QuickVue ® In-line Strep A test
Test in Laboratory
Ordered by
Medinor A/S, Postbox 321, Langebjerg 35, 4000 Roskilde

Rapport from laboratory testing
In SKUP

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Testing of QuickVue® In-line Strep A test

CONTENT

SUMMARY

Background Medinor AS ordered a SKUP laboratory testing of QuickVue® In-line Strep A in September 2003 due to great interest from GP. In Scandinavia, there is no consensus on diagnosis and treatment of hemolytic streptococci.

Principle of the test. QuickVue® In-line Strep A test is an immunochromogen method. A throat swab specimen is collected and inserted into the Swab Chamber of the Test Cassette. The Extraction Solutions are mixed and added to extract the antigenic component of the bacteria. The extracted sample flows through a label pad containing rabbit polyclonal anti-strep A antibody and a blue control label. If the extracted solution contains strep A antigen, it will be seen as a pink-to-purple Test Line. A blue Control Line should always appear in a properly functioning Test Cassette. If strep A is not present or present at very low levels, only a blue Control Line will be visible. The result of the test should be read after 5 minutes at 15-30^0 C.

Analytical quality counts 50 % of the total validation. Parameters evaluated:
1) Equivalence point. 2a) Specificity, defined by measuring other streptococci (True negative)/ (false positive + true negative). 2b) Specificity, defined from Equivalence point (True negative)/ (false positive + true negative). 3) Validation of practical use: intra-person and inter-person variation. 4) Percent of tests not valid. 5) Does the test turn positive at the time told in the insert? 6) Does the result change during time?

Practability counts 50 % of the total validation. Parameters evaluated: insert, time, possibility of quality control, operation of the test, and other factors. The results of the evaluation are indicated as follows: not relevant, not satisfactory = 0 point, less satisfactory = 1, satisfactory = 2 and very satisfactory = 3 points. Each of the 5 areas has to achieve $\geq$ 2 points.

Method

To decide the detection limits of QuickVue® In-line Strep A test we used serial dilutions of a known amount of *S. pyogenes* in seven different concentrations, one mix of four other streptococci-strains and a positive and a negative control. The extraction solution is filled into the chamber after the swab has been placed there. The result of the tests is read by 4 independent persons.

Results, *analytical quality.*

1) Equivalence point: about 8.5×10^5 hemolytic streptococci/ml.

2a) Specificity: *95.3 %. (61 of 64).*

2b) Specificity: *96.25 % $\leq 8.5 \times 10^4$* ***hemolytic streptococci/ml. (308 readings of 320)***

3a) Intra-person reading: *No disagreement.*

3b) Inter-person disagreement of reading: *1.4 % of the test (2/144).*

4) Invalid tests*: 0.4 % (3 of 640).*

5) The test is positive at 5 minutes: yes*.*

6) False positive later than 5 minutes*: see text, table1 and photos.*

6b) False negative: *0 % at a concentration of > 8.5×10^5/ml.*

Results, *practability.* The 4 test persons could distinguish between True positives and False positives, however this can not be expected in routine. See comments.

Conclusion

QuickVue In-line® Strep A test does not fulfil the criteria for good performing in this analysis. The reason why, is the possibility of false positives due to a transitory, diffuse, red band that passes some of the test windows. The band appears within a space of 2 to 15 minutes, and the duration of the bands is about 90 seconds. Twenty-four % of the tests had to be "re-started" after 60 seconds. There is no correlation between the bands and the "re-starting" of the test. We do not expect that QuickVue In-line will perform better in less standardised conditions in the hands of General Practitioners.

PLANNING of QuickVue In-line Strep A LABORATORY TESTING

In September 2003 Medinor had two tests in which the general practitioners were very interested. A laboratory test according to the protocol was ordered and was performed in November 2003. The results of the test were not satisfactory. The procedures of the insert could not be followed, and it was expected by the company, that there had been a production failure on the tests. A new laboratory test was performed February 2004.

