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# Staphaurex Plus*

## INTENDED USE

Staphaurex Plus* is a rapid latex agglutination test for the identification of staphylococci which possess clumping factor, protein A and/or surface antigens characteristic of *Staphylococcus aureus*.

## SUMMARY AND EXPLANATION OF THE TEST

*S. aureus* possess a number of properties which are used to confirm identification. These include free coagulase, clumping factor (bound coagulase), thermonuclease and protein A[1]. The tube coagulase test detects free coagulase and is considered as a reference test for *S. aureus*[1]. This test, however, takes 4 to 24 hours and plasma may show a lot-to-lot variation[2]. Over the past decade particle agglutination assays have been developed which give a much more rapid identification[3,4]. These first generation assays are based on latex particles or red cells coated with either fibrinogen alone, to detect clumping factor, or fibrinogen and immunoglobulin G (IgG), to detect both clumping factor and staphylococcal protein A.

Recently it has been shown that these tests can fail to detect certain strains of *S. aureus*, particularly a proportion of methicillin/oxacillin resistant strains (MRSA)[5,6,7]. Some of these strains may express undetectable levels of clumping factor and protein A[8].

Two antigens, somatic type 18[9] and capsular type 5[10,11] have been associated with the methicillin-resistant phenotype. The incorporation of antisera to these antigens may improve the sensitivity of agglutination assays for MRSA strains. Investigations on strains that are negative in rapid assays have shown that antibodies to a single somatic or capsular antigen are insufficient to detect all strains that are negative with the first generation of particle agglutination tests. Staphaurex Plus* uses latex beads coated with fibrinogen to detect the majority of clinical strains and IgG specific for a carefully selected group of strains that are negative in the first generation tests.

## PRINCIPLE OF THE PROCEDURE

The Staphaurex Plus* Test Latex consists of yellow latex particles which have been coated with fibrinogen and rabbit immunoglobulin G (IgG) specific for *S. aureus*. When a drop of the reagent is mixed on a card with *S. aureus* organisms, rapid agglutination occurs through the interaction of (i) fibrinogen and clumping factor, (ii) the Fc portion of IgG and protein A or (iii) specific IgG and cell surface antigens.

Some strains of *Staphylococcus spp*., particularly *S. saprophyticus*, may cause non-specific aggregation of latex particles. Therefore a Control Latex is provided to assist with the identification of non-specific reactions.

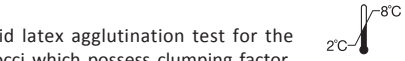
## REAGENTS

KIT CONTENTS

| Staphaurex Plus* | ZL33/R30950102 150 Tests | ZL34/R30950201 450 Tests |
|---|---|---|
| 1. Test Latex (Yellow cap) | 1 dropper bottle | 3 dropper bottles |
| 2. Control Latex (Grey cap) | 1 dropper bottle | 3 dropper bottles |
| 3. Disposable Reaction Cards (RT64/R30369001) | 2 packs | 6 packs |
| 4. Disposable Mixing Sticks | 3 bundles | 9 bundles |
| 5. Instructions for Use | 1 | 1 |

DESCRIPTION OF REAGENTS, PREPARATION FOR USE AND RECOMMENDED STORAGE CONDITIONS

See also **Warnings and Precautions**.




The latex suspensions are provided ready to use and should be stored in an upright position at 2 to 8°C, where they will retain activity at least until the date shown on the bottle label. Do not freeze. Avoid storage at room temperature (15 to 30°C). Do not stand the reagent in bright light on the bench.

TEST LATEX ⚠

**Test Latex**

A buffered suspension of yellow polystyrene latex particles coated with human fibrinogen and rabbit IgG. Contains 0.05% Bronidox® preservative[12].

Materials of human origin have been tested for the presence of hepatitis B surface antigen, anti-HCV and anti-HIV-1/HIV-2 and found to be negative.

CONTROL LATEX

**Control Latex**

A buffered suspension of yellow polystyrene latex particles coated with a bovine serum protein unreactive with *S. aureus*. Contains 0.05% Bronidox® preservative[12].

Reaction Cards and Mixing Sticks should be stored at room temperature (15 to 30°C). Staphaurex Plus* (ZL33/R30950102 and ZL34/R30950201) was developed using RT64/R30369001 Disposable Reaction Cards. Do not substitute another disposable slide for the RT64/R30369001 Disposable Reaction Cards when samples are tested using Staphaurex Plus*.

