Trinity Biotech

Urgent Field Safety Notice

01 October 2014

Product Name: Uni-Gold™ S. pneumoniae

Product Code: 1204420

Lot Numbers: 8817K **Expiry Date:** 2015/02

Type of Action: Device Modification

Dear Valued Customer:

We would like to inform you that as a result of additional studies, Trinity Biotech MarDx USA revised the Uni-Gold™ S. pneumoniae Instructions for Use (IFU) to include the claim for the qualitative detection of *StreptococcuS. pneumoniae* in cerebral spinal fluid (CSF) within the Intended Use section and further reference to CSF in other sections of the Instructions For Use (IFU).
In April 2014, this revision was released as 1204420-29EN Uni-Gold™ S. pneumoniae Instructions for Use (IFU), **Rev 3.** However an investigation of a customer complaint has confirmed that previously stocked inventory of Uni-Gold™ S. pneumoniae, Product Number 1204420, Lot Number **8817K** contained the older version of the Instructions for Use (IFU), 1204420-29EN Uni-Gold™ S. pneumoniae Instructions For Use (IFU), **Rev 2**.

Due to this finding, it was decided to initiate a Urgent Field Safety Notice. Customers are instructed to discard the older version of the Instructions For Use (IFU), 1204420-29EN Uni-Gold™ S pneumoniae, **Rev. 2** and replace with the current version of 1204420-29EN Uni-Gold™ S pneumoniae Instructions For Use (IFU), **Rev 3** that has been provided in this notification. The new version includes the CSF claim.

Therefore we ask you to comply with the following:

- Discard the older IFU (Rev 2);
- Distribute the correct revision of IFU (Rev 3) to all impacted End Users;
- Place correct revision of IFU (Rev 3) in all remaining inventory;
- Complete the attached faxback form;

A thorough investigation into the root cause has been initiated and any corrective/preventive actions will be implemented as appropriate.

We wish to sincerely apologize for any inconvenience caused as a result of this Field Safety Notice. Trinity Biotech is committed to offering quality products and superior customer service. If you have any questions or comments arising from this customer communication, please contact us at the following:
Tel: +353-1-2769800 – contact Infectious Disease Technical Support Team
Fax: +353-1-2769888 – attention Infectious Disease Technical Support Team
e-mail: infectousdiseasetechsupport@trinitybiotech.com

Signed:

Tracey Murphy
Head of QA/RA

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Registered in Ireland. Registration number 239206
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Trinity Biotech

Urgent Field Safety Notice
FAX BACK FORM

Please complete and promptly return to:

Yvonne Kenny, Regulatory Affairs Department, Trinity Biotech

Email: yvonne.kenny@trinitybiotech.com **OR** Fax: + 353-1-2769888

01 October 2014

Product Name: Uni-Gold™ S. pneumoniae

Product Code: 1204420

Lot Numbers: 8817K **Expiry Date:** 2015/02

Type of Action: Device Modification

Customer Name: **XXX**
Customer Address: **XXX**

Dear <Name>

Further to the attached communication, you are requested to complete the following information:

- I have read the attached Customer Notification Yes/No
- I have placed the correct revision of IFU (Rev 3) in all remaining inventory Yes/No
- I have distributed the correct revision of IFU (IFU) to all impacted customers Yes/No

Printed Name: _____ Signed: _____

Title: _____ Date: _____

Fax: _____ Phone: _____

Comments: _____

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Uni-Gold™ S. pneumoniae

20 Tests

Store Kit at +2 to +30°C

REF 1204420

Pour d'autres langues
Für andere Sprachen
Para otras lenguas
Per le altre lingue
Dla innych języków
Para outras línguas
Για τις άλλες λώσσες
För andra språk
For andre språk

www.trinitybiotech.com

COOPERATION

Uni-Gold™ S. pneumoniae was developed in cooperation with Statens Serum Institut, SSI Diagnostica, Denmark.