Department of Clinical Microbiology, Odense University Hospital (Dpt.. KMA, OUH), and Professor Hans Jørn Kolmos is the "reference laboratory" in Denmark.

In Scandinavia, there is no consensus of diagnosis and treatment of hemolytic streptococci. Denmark is homogenous compared to Norway and Sweden, because Denmark has used the methods of Statens Serum Institute (SSI) as a golden standard for diagnosis of Strep A.

This is the 4th test made by SKUP with results on ordinal scale. It is expected that the Strep A laboratory tests will create precedence for coming tests of Strep A and other tests on ordinal scale.

It has been a wish from the General Practitioners in Denmark that analytical quality and practability are weighted equally.

The goal of the laboratory tests is to investigate the analytical performance and the practability under standardised and optimal conditions. Bad tests with false positive or false negative results, a high variation in reading (intra- and inter-personal) or a high time consumption for analysis can be sorted out at this point.

- The laboratory testing is done in department KMA and department KKA, Odense University Hospital.
- Esther Jensen is responsible for the testing.

  The work is done by the lab. technicians Ann Mains, Nina Brøgger, Ann Jepsen, KKA, and Elisa Knudsen, Anette Knudsen, KMA. Secretary Jette Hedelund, KKA and medical doctor Hanne Holt (KMA) and Esther Jensen (KKA)

  Esther Jensen and Hanne Holt have written the protocol. The protocol is approved by SKUP and has to be approved by the claimant.

- SKUP writes a contract with the claimant.
- The claimant gives SKUP the disposal of the equipment necessary for testing. Teaching is not expected before performing the test, as it is not demanded before sale.
- Calculating of data is done by SKUP. (Esther Jensen).
- Esther Jensen writes the report of the testing. The report is approved by Hanne Holt, KMA. Then it is sent to the claimant and SKUP. Both get the opportunity to discuss and comment the report.
- After (analysis) the report is published by SKUP, if the test is sold in Scandinavia.
- A good laboratory test is expected to be followed by an investigation in General Practice under "real" conditions. The results in General Practice is not expected to be better than the laboratory test.

ADDRESSES

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Department of Clinical Microbiology (KMA)
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METHOD
Qualitative detection of group A streptococcal antigen. The streptococci can be dead or alive.

Principle of the test.
To perform the test, a throat swab specimen is collected and inserted into the Swab Chamber of the Test Cassette. The Extraction Solutions are mixed, resulting in a green color change, and added to the swab in the Swab Chamber in order for the antigenic component of the bacteria to be extracted. Extraction begins instantaneously, after which the extracted solution flows from the Swab Chamber onto the test strip by capillary action. The extracted sample flows through a label pad consisting of a pink label containing rabbit polyclonal anti-strep A antibody and a blue control label. If the extracted solution contains strep A antigen, the antigen will bind to the antibody on the pink test label which, in turn, will bind a rabbit polyclonal anti-strep A antibody spotted on the membrane, resulting in the formation of a pink-to-purple Test Line. A blue Control Line will also appear next to the letter "C" on the Test Cassette indicating that the reagents were mixed and added properly, proper volume of fluid entered the Test Cassette and capillary flow occurred. A blue Control Line should always appear in a properly functioning Test Cassette. If strep A is not present or present at very low levels, only a blue Control Line will be visible.

Reagents and materials supplied.
QuickVue® In-line Strep A test
Content: 25 individually packaged Test Cassette, lot 145800, Expiration date December 7th 2004
25 individually packaged sterile rayon-tipped swabs lot 8001. Expiration date 2008/09
25 Extraction Solution Bottles 4M Sodium Nitrite (0.6 mL), and 0,2M Acetic Acid (0.65 mL) inside glass ampule, lot 145228, Expiration date November 26th 2004.
1 Positive Control Swab (+): Heat-inactivated group A Streptococcus, lot 144973,
1 Negative Control Swab (-): Heat-inactivated group A Streptococcus, lot 144228,
1 Package Insert.
1 Procedure Card.
5 Tubes and 5 Disposable Droppers for use with Proficiency Testing Samples only. Refer to the Proficiency Testing Section for instructions for use.

