into the infected body fluid such as serum or cerebrospinal fluid (CSF) and is excreted in the urine[5,13]. The antigen in these body fluids can be detected by sensitive immunological methods including counterimmunoelectrophoresis and latex agglutination[5]. One of the serological groups of N. meningitidis most commonly associated with meningococcal infections is group B[1,7]; about 80% of neonatal E. coli meningitis is caused by strains carrying K1 antigen[11].

3 PRINCIPLE OF THE TEST

The Wellcogen N. meningitidis B/E. coli K1 reagent consists of polystyrene latex particles which have been coated with monoclonal antibodies specific to meningococcus group B antigen. These latex particles agglutinate in the presence of sufficient homologous antigen, either in body fluids or cultures of the organism.

The polysaccharide K1 antigen of E. coli shows structural[9] and immunological[4,8] identity with meningococcus group B antigen, and the Wellcogen N. meningitidis B/E. coli K1 reagent does not distinguish between them. Therefore the reagent may be used to assist in the diagnosis of meningococcal meningitis and neonatal E. coli meningitis.

Some body fluid samples cause non-specific aggregation of latex particles, and a Control Latex preparation is provided in order to identify these samples.

4 SYMBOL DEFINITIONS

REF	Catalogue Number
IVD	In Vitro Diagnostic Medical Device
Σ	Contains sufficient for <n> tests
	Consult Instruction for Use (IFU)
2°C 8°C	Temperature Limitation (Storage Temp.)
LOT	Batch code (Lot Number)
	Use by (Expiration Date)
	Manufacturer
	Add water

5 KIT CONTENTS, PREPARATION FOR USE AND STORAGE

The Wellcogen N. meningitidis B/E. coli K1 kit includes sufficient reagents to perform Σ 30 tests.

See also **Precautions**, section **6**.

All components should be stored at 2 to 8°C under which condition they will retain their activity until the expiry date of the kit.

Before use, bring all reagents to room temperature (18 - 30°C) and mix. Return the unused reagents to the refrigerator after use.

Instructions for Use
Disposable Reaction Cards (1 pack)
Disposable Mixing Sticks (2 bundles)
Disposable Droppers (1 container)
Black rubber teat (1)

TEST LATEX

Test Latex

One dropper bottle (brown cap) containing a 0.5% suspension of polystyrene latex particles in glycine saline buffer, pH 8.2 with 0.05% Bronidox® preservative. The latex particles are coated with murine monoclonal antibody to N. meningitidis group B antigen.

CONTROL LATEX

Control Latex

One dropper bottle (dark blue cap) containing a 0.5% suspension of polystyrene latex particles in glycine saline buffer, pH 8.2 with 0.05% Bronidox® preservative. The latex particles are coated with murine monoclonal antibody to Bordetella bronchiseptica.

The latex suspensions are provided ready for use and should be stored at 2 to 8°C in an upright position, until the expiry date of the kit. After prolonged storage some aggregation or drying of the latex may have occurred around the top of the bottle. Under these circumstances the bottle of latex should be shaken vigorously for a few seconds until resuspension is complete. DO NOT FREEZE.

CONTROL +

Polyvalent Positive Control

One bottle (blue cap) containing freeze-dried bacterial extracts including antigen from a representative strain of N. meningitidis group B and/or E. coli K1 antigen. Contains 0.01% bronopol before reconstitution and 0.004% when reconstituted.

Reconstitute using 3.6 ml of sterile distilled water. After the addition of water allow the bottle to stand for a few minutes and then swirl to mix. Store reconstituted antigen at 2 to 8°C for up to 6 months.

CONTROL −

Negative Control

One dropper bottle (white cap) containing Glycine saline buffer, pH 8.2, with 0.05% Bronidox® as preservative.

6 PRECAUTIONS

IVD

The reagents are for in vitro diagnostic use only.

For professional use only.

Please refer to the Safety Data Sheet (SDS) and product labelling for information on potentially hazardous components.

HEALTH AND SAFETY INFORMATION

6.1 In accordance with the principles of Good Laboratory Practice it is strongly recommended that body fluids should be treated as potentially infectious and handled with all necessary precautions.