## WARNINGS AND PRECAUTIONS

IVD

For *in vitro* diagnostic use only.

For professional use only.

Please refer to the manufacturer's safety data sheet and the product labelling for information on potentially hazardous components.

HEALTH AND SAFETY INFORMATION

1. CAUTION: This kit contains human sourced components. No known test can offer complete assurance that products derived from human sources will not transmit infection. Therefore, all human sourced material should be considered potentially infectious. It is recommended that these reagents and test specimens be handled using established good laboratory working practices.
2. 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. Materials used to clean spills, including gloves, should be disposed of as biohazardous waste.
3. Wear laboratory coat, disposable gloves and eye protection while handling specimens and performing the assay. Wash hands thoroughly when finished.
4. When used in accordance with the principles of Good Laboratory Practice, good standards of occupational hygiene and the instructions in these Instructions for Use, the reagents supplied are not considered to present a hazard to health.

ANALYTICAL PRECAUTIONS

1. Do not use the reagents beyond the stated expiry date.
2. Latex reagents should be brought to room temperature (15 to 30°C) before use. Latex reagents which show signs of aggregation or 'lumpiness' before use may have been frozen and should not be used.
3. 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 proceeding.
4. Do not touch the reaction areas on the cards.
5. Do not interpret agglutination that appears after 30 seconds as a positive result. Prolonged rocking can result in false-positive reactions with some coagulase-negative isolates.
6. Microbiological contamination of reagents must be avoided as this may reduce the life of the product and cause erroneous results.

## SPECIMEN COLLECTION AND STORAGE

For details of specimen collection and treatment a standard text book should be consulted[1]. Cultures may be tested from any of the following media:

Blood agar
Nutrient agar
Tryptone soya agar
Tryptone soya agar with 5% blood
Columbia blood agar
Columbia CNA agar
Mueller Hinton agar with 5% blood
Baird-Parker agar
Mannitol-salt agar†

†Note: specimens grown on media containing antibiotics or a high-salt-supplemented medium such as Mannitol-salt agar may give an agglutination containing stringy aggregates.

THE USE OF FRESH CULTURES GROWN OVERNIGHT IS RECOMMENDED.

## PROCEDURE

MATERIALS PROVIDED

Sufficient materials are provided for 150 (ZL33/R30950102) or 450 (ZL34/R30950201) tests, see **Kit Contents**.

TEST PROCEDURE

Please read **Analytical Precautions** carefully before performing the test.

| | | |
|---|---|---|
| **Step 1** | Shake vigorously and examine the latex reagents for aggregation before use. Refer to **Quality Control** Section and **Visual Inspection** for additional instructions. | |
| **Step 2** | For each test sample place one drop of **Test Latex** in one circle on a Reaction Card (RT64/R30369001) and one drop of **Control Latex** in a separate circle. Ensure that the dropper bottles are held vertically to dispense an accurate drop. | **1 drop** |
| **Step 3** | Using a mixing stick, remove sufficient growth from a pure culture or well-isolated colonies to cover the blunt end of the stick. As a guide, an amount of growth roughly equivalent to six average-sized colonies should be used. | |
| **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 too vigorously or the surface of the card may be damaged. Some strains, particularly of species other than *S. aureus* remain difficult to emulsify and this should be noted, since lumps of unemulsified culture can make the latex appear 'rough' or 'stringy' when read. Spread the latex over approximately half the area of the circle. Discard the mixing stick for safe disposal. | **Emulsify sample** |
| **Step 5** | Using a separate stick, emulsify a similar culture sample in the **Control Latex**, as stated in Step 4. Discard the mixing stick for safe disposal. | **Emulsify sample** |
| **Step 6** | Rock the card slowly for up to 30 seconds while observing for agglutination. The card should be held at normal reading distance (25 to 35 cm) from the eyes. Do not use a magnifying lens. | **Rock** |
| **Step 7** | Discard the used Reaction Card for safe disposal. | |

## RESULTS

**Positive Result**

Agglutination of the Test Latex accompanied by a lack of agglutination of the Control Latex indicates the presence of either coagulase, protein A or antigens commonly found on *S. aureus* in the culture under test. Most positive reactions will be almost instantaneous. False positive results can occur if the test is read after more than 30 seconds.