Lot nr. 700882, Expiration date November 26th 2004.

Producer: Quidel Corporation, Worldwide Headquarters, 10165 McKellar Court, San Diego, Californien 92121 USA, www.quidel.com

Agent in Denmark: Medinor A/S, Postbox 321, Langebjerg 35, DK-4000 Roskilde, Denmark

Test period: February 2004

Writing of Report: February 2004

Material

For the serial dilutions the reference strain *S. pyogenes* (ATCC 19615) was used. For the the mixture of different streptococci the following four rutine isolates from throat specimens were used: hemolytic streptococcus group C, hemolytic streptococcus group F, hemolytic streptococcus group G and an alfa-hemolytic streptococcus.

The grouping was done by Streptococcal Grouping Kit, Oxoid.

For dilution, a phosphate buffered saline (PBS) from SSI, art nr. 3892, was used.

5 % blood agar plates (Danish Blood Agar, Statens Serum Institute (SSI), with 5% horse blood), art nr. 677

SSI transport medium (Stuarts) art. nr. 944

Serumbouillon (bovine bouillon with defibrinogenated blood and horse serum, SSI) art nr. 1040

Method

1. Preparation of tests used in the analysis.

A tube of 10 ml broth is inoculated with *S. pyogenes* and incubated 18-24 timer at 35 °C. This culture is used for making a 10-fold dilution series in seven different concentrations: 10^6 colony forming units (cfu)/ml – 10^0 (cfu)/ml. The number of bacteria in the broth is determined by inoculating 0.1 ml of each dilution on two 5 % blood agar plates (in duplicates). After 18-24 hours incubation in 5 % CO_2, plates with 30-300 cfu are used for colony counting and calculating of the average streptococci concentration.

In the same way dilutions are made of β-haemolytic streptococci group C, G og F and α-haemolytic streptococci. The concentration of 10^7 cfu/ml is used for the preparation of a mixture with equal amounts of the 4 streptococci strains. From each of the seven concentrations of *S. pyogenes*, from the mix of streptococci and from the 100 % PBS, in total nine different concentrations, 16 tests is taken randomly, all together 9 x 16 = 144 tests for the investigation of the Strep A test. The positive and negative control from the box was each tested 8 times. According to the insert, the test was positive at 5×10^5 cfu/ml. The concentration of the positive control is not mentioned in the insert. The Negative control is group C streptococci.

2. Investigation of stability in SSI transport medium (Stuarts).

Due to future investigations in General Practice (to compare results from general practice with results from the department of microbiology) we investigated changes in the concentration of *S. pyogenes* after transportation in Stuarts transport medium in the following way:

From dilution series of *S. pyogenes* in the concentrations 10^6 cfu/ml - 10^0 cfu/ml 5 % blood agar plates are spread with charcoal swabs. The spreading is done 5 times from each dilution, n = 5. The same procedure is repeated after the charcoal swap have been stuck in the SSI´s transport medium for a few seconds (n = 5) and after 24 hours at room temperature (n=5). The concentration of *S. pyogenes* is calculated from agars with 30 to 300 cfu/ml, as described previously

DEMANDS TO ANALYTICAL QUALITY AND TO PRACTABILITY

No international (Golden) Standard for Strep A-test does exist for laboratory testing or test in General Practice.

Analytical quality and practability is each weighted 50 % of the total validation in this protocol. Each of the 5 areas within Analytical quality and practability has to achieve ≥ 2 points.
Each area is subdivided and each subdivision has 5 possible results.