6.2 When handling radiometric blood culture medium, the basic rules of radiation safety should be followed. These include:

a) Radioactive material should be stored in a designated area in an approved container.
b) Handling of radioactivity should take place in a designated area.
c) No mouth pipetting of radioactive material should be carried out.
d) No eating, drinking or smoking should take place in the designated area.

e) Hands should be washed thoroughly after using radioactive material.
f) The local Radiation Safety Officer should be consulted concerning disposal requirements.

6.3 Non-disposable apparatus should be sterilised by any appropriate procedure after use, although the preferred method is to autoclave for 15 minutes at 121°C. Disposables should be autoclaved or incinerated. Spillage of potentially infectious materials should be removed immediately with absorbent paper tissue and the contaminated areas swabbed with a standard bacterial disinfectant or 70% alcohol. Do NOT use sodium hypochlorite. Materials used to clean spills, including gloves, should be disposed of as biohazardous waste.

6.4 Do not pipette by mouth. Wear disposable gloves and eye protection while handling specimens and performing the assay. Wash hands thoroughly when finished.

6.5 When used in accordance with the principles of Good Laboratory Practice, good standards of occupational hygiene and the instructions stated in these Instructions for Use, the reagents supplied are not considered to present a hazard to health.

ANALYTICAL PRECAUTIONS

6.6 Do not use the reagents beyond the stated expiry date.

6.7 Latex reagents should be brought to room temperature (18 to 30°C) before use. Latex reagents which show signs of aggregation or 'lumpiness' before use may have been frozen and must not be used.

6.8 It is important when using dropper bottles that they are held vertically and that the drop forms at the tip of the nozzle. If the nozzle becomes wet an incorrect volume will form around the end and not at the tip; if this occurs dry the nozzle before progressing.

6.9 The reagents provided with each kit are matched in performance and should not be used in conjunction with reagents from a kit having a different lot number.

6.10 Do not touch the reaction areas on the cards.

6.11 Mechanical rotators may be used in this assay. The following characteristics have been found to be satisfactory:

a) Orbital rotators (also known as dimensional rotators) operating at 25 rpm with approximate rotating angle of 9 to 10.5 degrees or operating at 18 rpm with a rotating angle of 16 to 17.5 degrees.

6.12 Avoid microbial contamination of reagents as this may lead to erroneous results.

7 SPECIMEN COLLECTION AND STORAGE

7.1 **Body fluid samples** (e.g. CSF, serum, urine) should be tested as soon after collection as possible. If the fluid cannot be tested immediately it may be stored overnight at 2 to 8°C, or for longer periods frozen at –15 to –25°C. If bacteriological analyses are required on the sample, these should be set up prior to performing the latex test, to avoid contaminating the sample.

7.2 **Blood cultures** may be sampled and tested after 18 to 24 hours incubation at 37°C and/or as soon as bacterial growth is observed.

7.3 **Plate cultures**. Isolated colonies growing on enriched agar medium (e.g. blood, chocolate agar) may be tested after overnight incubation at 37°C. A Gram stain should be performed to assist with the interpretation of the latex test result.

8 TEST PROCEDURE

REQUIRED MATERIALS PROVIDED

See **Kit Contents**, section **5**.

MATERIALS REQUIRED BUT NOT PROVIDED

Boiling water bath
Laboratory centrifuge or membrane filters (0.45 µm)
Rotator (optional – refer to **Precautions**, section **6**)

PREPARATION OF CLINICAL SPECIMENS

8.1 **Body fluid samples** must be heated[3] before testing by the Wellcogen procedure to minimise non-specific reactions. The following procedures are recommended:

a) For CSF and urine, heat the sample for 5 minutes in a boiling water bath. Cool the sample to room temperature (18 to 30°C) and clarify by centrifugation or membrane filtration (0.45 µm) prior to testing. For maximum sensitivity urine samples may be concentrated up to 25-fold in a Minicon® B-15 concentrator. Clarify as above before testing.

b) For serum, add 3 volumes 0.1M disodium ethylenediaminetetra-acetate (EDTA) pH 7.4 per 1 volume serum, heat the sample for 5 minutes in a boiling water bath, cool to room temperature (18 to 30°C) and clarify as above. A suitable EDTA solution (10 ml) is available (Code No. ZL29/R30164501).

8.2 **Blood cultures**. Centrifuge a 1 to 2 ml sample to pellet the red blood cells, for example at 1000 g for 5 to 10 minutes. Perform the latex test on the supernatant.