INTENDED USE

Trinity Biotech Uni-Gold™ S. pneumoniae is a single use rapid immunoassay for the qualitative detection of *Streptococcus pneumoniae (S. pneumoniae)* antigen in urine of patients with pneumonia and in cerebral spinal fluid (CSF) of patients with meningitis. This test is intended, in conjunction with culture and other methods, as an aid in the diagnosis of suspected *S. pneumoniae* infections. For *In Vitro* Diagnostic Use.

SUMMARY AND EXPLANATION

S. pneumoniae is a key pathogen in invasive infection and WHO estimates that 1.6 million people die of severe pneumococcal infections every year[1]. *S. pneumoniae* is the leading cause of community-acquired pneumonia and may be the most important agent in community-acquired pneumonia of unknown etiology.

S. pneumoniae is a major cause of meningitis, leading to high morbidity and mortality in paediatric and adult patients[1,2]. It can occur spontaneously and can progress from mild illness to coma within hours.

A rapid diagnosis of pneumococcal infection can be performed by a rapid antigen test, as pneumococcal polysaccharide antigen (PPA) appears early in infection in urine and CSF[3,4,5]. Detection of PPA provides a simple, rapid method for the diagnosis of pneumococcal infection. This impacts positively on patient morbidity and mortality, and is important for the effectiveness of antibiotic therapy.

Uni-Gold™ S. pneumoniae is an immunochromatographic membrane assay used to detect PPA and aid in the rapid and accurate diagnosis of pneumococcal pneumonia using urine and meningitis using CSF.

PRINCIPLE OF THE TEST

Uni-Gold™ S. pneumoniae is a single use rapid lateral flow immunoassay which detects the presence of *S. pneumoniae* antigen in human urine and CSF.

Uni-Gold™ S. pneumoniae rapid test consists of anti-*S. pneumoniae* antibodies coated onto the test line region and anti-species specific IgG coated onto the control line region of the test strip. A conjugate of anti-*S. pneumoniae* antibodies and coloured latex particles are dried onto inert glass fibre below the nitrocellulose. A permanent blue line is printed on the laminate cover between the test line and the control line regions. As *S. pneumoniae* antigen in the sample passes over the conjugate region, it combines with the antibody/red latex to form a complex. This complex migrates up the nitrocellulose strip and binds to the antibodies in the test region forming a visible pink/red band.

Excess conjugate forms a second pink/red band in the control region of the device. The control line should always appear as a visible pink/red band in the control region of the device to indicate that the test device is functioning correctly.

REAGENTS

MATERIALS SUPPLIED

- 1204420-D Test Devices: 20 pouched test strips, each pouch containing one test strip and dessicant.
- 1204420-B Extraction Buffer: 2.0 mL of buffered solution preserved with <0.09% sodium azide.
- 1204420-P Positive Control: 0.5 mL of inactivated *S. pneumoniae* antigen preserved with <0.09% sodium azide (Red cap).
- 1204420-N Negative Control: 0.5 mL of phosphate buffered saline solution preserved with <0.09% sodium azide (Black cap).
- 90-1753 Disposable transfer pipettes: 20 disposable single use pipettes, used to add sample to the test tube.
- 99-8003 Test tubes: 20 disposable single use plastic tubes.
- Test Tube Holder Cardboard tube holder
- Package insert

MATERIALS REQUIRED BUT NOT SUPPLIED

- Timer or stopwatch.
- Standard containers for collection of urine, or CSF transport tubes.
- Biohazard disposal container.
- Disposable gloves.

STORAGE AND STABILITY

- Store all components between 2-30°C.
- Do not freeze or overheat.
- This product should not be used beyond the expiration date printed on the outer package label.
- The test kits should be kept away from direct sunlight, moisture and heat.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- For professional use only.
- Directions should be read and followed carefully.
- Test devices, tubes and pipettes are for single use only. Do not reuse.
- Do not use kits or reagents beyond the stated expiration dates.
- Reagents are provided at the necessary working strength. Do not dilute reagents.
- Microbial contamination of regents may decrease the accuracy of the assay.
- Treat all materials as if they were infectious and dispose of all material in accordance with local regulation. Liquid waste should be disposed of in a 1% sodium hypochlorite solution or in accordance with local requirements for disposal of infectious material.
- Extraction buffer, positive control and negative control contains <0.1% sodium azide. Sodium azide is toxic if ingested and forms potentially explosive copper and lead azide compounds in waste plumbing lines. Should the reagents come in contact with copper or lead waste plumbing, flush the waste line with large quantities of water to prevent the formation of potentially explosive compounds.
- The test strip is sealed in a protective foil pouch. Do not use if pouch is opened or damaged.
- Only remove test strips from pouches immediately before use.
- Do not touch the reaction area of test strip.
- Do not use damaged strips.
- Do not interchange reagents between kits with different lot numbers.