**Negative Result**

Lack of agglutination in both reagents means that the culture under test is unlikely to be *S. aureus*.

**Non-interpretable Result**

Visible agglutination of the Control Latex, whether stronger or weaker than the Test Latex, indicates a non-specific reaction.

QUALITY CONTROL

Quality control testing should be run with each shipment and new kit lot number received. Each laboratory should follow their state and local requirements.

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. If there is evidence of clumping before addition of the test sample the suspension should 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.

**Control procedure**

The performance of the Test and Control Latex reagents should be confirmed using fresh, overnight cultures of reference strains of bacteria, following the method described in **Test Procedure**. Suitable reference strains are shown below.

| SPECIES | EXPECTED RESULT | |
|---|---|---|
| | TEST LATEX | CONTROL LATEX |
| *S. aureus* (ATCC® 25923™) | + | – |
| *S. epidermidis* (ATCC® 12228™) | – | – |

INTERPRETATION OF RESULTS

A positive reaction indicates the presence of one or more of clumping factor, protein A or cell surface antigens in the culture under test and a negative result indicates their absence.

## LIMITATIONS OF THE PROCEDURE

1. Specimens grown on media containing antibiotics or a high-salt-supplemented medium such as mannitol-salt agar may give an agglutination containing stringy aggregates.
2. Some species of staphylococci in addition to *S. aureus* notably *S. hyicus, S. intermedius, S. lugdunensis* and *S. schleiferi*, may give positive results in coagulase tests and may also react in rapid latex procedures. If necessary these species may be identified by biochemical test procedures. *S. hyicus* and *S. intermedius* are encountered rarely in the clinical laboratory.
3. Some other coagulase negative staphylococcal species, such as *S. capitis* possess plasma protein binding factors, which do not react in the Staphaurex Plus* test. However, a few strains identified biochemically as *S. saprophyticus* have given weak positive reactions and further identification of urinary isolates may be required.
4. Some streptococci and possibly other organisms possess immunoglobulin or other plasma protein binding factors which can react in the latex test and there are several bacteria such as *E. coli*, which are able to non-specifically agglutinate latex particles. To eliminate potential interference from these organisms a Gram stain and catalase test should be performed so that only organisms with staphylococcal morphology are tested.
5. All questionable results should be checked for purity and identified by an alternative method.

## EXPECTED RESULTS

Strong agglutination with *S. aureus* cultures, no agglutination with staphylococci which possess neither clumping factor, protein A or surface antigens characteristic of *S. aureus*.

## SPECIFIC PERFORMANCE CHARACTERISTICS

The performance of Staphaurex Plus* has been evaluated in four North American and two European microbiological reference laboratories on a total of 646 routine (presumed staphylococcal) clinical isolates and 671 stored cultures. The cultures were tested in parallel with the tube coagulase procedure, Gram stain and at least one alternative rapid test for the identification of *S. aureus*. The results are summarised **Tables 1** and **2**.

CLINICAL ISOLATES

**Methicillin Resistant *S. aureus* (MRSA)**

A total of 151 fresh *S. aureus* cultures shown to be resistant to one or more antibiotics were tested in the American and European reference laboratories. Staphaurex Plus* correctly identified 150 of these isolates. The discrepant isolate was positive with a tube coagulase test and an alternative rapid latex test.

The sensitivity of Staphaurex Plus* on this group of MRSA cultures is estimated to be 99.34% (150/151).

**Methicillin Sensitive *S. aureus* (MSSA)**

Staphaurex Plus* correctly identified 335 of 337 confirmed *S. aureus* cultures from the microbiological reference laboratories. The discrepant isolates included one which also gave a negative result with the alternative rapid latex test.

The sensitivity of Staphaurex Plus* on this group of MSSA cultures is estimated to be 99.41% (335/337).

**Other staphylococci**

A total of 157 fresh non-*S. aureus* staphylococcal isolates were also tested. Staphaurex Plus* gave a negative result with 150 of these isolates which included *S. saprophyticus, S. epidermidis* and *S. haemolyticus*. The remaining seven cultures which gave a positive result with Staphaurex Plus* included three which were also positive with an alternative rapid latex test.