If a non-specific reaction occurs with a blood culture supernatant (see **Interpretation of Results**, section **10**), heat the sample in a boiling water bath for 5 minutes, cool to room temperature (18 to 30°C), clarify by centrifugation and repeat the test.

8.3 **Plate cultures**. Test directly from culture plate.

PROCEDURE

It is recommended that the section on **Precautions**, section **6**, is read carefully before performing the test.

NOTE: If there is only a limited volume of test sample available, it should be used with the Test Latex first and if a positive result is obtained the sample should be tested with the Control Latex. If sufficient sample is available, it should be tested against both the Test and Control Latexes simultaneously.

a, b)	**Body fluid samples and blood culture supernatants**	
Step 1	Process the sample as described under **Preparation of Clinical Specimens**, section **8**.	
Step 2	Shake the latex reagents.	
Step 3	For each test sample place 1 drop of **Test Latex** in one circle on a Reaction Card, and 1 drop of **Control Latex** in a separate circle. Ensure that the dropper bottles are held vertically to dispense an accurate drop. (See **Precautions**, section **6**).	**1 drop**
Step 4	Using a Disposable Dropper, dispense 1 drop (approximately 40 µl) of **Test Sample** next to each drop of latex.	**1 drop**
Step 5	**Mix** the contents of each circle with a Mixing Stick and spread to cover the complete area of the circle. Use a separate stick for each circle and discard it for safe disposal after use.	
Step 6	**Rock** the card slowly and **observe** for agglutination for 3 minutes, holding the card at normal reading distance (25 to 35 cm) from the eyes. Do not use a magnifying lens. Mechanical rotation (3 minutes) may be used (see **Precautions**, section **6**). The patterns obtained are clear cut and can be recognised under all normal lighting conditions.	**3 mins**
Step 7	Discard the used Reaction Card for safe disposal.	
c)	**Plate cultures**	
Step 1	Shake the latex reagents.	
Step 2	For each culture to be tested place 1 drop of **Test Latex** in one circle on a Reaction Card and 1 drop of **Control Latex** in a separate circle. Note: it is essential to use the **Control Latex** for suspected E. coli cultures.	**1 drop**
Step 3	Take a Mixing Stick and pick up some of the culture by touching it with the flat end of the stick. As a guide, an amount of growth roughly equivalent to 1 large colony should be picked.	**sample of growth**
Step 4	**Emulsify** the sample of culture in the drop of **Test Latex** by rubbing with the flat end of the stick. Rub thoroughly, but not so vigorously as to damage the surface of the card. Spread the latex to cover as much of the circle as possible. Discard the Mixing Stick for safe disposal.	
Step 5	Using a separate stick, **emulsify** a similar sample of culture in the **Control Latex**.	
Step 6	**Rock** the card slowly and **observe** for agglutination for 20 seconds, holding the card at normal reading distance (25 to 35 cm) from the eyes. Do not use a magnifying lens. The patterns obtained are clear cut and can be recognised under all normal lighting conditions.	**20 secs**
Step 7	Discard the used Reaction Card for safe disposal.	

9 QUALITY CONTROL

The following procedures should be carried out initially with each shipment of test kits and with each run of test samples. In practice, a run may be defined as a testing period of up to 24 hours. Any departure from the expected results indicates that there may be a problem with the reagents, which must be resolved before further use with clinical samples.

VISUAL INSPECTION

The latex suspensions should always be inspected for aggregation as they are dropped onto the reaction card and if there is evidence of clumping before addition of the test sample, the suspension must not be used. After prolonged storage some aggregation or drying may have occurred around the top of the bottle. If this is observed, the bottle should be shaken vigorously for a few seconds until resuspension is complete.

POSITIVE CONTROL PROCEDURE

The reactivity of the test can be confirmed by adding Polyvalent Positive Control to a reaction circle in which the test sample has not agglutinated the Test Latex after 3 minutes rotation.

Step 1	Use a Disposable Dropper to add 1 drop of Positive Control to the circle containing Test Latex and specimen.	**1 drop**
Step 2	Mix using a Mixing Stick and discard it for safe disposal.	
Step 3	Rock the card manually or by a rotator for a further 3 minutes. After this time, definite agglutination should be visible in the Test Latex.	**3 mins**
Step 4	Discard the used Reaction Card for safe disposal.	