SPECIMEN COLLECTION AND TRANSPORT

Urine and CSF specimens collected for routine examination can be used with Uni-Gold™ S. pneumoniae. Urine specimens should be collected in clean, standard sterile containers and CSF should be collected in CSF transport tubes.

Ensure all samples are brought to room temperature (15-30°C) and are properly mixed prior to running the test.

URINE

- Test specimens stored at room temperature (15-30°C) within 24 hours of collection. Specimens with excess urates, phosphates or other dissolved salts may develop salt crystals after storage.
- Specimens stored at 2-8°C may be kept for up to 14 days before testing.
- Frozen samples (-20°C) may be stored for up to 14 days before testing. Ensure frozen samples are fully thawed and mixed prior to testing. Avoid multiple freeze-thaw cycles.
- Ensure all samples are brought to room temperature (15-30°C) and are properly mixed prior to running the test.
- Boric acid may be used as a preservative for stored urine samples.

CSF

- Test specimens stored at room temperature (15-30°C) within 24 hours of collection.
- Specimens stored at 2-8°C may be kept for up to 1 week before testing.
- If samples are to be kept longer than 1 week they should be stored frozen (≤ -60°C) before testing. Avoid multiple freeze-thaw cycles.

QUALITY CONTROL

Good Laboratory Practice (GLP) recommends the use of control specimens to ensure proper device performance at least once daily. Uni-Gold™ S. pneumoniae controls are used to verify correct device performance, operator procedure and result interpretation. The positive control will produce a reactive test result and the negative control will produce a non-reactive test result (refer to the Interpretation of Results section).

It is recommended that positive and negative controls are run:

- By all new operators who will perform testing on patient specimens.
- With each new kit lot and whenever a new shipment of test kits is received.
- At periodic intervals as specified in the Laboratory Quality Assurance Programme.

Uni-Gold™ S. pneumoniae controls must give the expected reactive or non-reactive results. If the test results are not valid repeat the test with a new device. Refer to Test Procedure section for instructions on the use of these reagents. It is the responsibility of each laboratory using the Uni-Gold™ S. pneumoniae to establish an adequate quality assurance programme to ensure the performance of the device under its specific conditions of use. Contact Trinity Biotech should unexpected results occur.

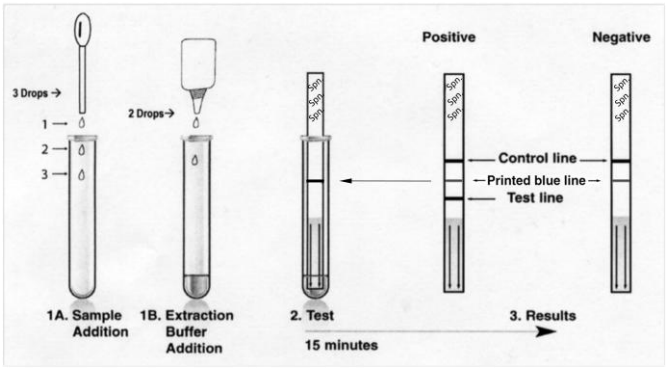
Each Uni-Gold™ S. pneumoniae device has a built in procedural control that demonstrates assay validity. When a pink/red line appears at the control line position this indicates the device has performed correctly. The control line will appear on all valid tests, whether or not the sample is reactive or non-reactive (refer to the Interpretation of Results section).