-		not relevant
0	Point	unsatisfactory
1	Point	less satisfactory
2	Points	satisfactory
3	Points	very satisfactory

Analytical quality. Parameters evaluated:

1) Equivalence point
2a) Specificity, defined by measuring other streptococci (True negative)/(false positive + true negative).
2b) Specificity, defined from Equivalence point (True negative)/(false positive + true negative).
3) Validation of practical use: intra-person and inter-person variation: 9 concentrations are read 16 times each by four different and independent persons.
4) Percent of test not valid, defined by insert (no control line and/or diffuse background)
5) Sturdiness: Does the test turn positive at the expected time, as told in the insert? The test is read to the reading time, specified in the insert plus this specified reading time times 0.5 and 2. Does the result change during time?

Practability. Parameters evaluated (Table 2).

- manual /insert
- time factors
- possibilities for quality control
- operation of the test
- other factors

Quality Control.
Built-in Control Features.
The QuickVue In-Line Strep A test contains built-in control features. The manufacturer´s recommendation for daily quality control is to document these controls for the first sample tested each day.

- A control of the extraction procedure is provided by a color change from clear to green as the extraction solutions are mixed. The color change is an indication of extraction reagent integrity and is also an indication that the extraction procedure was correctly performed.

- The two color result format provides a clear-cut readout for positive and negative results. The appearance of a blue Control Line next to the letter ”C” provides several forms of control. First, detection components for the specimen and internal control are processed concurrently using identical procedures; therefore, the appearance of the Control Line ensures that functional activity of the detection component is maintained. Secondly, the appearance of the Control Line also ensures that the foil pouch integrity has been maintained and the Test Cassette has been stored in such a manner as not to compromise its functionality. Third, the appearance of the Control Line indicates that proper volume of fluid entered the Test Cassette and capillary flow occurred. This would indicate that the Test Cassette was assembled properly, by acting as a check for all membrane interfaces and proper positioning of components. If the Control Line does not devolop within 5 minutes, the test result is invalid.

A negative background control is provided by the clearing of background color in the Result Window and indicates that there were no immunological interfering substances in the specimen. This area should be white to light pink within 5 minutes and not interfere with the reading of the test result. If background color remains in the Result Window which interferes with your ability to read the test result, your result may be invalid. In this case, contact Quidel Technical Assistance.

Positive and Negative Quality Control.

External controls may be used to assure that the reagents and assay procedure are performing properly, if required by your laboratory´s quality assurance plan. Positive and Negative Control Swabs are supplied in the kit. The Positive Control Swab (+) is stored in the pink-capped tube; the Negative Control Swab (-) is stored in the blue-capped tube. It is recommended that the positive control used by your laboratory be traceable to ATCC strain 19615. and the negative kontrol be traceable to an ATCC non-group A Strep organism.

To test using a Positive or Negative Control Swab, remove the Control Swab from its container and insert it into the QuickVue In-Line Strep A Test Cassette Swab Chamber. Continue with the assay as instructed in the **Test Procedure** Section.

To test using a liquid control (Catalog #00354), shake the Control Solution Bottle vigorously. Hold the bottle vertically and place one free falling drop of liquid Control on a sterile rayon-tipped swab provided in the kit. Insert the Swab into the QuickVue In-Line Strep A Test Cassette Swab Chamber. Continue with the assay as instructed in the **Test Procedure** Section.

Positive and Negative controls should be tested with each new lot or shipment of test materials once for each 25 test kit, and with each new operator within that 25 test kit, and as otherwise required by your laboratory´s standard quality control procedures.

If controls do not perform as expected, do not use the test results. Repeat the test or contact Quidel Technical Assistance.

TESTING

(under standardised and optimal conditions in the laboratorium)

160 Strep A test was produced by a doctor and a lab technician from KMA, OUH.

The 9 different strain solutions, each divided in 2-3 glasses plus the negative and positive control were produced randomly 16 times each (in total 16 × 9 + 8 +8 test). The different 11 solutions is a pure diluent, 7 dilutions of a know amount of *S. pyogene*s, a mix of four other streptococci, a positive and a negative control.