NEGATIVE CONTROL PROCEDURE

If at least one test sample within a run gives a negative result with Test and Control Latexes (or Test Latex only where no Control Latex has been used), this constitutes a valid negative control for the reagents and no further testing is necessary.

If a test sample gives agglutination with the Test Latex and no agglutination with the Control Latex then the Test Latex should be tested either with the Negative Control or uninoculated blood culture medium, as appropriate (see below).

Step 1	Place 1 drop of Test Latex in one circle on a Reaction Card.	**1 drop**
Step 2	Dispense 1 drop of Negative Control or uninoculated blood culture medium next to the Test Latex.	**1 drop**
Step 3	Mix using a Mixing Stick and discard it for safe disposal.	
Step 4	Rock the card manually or by a rotator for a further 3 minutes. After this time, there should be no significant agglutination in the Test Latex.	**3 mins**
Step 5	Discard the used Reaction Card for safe disposal.	

For tests with body fluid samples, the Negative Control provided with the kit should be used.

For tests with blood cultures a sample of uninoculated blood culture medium from the same source as the specimen should be used as a negative control. Testing uninoculated media is important as false-positives can occur with some formulations of blood culture media.

NOTES:

1. Previously assayed positive and negative samples, aliquoted and stored at –15 to –20°C or below, may be used as positive and negative controls respectively, if desired. The Positive Control can also be used in place of the test sample.
2. For colony identification the performance of the Test and Control Latex reagents may be confirmed using fresh, overnight cultures of reference strains of bacteria, following the method described in **Test Procedure** (c). Suitable reference strains are:
   ATCC 13090 – N. meningitidis group B (positive reactivity)
   ATCC 23503 – E. coli type K1 (positive reactivity)
   ATCC 13077 – N. meningitidis group A (negative reactivity)
   ATCC 13090 and ATCC 23503 should give agglutination with the Test Latex and no significant agglutination in the Control Latex, ATCC 13077 should give no significant agglutination with either the Test or Control Latex.

10 RESULTS

READING OF RESULTS

A **positive** reaction is indicated by the development of an agglutinated pattern within 3 minutes (20 seconds for colony testing) of mixing the latex with the test sample, showing clearly visible clumping of the latex particles (Figure 1).

The speed of appearance and quality of agglutination depend on the strength of the antigen, varying from large clumps which appear within a few seconds of mixing, to small clumps which develop rather slowly. In culture identification, most positive reactions will be almost instantaneous.

Figure 1

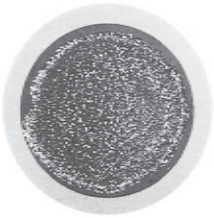

Figure 2

In a **negative** reaction the latex does not agglutinate and the milky appearance remains substantially unchanged throughout the test (Figure 2). Note, however, that faint traces of granularity may be detected in negative patterns, depending on the visual acuity of the operator. In culture identification, some strains may cause a "stringy" aggregation of the latex with a milky background; this should be interpreted as a negative reaction.

The latex particles are not the same as those used in other Wellcogen kits and give finer agglutination.

INTERPRETATION OF RESULTS

Positive Result

Clear agglutination of the Test Latex accompanied by a lack of agglutination of the Control Latex indicates the presence of meningococcus group B or E. coli K1 antigen in the body fluid or blood culture, or confirms the identity of the culture. As a general rule a positive result with a neonatal specimen suggests E. coli K1 infection; with older patients, meningococcus group B is more likely.

Negative Result

With a body fluid or blood culture supernatant, lack of agglutination in both reagents means that no meningococcus group B or E. coli K1 antigen is detectable in the test fluid – it does not eliminate the possibility of meningococcal or E. coli infection, and if symptoms persist it may be desirable to perform the test on subsequent or alternative specimens, or after concentration of the urine specimen.

With a culture, lack of agglutination in both reagents indicates that it is unlikely to be N. meningitidis group B or E. coli K1.