LIMITATIONS

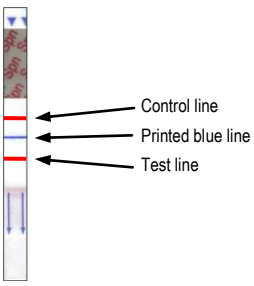
- Uni-Gold™ S. pneumoniae must be used in accordance with the instructions in this package insert to obtain an accurate result.
- A negative test result does not exclude the possibility of the presence of *S. pneumoniae*. This may occur when the antigen level in the sample is below the detection level of the test. Correlation between the amount of antigen in a sample and clinical presentation has not been established. Alternatively, an infection caused by other streptococci species or subgroups may be present.
- Uni-Gold™ S. pneumoniae detects *S. pneumoniae* antigen in urine and CSF samples. The level of the antigen may vary depending on the individual patient and the stage of disease. The test cannot be used to derive a relationship between the intensity of the visible bands and the occurrence or severity of clinical symptoms.
- The results obtained are intended to aid in diagnosis only. All *in vitro* diagnostics test results must always be interpreted by the clinician in combination with the clinical evaluation, medical history, and/or other laboratory results to properly diagnose patients.
- The diagnosis of *S. pneumoniae* infection cannot be based on clinical or radiological evidence alone. There is no single satisfactory laboratory test for *S. pneumoniae*. For this reason, culture results, PCR and/or antigen detection methods should be used in conjunction with clinical findings, e.g. chest X-rays, to make an accurate diagnosis.
- Reading test results before or after the 15 minute read time may give incorrect results.
- Proper specimen collection and processing are essential to achieve the optimal performance of the assay.
- If the incorrect volume of sample is used with Uni-Gold™ S. pneumoniae, false positive or false negative results may occur.
- The extraction buffer is key to the performance of the test. If insufficient extraction buffer is added to a sample prior to testing with Uni-Gold™ S. pneumoniae, false positive results may occur.
- The effect of vaccination or treatment with antibiotics on the performance of the Uni-Gold™ S. pneumoniae has not been established.
- Uni-Gold™ S. pneumoniae has not been validated for use with samples from children.
- Uni-Gold™ S. pneumoniae has been validated using urine and CSF samples only. Other samples (e.g. plasma, serum or other body fluids) that may contain *S. pneumoniae* antigen have not been evaluated. The test cannot be used on environmental samples.
- Uni-Gold™ S. pneumoniae has not been validated using urine samples that have been boiled or concentrated prior to testing.

TEST PROCEDURE

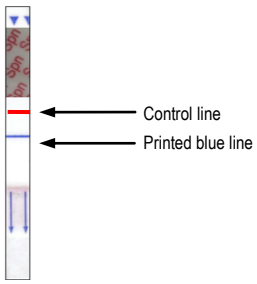
1. Ensure the Uni-Gold™ S. pneumoniae kit is at room temperature (15-30˚C). Gently mix the extraction buffer before use.
2. Fold test tube holder according to pictorial instructions printed on the test tube holder.
3. Label test tubes with appropriate patient information and place in rack.
4. Sample preparation (diagram 1A and 1B below)
   - Ensure specimens are at room temperature (15-30°C) prior to testing.
   - Mix samples thoroughly. Treat patient samples and controls in the same way.
   - Fill the pipette with sample and holding it vertically, add three (3) drops of the sample to the test tube.
   - Holding the dropper bottle vertically, add two (2) drops of extraction buffer.
   - Mix gently.
5. Remove each test strip from its pouch immediately before inserting it into the sample/extraction buffer mix.
6. Hold the "Spn" section of the test strip, insert the strip into the test tube (arrows pointing downwards (diagram 2 below). Time the assay from this point, incubate for 15 minutes.
7. Read assay results immediately at 15 minutes (diagram 3 below). Do not read strips after 15 minutes as the results may be inaccurate.
8. Discard the test strip after result is interpreted.