The specificity of Staphaurex Plus* on this group of non-*S. aureus* staphylococcal cultures is estimated to be 95.54% (150/157).

**Overall Performance of Staphaurex Plus* in Comparison with Tube Coagulase on *S. aureus* Isolates**

| | |
|---|---|
| Relative Sensitivity | 99.4% |
| Relative Specificity | 95.5% |
| Overall agreement | 98.4% |

NOTE: Staphaurex Plus* gave a non-interpretable result with 0.15% (1/646) of the fresh cultures, which has been excluded from the summary above.

STORED CULTURES

**Methicillin Resistant *S. aureus* (MRSA)**

A total of 282 stored *S. aureus* cultures shown to be resistant to one or more antibiotics were tested. Staphaurex Plus* correctly identified 281 of these isolates. The discrepant culture was positive with a tube coagulase test and negative with an alternative rapid latex test.

The sensitivity of Staphaurex Plus* on this group of MRSA cultures is estimated to be 99.65% (281/282).

**Methicillin Sensitive *S. aureus* (MSSA)**

Staphaurex Plus* correctly identified 242 of 248 confirmed *S. aureus* cultures from the microbiological reference laboratories. The discrepant cultures included four which also gave a negative result with the alternative rapid latex test.

The sensitivity of Staphaurex Plus* on this group of MSSA cultures is estimated to be 97.6% (242/248).

**Other staphylococci**

A total of 139 stored non-*S. aureus* staphylococcal cultures were also tested. Staphaurex Plus* gave a negative result with 132 of these isolates which included *S. saprophyticus, S. epidermidis* and *S. haemolyticus*. The remaining seven cultures which gave a positive result with Staphaurex Plus* included two which were also positive with an alternative rapid latex test.

The specificity of Staphaurex Plus* on this group of non-*S. aureus* staphylococcal cultures is estimated to be 95.0% (132/139).

**Overall Performance of Staphaurex Plus* in Comparison with Tube Coagulase on stored *S. aureus* Cultures**

| | |
|---|---|
| Relative Sensitivity | 98.7% |
| Relative Specificity | 95.0% |
| Overall agreement | 97.9% |

NOTE: Staphaurex Plus* gave a non-interpretable result with 0.3% (2/671) of the stored cultures, which has been excluded from the summary above.

**Table 1**

**Reactivity of Staphaurex Plus* on Presumed Staphylococcal Clinical Isolates[a]**

| | Staphaurex Plus* result | | |
|---|---|---|---|
| | Positive | Negative | Total |
| Methicillin Resistant *S. aureus* (MRSA) | 150 | 1 | 151 |
| Methicillin Sensitive *S. aureus* (MSSA) | 335 | 2 | 337 |
| Non-*S. aureus* isolates[b] | 7 | 150 | 157 |

[a] Staphaurex Plus* gave a non-interpretable result with 1 sample. This has been excluded from the table.

[b] includes *S. saprophyticus, S. epidermidis* and *S. haemolyticus*.

**Table 2**

**Reactivity of Staphaurex Plus* on Stored Staphylococcal Cultures[a]**

| | Staphaurex Plus* result | | |
|---|---|---|---|
| | Positive | Negative | Total |
| Methicillin Resistant *S. aureus* (MRSA) | 281 | 1 | 282 |
| Methicillin Sensitive *S. aureus* (MSSA) | 242 | 6 | 248 |
| Non-*S. aureus* cultures[b] | 7 | 132 | 139 |

[a] Staphaurex Plus* gave a non-interpretable result with 2 samples. These have been excluded from the table.

[b] includes *S. saprophyticus, S. epidermidis* and *S. haemolyticus*.

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## PACKAGING

REF ZL33/R30950102..... 150 tests
ZL34/R30950201..... 450 tests

**Symbol legend**

| | |
|---|---|
| REF | Catalog Number |
| IVD | *In vitro* diagnostic medical device |
| | Consult instruction for use (IFU) |
| | Temperature limitation (Storage Temp.) |
| LOT | Batch code (Lot Number) |
| | Use by (Expiration Date) |
| | Caution, consult accompanying documents |
| | Manufacturer |

CE

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ATCC® is a registered trademark of American Type Culture Collection.
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IFU X7826 revised March 2012 Printed in the UK



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