Non-interpretable Result

Visible agglutination of the Control Latex, whether stronger or weaker than the Test Latex, indicates a non-specific reaction. In most cases, non-specific reactions with body fluids may be eliminated by heating and clarifying the sample (see **Preparation of Clinical Specimens**, section **8**). If a non-specific reaction occurs with a blood culture supernatant, heat the sample in a boiling water bath for 5 minutes, cool to room temperature (18 to 30°C), clarify by centrifugation and repeat the test.

11 PERFORMANCE LIMITATIONS

11.1 A positive result in the test depends on the presence of a detectable level of antigen in the body fluid or blood culture medium.

11.2 Limited clinical data are available for the detection of antigen in urine or serum using this reagent.

11.3 In addition to E. coli K1 which has already been mentioned, there have been reports of other unrelated bacteria which possess common antigens[2] and, as with any immunological test system, the possibility of cross reactions occurring in the latex test can not be ruled out.

11.4 E. coli cultures bearing K antigens other than K1 are particularly prone to give non-specific reactions.

12 EXPECTED RESULTS

Samples containing a detectable level of N. meningitidis B/E. coli K1 antigen will give an agglutination reaction with the Test Latex.

13 PERFORMANCE CHARACTERISTICS

Clinical studies were carried out in 12 laboratories using body fluid samples (fresh and stored frozen) and blood culture supernatants. Both traditional and radiometric cultural techniques were used in the blood culture studies.

SENSITIVITY

The sensitivity of Wellcogen N. meningitidis B/E. coli K1 was established from tests on samples found to be culture positive for the homologous organisms or for which there was other evidence of infection (clinical diagnosis plus a positive result in another antigen test).

Table 1 shows the numbers of each type of fresh samples tested with the latex together with the number of positive results obtained.

The sensitivity of Wellcogen N. meningitidis B/E. coli K1 in detecting bacterial antigen in fresh CSF from patients infected with N. meningitidis group B was 64% (7/11). Tests were also carried out on stored (frozen) samples from patients with N. meningitidis group B infection. The results indicated that the antigen in most of the samples had deteriorated on storage. The Wellcogen N. meningitidis B/E. coli K1 test detected antigen in 9 out of 18 of the stored samples tested. The same 9 samples were detected by other antigen tests (CIE/ Latex) carried out at the same time. One additional sample gave a non-specific reaction with the Wellcogen latex and a positive result in CIE.

Antigen was detected in 4/6 stored CSF samples from patients with infections due to E. coli K1. The two Wellcogen latex negative samples also failed to react in CIE.

Limited data on serum and urine specimens are available at present (Table 1).

Wellcogen N. meningitidis B/E. coli K1 detected antigen in 5/7 blood cultures from which N. meningitidis group B was isolated (Table 1). Another study using Wellcogen N. meningitidis B/E. coli K1 has shown similar results[14].

SPECIFICITY

The specificity of Wellcogen N. meningitidis B/E. coli K1 was evaluated using 138 body fluid (fresh and frozen) and 461 blood culture samples from patients with bacterial or aseptic meningitis and other unrelated conditions.

The organisms isolated from the infected samples were Haemophilus influenzae type b, Streptococcus pneumoniae, N. meningitidis groups A, C, W135, E. coli, Klebsiella pneumoniae, Proteus mirabilis, Staphylococcus epidermidis, beta-haemolytic streptococcus group A + streptococcus group B and Streptococcus sanguis.

The specificity of Wellcogen N. meningitidis B/E. coli K1 in tests on body fluids and blood culture supernatants was 100% (138/138) and 99% (458/461) respectively (Table 1). The bacteria isolated from the 3 positive blood cultures were: a beta-haemolytic streptococcus group A (aerobic and anaerobic cultures from the same patient) and a coagulase negative staphylococcus. One CSF sample from a patient with a N. meningitidis group C infection gave a non-specific reaction.

Identification of Plate Cultures

N. meningitidis and E. coli cultures grown on an enriched agar medium were tested in hospital laboratories and at the development laboratory. All N. meningitidis group B and E. coli K1 cultures were correctly identified. There were no cross-reactions with other groups of N. meningitidis or other E. coli K antigens (Table 2). A high proportion of the E. coli cultures with other K antigens which were tested gave non-specific reactions (Table 2).