INTERPRETATION OF RESULTS

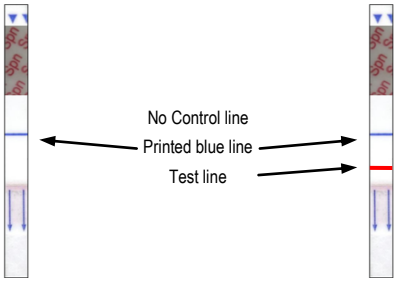


Positive Result: Two pink/red colored lines of any intensity located above and below the central blue printed line. This indicates a reactive result that is interpreted as positive for *S. pneumoniae* antigen.



Negative Result: A single pink/red control line of any intensity above the central blue printed line. There is no line at the test line position. This indicates a non-reactive result that is interpreted as negative for *S. pneumoniae* antigen.

Invalid Result: No line appears on the strip at the control line position. This is an invalid result and cannot be interpreted. This is irrespective of whether or not a pink/red line appears at the test line position. If either condition occurs, the test should be repeated with a new device.



Please note that any reference to a 'line' or a 'line of any intensity' at the test region (below central blue line) of the strip is only deemed a positive test line if it is 'pink/red' in color. Similarly for the control line, a 'line' or a 'line of any intensity' at the control region (above central blue line) of the strip is only deemed valid if it is 'pink/red' in color.

PERFORMANCE CHARACTERISTICS

The performance of Uni-Gold™ S. pneumoniae was evaluated on 298 retrospective urine samples at an external clinical laboratory.

Clinical Sensitivity & Specificity

The sensitivity and specificity of the test with urine was compared against blood culture with retrospective samples as shown in the following table.

S. pneumoniae		Blood Culture	
		(+) Positive	(-) Negative
Uni-Gold™	(+) Positive	64	17
	(-) Negative	9	208
	Total	73	225

Sensitivity: 87.7% (64/73) 95%CI 77.4 – 93.9%

Specificity: 92.4% (208/225) 95%CI 87.9 – 95.4%

Concordance Study

Uni-Gold™ S. pneumoniae was compared to a commercially available lateral flow test on 298 retrospective urine samples. The percent agreement of Uni-Gold™ S. pneumoniae versus the comparator device was as follows:

S. pneumoniae		Comparator Device	
		(+) Positive	(-) Negative
Uni-Gold™	(+) Positive	66	15
	(-) Negative	0	217
	Total	66	232

Overall Agreement: 95%

Uni-Gold™ S. pneumoniae was compared to a commercially available lateral flow test on 45 retrospective CSF samples. The results of the Uni-Gold™ S. pneumoniae versus the comparator device are as follows:

S. pneumoniae		Comparator device	
		(+) Positive	(-) Negative
Uni-Gold™	(+) Positive	0	0
	(-) Negative	0	45
	Total	0	45

Expected Values

The performance of Uni-Gold™ S. pneumoniae was evaluated at internal and external laboratories. Both male and female urine samples were collected from hospitals throughout Northern Europe. The retrospective study included 73 positive samples and 225 negative samples confirmed by blood culture. No differences were observed in clinical performance between male or female populations.

Serotype detection

Antigen from 92 different *S. pneumoniae* serotypes was purified and diluted into negative urine. When tested with Uni-Gold™ S. pneumoniae, all 92 serotypes were detected.

Analytical Sensitivity:

The limit of detection was determined for both urine and CSF by spiking purified antigen into negative specimens. The samples were diluted and tested with the Uni-Gold™ S. pneumoniae to determine the lowest concentration that produced a positive result. The limit of detection for Uni-Gold™ S. pneumoniae for both urine and CSF was 45 pg/mL.

Cross Reactivity.