The 160 Strep A test is read blindly to the time 2, 5 and 10 min by 4 independent doctors, lab technicians or secretaries from the department of clinical chemistry, OUH.
All together 480 (3 x 160) readings per person, in total 1920 (4 x 480) readings in the result table.
All readings are done to specified time plus 15 seconds. All tubes contain 90% to 100 % PBS (salt-diluent).
The readings were done on a cloudy day in a room with day light combined with artificial light. At the time for testing the temperature in the room was 22° C.

RESULTS

4 persons read randomly 9 concentrations of Strep A 16 times plus the positive and negative controls at the time 2, 5 og 10 minutes

Table 1 2 minutes	person 1 positive	person 2 positive	person 3 positive	person 4 positive	In total positive	In total
Concentration, n=16	n=	n=	n=	n=	n=	n=
PBS	0	0	0	0	0	64
Other Streptocci	0	0	0	0	0	64
$8.5x10^0$	1	1	0	0	2	64
$8.5x10^1$	0	0	0	0	0	64
$8.5x10^2$	0	0	0	0	0	64
$8.5x10^3$	1	1	0	0	2	64
$8.5x10^4$	0	0	0	0	0	64
$8.5x10^5$	2	3	4	0	9	64
$8.5x10^6$	16	16	15	16	63	64
Negative control	0	0	0	0	0	32
positive control	8	8	8	8	32	32

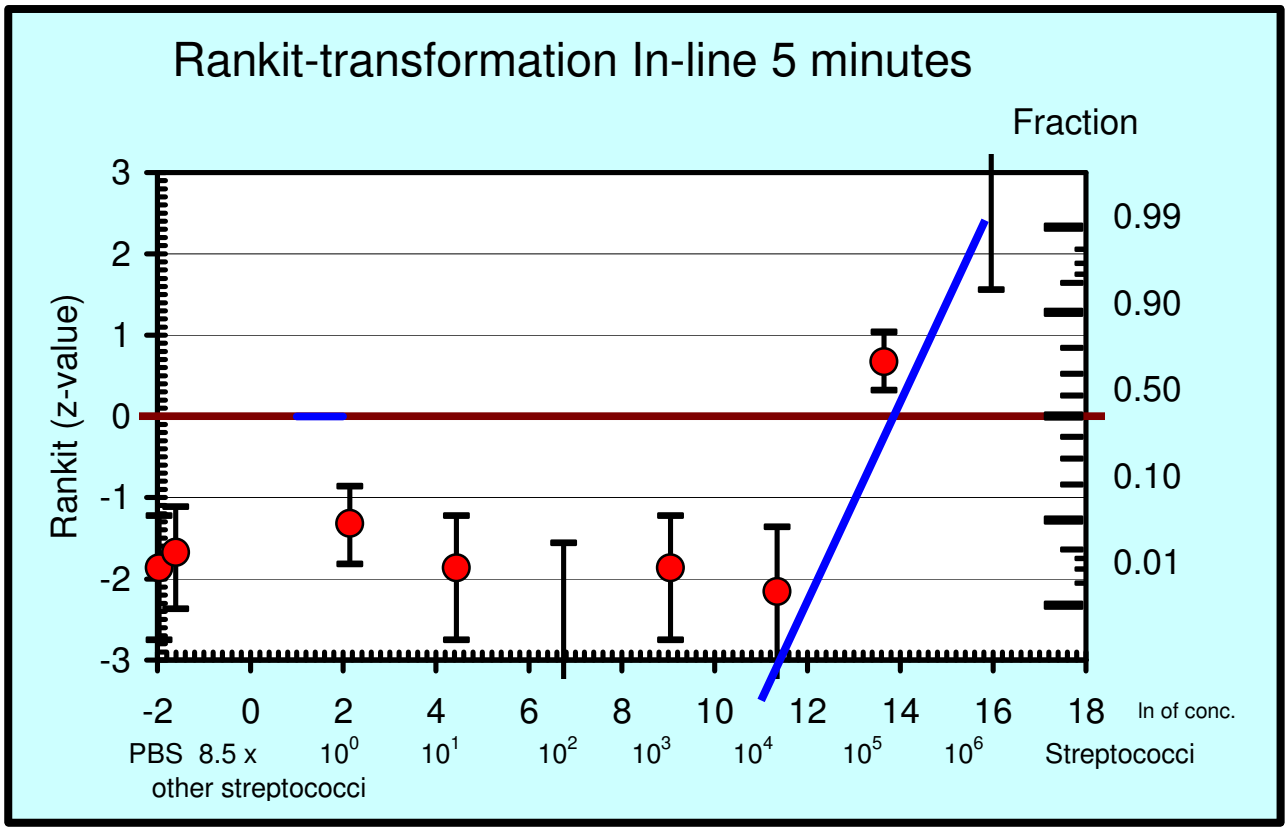
5 minutes	person 1 positive	person 2 positive	person 3 positive	person 4 positive	In total positive	In total
Concentration, n=16	n=	n=	n=	n=	n=	n=
PBS	1	1	0	0	2	64
Other Streptococci	1	2	0	0	3	64
$8.5x10^0$	3	3	0	0	6	64
$8.5x10^1$	1	1	0	0	2	64
$8.5x10^2$	0	0	0	0	0	64
$8.5x10^3$	1	1	0	0	2	64
$8.5x10^4$	0	0	1	0	1	64
$8.5x10^5$	11	13	15	9	48	64
$8.5x10^6$	16	16	16	16	64	64
Negative control	0	0	0	0	0	32
positive control	8	8	8	8	32	32