Table 1

Results of clinical studies on Wellcogen N. meningitidis B/E. coli K1

	Sensitivity[a]		Specificity[b]	
Sample	No. tested	No. positive	No. tested	No. positive
CSF:				
N. meningitidis B	11	7	128	0
E. coli K1[c]	6	4	128	0
Serum:				
N. meningitidis B	2	1	3	0
Urine:				
N. meningitidis B	2	1	7	0
Blood Culture:				
N. meningitidis B	7	5	461	3[d]

[a] Samples found to be culture positive or positive by another antigen test plus clinical diagnosis.

[b] Samples negative for N. meningitidis B/E. coli K1 by culture and alternative antigen test.

[c] Samples stored frozen. All other samples tested fresh.

[d] Aerobic and anaerobic cultures (beta-haemolytic strep A) for same patient; coagulase negative staphylococcus.

Table 2

Identification of cultures using Wellcogen N. meningitidis B/E. coli K1

Culture[a]	+	–
N. meningitidis group A	0	16
N. meningitidis group B	10	0
N. meningitidis group C	0	18
N. meningitidis group 29E	0	8
N. meningitidis group W135	0	7
N. meningitidis group X	0	4
N. meningitidis group Y	0	5
N. meningitidis group Z	0	3
E. coli K1	7	0
E. coli other antigens	0	13[b]

[a] Cultures identified by slide agglutination.

[b] An additional 10 cultures gave non-specific reactions.

14 BIBLIOGRAPHY

1 **Band, J.D., Chamberland, M.E., et al (1983).**
Trends in meningococcal disease in the United States, 1975-1980.
J. Infect. Dis., 148, 754.

2 **Bøvre, K., Bryn, K., et al (1983).**
Surface polysaccharide of Moraxella non-liquefaciens identical to Neisseria meningitidis group B capsular polysaccharide. A chemical and immunological investigation.
NIPH Annals, 6, 65.

3 **Doskeland, S.O. and Berdal, B.P. (1980).**
Bacterial antigen detection in body fluids: methods for rapid antigen concentration and reduction of nonspecific reactions.
J. Clin. Microbiol., 11, 380.

4 **Fallon, R.J. and McIllmurray, M.B. (1976).**
Escherichia coli K1.
Lancet, i, 201.

5 **Feigin, R.D., Wong, M., et al (1976).**
Countercurrent immunoelectrophoresis of urine as well as of CSF and blood for diagnosis of bacterial meningitis.
J. Pediatr., 89, 773.

6 **Galazka, A. (1982).**
Meningococcal disease and its control with meningococcal polysaccharide vaccines.
Bull, W.H.O., 60, 1.

7 **Jones, D.M. and Eldridge, J. (1981).**
Meningococcal disease in England and Wales 1978-79 – a change in the serotype pattern.
J. Infect., 3, 134.

8 **Kasper, D.L., Winkelhake, J.L., et al (1973).**
Immunochemical similarity between polysaccharide antigens of Escherichia coli 07:K1(L):NM and group B Neisseria meningitidis.
J. Immunol., 110, 262.

9 **Lifely, M.R., Gilbert, A.S., et al (1981).**
Sialic acid polysaccharide antigens of Neisseria meningitidis and Escherichia coli: esterification between adjacent residues.
Carbohyd. Res., 94, 193.

10 **Peltola, H.** (1983).
Meningococcal disease: still with us.
Rev. Infect. Dis., 5, 71.

11 **Sarff, L.D., McCracken, G.H., et al (1975).**
The Lancet – Saturday 17 May 1975. Epidemiology of Escherichia coli K1 in healthy and diseased newborns.
Lancet, i, 1099.

12 **Slack, J. (1982).**
Deaths from meningococcal infection in England and Wales in 1978.
J. Royal Coll. Phys. London, 16, 40.

13 **Stevens, P., Young, L.S., et al (1983).**
Correlation of E. coli K-1 bacteremia and capsular polysaccharide antigenemia in acute and chronic infection.
Diagn. Microbiol. Infect. Dis., 1, 185.

14 **Williams, R.G. and Hart, C.A. (1988).**
Rapid identification of bacterial antigen in blood cultures and cerebrospinal fluid.
J. Clin. Path., 41, 691.

CE

Remel Europe Ltd
Clipper Boulevard West, Crossways
Dartford, Kent, DA2 6PT
UK

For technical assistance please contact your local distributor.

IFU X7712B, Revised June, 2014 Printed in the UK