No cross-reactivity was observed with *S. pneumoniae* negative urine samples containing the following organisms. Test concentrations ranged from 10^6 cfu/mL to 10^7 cfu/mL:

Acinetobacter (4)
Bacillus subtilis
Bordetella Pertussis
Branhamella catarrhalis
Candida albicans (4)
Corynebacterium aquaticum (2)
Corynebacterium spp.
E. cloacea (4)
E. coli (10)
E. faecalis (8)
Enterococcus durans
G. vaginalis
H. influenza a
H. influenza b
H. influenza c
H. influenza d
H. influenza e
H. influenza f
H. influenza non caps
H. influenzae (4)
H. parainfluenzae
K. oxytoca (2)
K. pneumoniae (3)
L. pneumophila (sg 1 Knoxville)
L. pneumophila (sg 3)
Lactobacillus catenaforme
Lactobacillus rhamnosus
Lactobacillus spp.
Listeria monocytogenes
M. morganii
Moraxella osloensis
Mycoplasma spp.
N. cineria
N. gonorrhoeae (3)
N. lactamica
N. meningitidis
N. polysak
P. mirabilis (2)
P. vulgaris (2)
P. aeruginosa (4)
P. stutzeri
Pseudomonas spp (2)
S. bredeney
S. epidermidis
S. mutans (2)
S. parasanquis
S. sanquis
S. thomson
S. typhimurium
S.glostrup
Serratia marcescens
S. aureus (6)
S. epidermidis (5)
S. saprophyticus(2)
Stenotrophomonas maltophilia
Streptococcus gr. A
Streptococcus Gr. A (colindale)
Streptococcus gr. B (10)
Streptococcus gr. C
Streptococcus gr. F
Streptococcus gr. G
Streptococcus gr. L

Clinical samples: Of 71 different organisms isolated from clinical samples (patients with UTI), 9 (12.7%) produced positive results with Uni-Gold™ S. pneumoniae. The organisms in question were *Aerococcus spp*. (2/3), *Citrobacter braakii* (1/1), *Enterobacter cloacae* (1/2), *Enterococcus spp*. (3/9), *Klebsiella pneumoniae* (1/7) and *Proteus mirabilis* (1/2).

Interfering Substances

The analytical sensitivity and specificity of the test was determined in urine samples containing potentially interfering substances at clinically relevant concentrations. Compounds were respectively spiked into positive and negative samples at medically relevant dosages (treatment) or were clinically obtained samples. The following compounds/conditions were tested: elevated glucose (2000mg/dL), protein (500mg/dL & 2000mg/dL), low pH (down to pH 5.0), elevated white blood cells, elevated red blood cells, HCG positive status and turbidity. No test interference was observed by any of the conditions or of the compounds at the concentrations tested above.

Reproducibility Study

Reproducibility testing was carried out on 12 blinded urine samples (both positive and negative samples) by two operators, twice daily for five days at three sites. 100% of the samples tested for *S. pneumoniae* produced the expected results.

REFERENCES

1. Community-acquired pneumonia. File TM. Lancet 2003, 362: 1991 – 2001.
2. Severe pneumococcal pneumonia. New strategies for management. Chiou CCC, Yu VL Curr Opin Crit Care 2006, 12: 470-476.
3. A 3-year prospective study of a urinary antigen-detection test for *Streptococcus pneumoniae* in community-acquired pneumonia: utility and clinical impact on the reported etiology. Ishida T, Hashimoto T, Arita M, Tojo Y, Tachibana H, Jinnai M. 2004 J Infect Chemother 10: 359-63.
4. Development of a sensitive, multiplexed immunoassay using xMAP beads for detection of serotype-specific *Streptococcus pneumoniae* antigen in urine samples. Sheppard CL, Harrison TG, Smith MD, George RC. 2011 J Med Microbiol 60: 49-55.
5. Rapid diagnosis of pneumococcal meningitis: implications for treatment and measuring disease burden. Saha SK, Darmstadt GL, Yamanaka N, Billal DS, Nasreen T, Islam M, Hamer DH. Pediatr Infect Dis J. 2005, 24(12):1093-8.

ORDERING INFORMATION

Cat. No.	Item	Quantity
1204420	Uni-Gold™ S. pneumoniae	20 devices

GUIDE TO SYMBOLS


Consult Instructions for Use

REF — Product Number

LOT — Lot Number

IVD — *In Vitro* Diagnostic Medical

BUF\EXT — Extraction Buffer


Use By


Caution, consult accompanying documents


Temperature limitation


Manufacturer


Irritant – Precaution
X_i - R36/37/38

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1204420-29 Rev. 3
4/2014