10 minutes	person 1 positive	person 2 positive	person 3 positive	person 4 positive	In total positive	In total
Concentration, n=16	n=	n=	n=	n=	n=	n=
PBS	0	0	0	0	0	64
Other Streptococci	0	0	0	0	0	64
$8.5x10^0$	1	1	0	0	2	64
$8.5x10^1$	2	2	0	0	4	64
$8.5x10^2$	0	0	0	0	0	64
$8.5x10^3$	1	1	0	0	2	64
$8.5x10^4$	1	1	1	0	3	64
$8.5x10^5$	14	16	15	9	54	64
$8.5x10^6$	16	15	16	16	64	64
Negative control	0	0	0	0	0	32
positive control	8	8	8	8	32	32

Comments to data in table 1 and table A.

It seems correct to read the test after 5 minutes. 100 % (64 of 64 at the conc. 8.5×10^6 and 32 positive controls were positive). The reason why only some of the expected negatives were negative, was that a transitory, diffuse, red band passed the test window. The band was present in approximately 90 seconds. The test persons could distinguish between true positives and false positives.

Equivalence point, Figure 1



In Figure 1 the fractions of the positive results of a dilution series of Strep A concentrations is shown in a Rankit-plot (Rankit is a linearization of the Gaussian distribution, where z is the distance from the average in standard deviations). The corresponding fractions is indicated on the right Y-axis and the abscissa (upper line) id natural logarithms (ln = log e) of the concentration while the lower line is the Strep A dilution series concentration. For each fraction the 95% confidence interval is plotted as well as the fraction 0.1, 0.5 and 0.9.

The Figure shows that QuickVue® In-line Strep A test has a wide range around the equivalence point and that there is a lot of false positives values not dependent of concentration with this test with living bacteria's.
All concentrations in the dilution row is read to the time 5 minutes. All concentrations $\geq 8.5 \times 10^6$ haemolytic streptococci/ml, are positive.

STABILITY OF *S. pyogenes* IN SSI transport medium (Stuarts)

By using the average cfu count from table B a concentration of 3.9×10^8 cfu/ml is achieved by direct sowing with charcoal on blood agar (39.2 cfu at 0,1 ml i dilution $1x10^{-6}$). After less than a minute in the transport medium from SSI the concentration was 4.9×10^7 cfu/ml and after 24 hours at room temperature in the SSI transport medium the concentration was calculated to 4.5×10^6/cfu/ml.

EVALUATION OF ANALYTICAL QUALITY AFTER 5 MINUTES

1) Equivalence point: about *8.5 × 10^5 Strep A/ml.*

2a) Specificity: *95.3 % (61 of 64).*

2b) Specificity: *96.25 % ≤ 8.5 × 10^3 Strep A/ml. (308 readings of 320).*

3a) Intra-person reading: *No disagreement.*

3b) Inter-person disagreement of reading: *1.4 % of the test (2/144).*

4) Invalid tests*: 0.4 % (3 of 640).*

5) The test is positive at 5 minutes: yes*.*

6) False positive later than 5 minutes*: see text, table1 and photos.*

7) False negative: *0 % ved koncentration > 8.5 × 10^5/ml.*

Analytical Quality

The analytical quality was not quite good.

Restarting of the test

136 tests performed according to the insert and the liquid were seen in the test field before 60 sec. 44 tests had no liquor in the test window within 60 seconds. Test no 171 in Figure 2.

Background

None of the tests had red background this time; (about 15% had it last time).

Control line

The location of the blue control band did not cause the same problems as last time. Three different locations are shown in Figure 3.

Different expression of tests

There is a very huge difference in the expression of the same concentration. In figure 4 the concentration is 8.5 x 10^4 in T1, T2 and T4. The concentration is 8.5 x 10^5 in T3. Fig 5 shows different colour intension of the concentration 8.5 x 10^5 while Figure 6 is concentration 8.5 x 10^6. The pictures are taken after breaking the code for the samples, the numbers indicate, that they are produced within 15 minutes. For concentration 8.5 x 10^5 6 tests were negative while 10 were positive when picture was taken. In previous testing it has been possible for the test persons to predict the concentration in most samples by colour expression. This also was the case for the first testing of In-line. (For a range close to the equivalence point this cannot be expected).

False Positives

Also in this lot, there were problems with the correct judgement due to a diffuse red band, which could pass the test area in 90 to 120 seconds. The four individual readers were agreeing when there were False Positive bands. The bands False Positive were photographed, Figure 5-10.

Two of the readers (one who participated last time and a new one, gave their answers positive and negative after what they believed the test were even if they saw a red diffuse band on the “reading time” the two others wrote positive, if there where a red band, but they also noticed, that this probably was a False Positive.

Of the 120 negative tests there were unexpected results in 14 in the period 2 to 10 minutes. It is still not clear why bands appear, where they should not. There is no correlation to restarting of the test.

Conclusion

QuickVue In-line® Strep A test does not fulfil the criteria for good performing in this investigation. The main problem is the possibility of false positives due to a transitory, diffuse red band that passes some of the test windows. The bands can occur after 2 to 15 minutes. The duration of the bands is about 90 seconds. Test person 1 and 2 described the red bands, if they were present, at 2, 5 or 10 minutes. Test person 3 and 4 made up their mind if the red band was a real positive or a false positive. For test persons aware of the problem, it is possible to distinguish between a real positive and a false positive.

Twenty-four percents of the tests had to be “re-started” after 60 seconds. There is no correlation between the bands and the “re-starting” of the test.

The test was performed of doctors and lab technicians from Clinical Biochemical Department and Clinical Microbiological Department under optimal and standardised conditions.

We do not expect that QuickVue In-line will perform better under less standardised conditions in the hands of general practitioners.

REFERENCES

1) A Model for setting Analytical Quality Specifications and Design of Control for Measurements on the Ordinal Scale. Per Hyltoft Petersen, Sverre Sandberg, Callum Fraser and Henk Goldschmidt. Clin Chem Lab Med 2000; 38 (6): 545-551.

2) Diagnosis of Group A Streptococcal Pharyngotonsillitis in generel Practice with Five Antigen Detection Test Kits and a rapid Kit for C-Reactive Protein. Steen Hofmann og Klaus Witt. Poster c22 ASM 99th General Meeting1999 (ingen artikel, n=2078, GP's=230)

3) Diagnostik af halsbetændelse. En multipraksisundersøgelse af tre antigendetektionssæt til påvisning af gruppe A-streptokokker i svælgpodninger. Jørgen Steen Andersen, Niels Jerne Borrild og Steen Hoffmann. Ugeskrift for Læger 1994; 156:46, 6869-6872

4) Detection of group A streptococcal antigen from throat swabs with five diagnostic kits in general practice. Hoffmann S. Streptococcus Department, Staten's Serum Institut, Copenhagen, Denmark. Diagn Microbiol Infect Dis. 1990 May-Jun;13(3):209-15.

5) Detection of group A streptococcal antigen from throat swabs by use of a latex agglutination test kit in general practice. Hoffmann S, Henrichsen J. Acta Pathol Microbiol Immunol Scand [B]. 1987 Apr;95(2):89-94

6) Inserts in Danish, Norwegian, Swedish and English.

7) SKUP report nr 24. OSOM Strep A test

TABLE A

Data

concentration	Prøve nr.	2 min	2 min	2 min	2 min	5 min	5 min	5 min	5 min	10 min	10 min	10 min	10 min
8.5×10^0	6	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	10	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	14	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	28	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	35	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	56	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	61	0	0	0	0	0	0	0	0	1	1	0	0
8.5×10^0	87	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	88	1	1	0	0	0	0	0	0	0	0	0	0
8.5×10^0	122	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	128	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	130	0	0	0	0	1	1	0	0	0	0	0	0
8.5×10^0	136	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	148	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^0	155	0	0	0	0	1	1	0	0	0	0	0	0
8.5×10^0	166	0	0	0	0	1	1	0	0	0	0	0	0
8.5×10^1	2	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	17	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	29	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	39	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	48	0	0	0	0	0	0	0	0	1	1	0	0
8.5×10^1	55	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	60	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	77	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	78	0	0	0	0	1	1	0	0	0	0	0	0
8.5×10^1	83	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	95	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	109	0	0	0	0	0	0	0	0	1	1	0	0
8.5×10^1	117	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	161	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	165	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^1	169	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	34	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	45	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	52					0	0	0	0	0	0	0	0
8.5×10^2	68	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	69	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	74	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	80	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	90	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	94	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	110	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	113	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	134	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	142	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	147	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	156	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^2	175	0	0	0	0	0	0	0	0	0	0	0	0
8.5×10^3	5	0	0	0	0	0	0	0	0	0	0	0	0

concentration	Prøve nr.	2 min	2 min	2 min	2 min	5 min	5 min	5 min	5 min	10 min	10 min	10 min	10 min
$8.5x10^3$	11	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	20	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	27	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	38	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	49	0	0	0	0	1	1	0	0	0	0	0	0
$8.5x10^3$	58	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	91	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	102	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	123	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	127	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	132	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	149	1	1	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	152	0	0	0	0	0	0	0	0	1	1	0	0
$8.5x10^3$	162	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^3$	170	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	13	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	30	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	33	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	44	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	50	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	65	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	71	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	79	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	98	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	105	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	116	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	125	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	137	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	144	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	154	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	164	0	0	0	0	0	0	0	0	0	0	0	0
$8.5x10^4$	172	0	0	0	0	0	0	1	0	1	1	1	0
$8.5x10^5$	8	0	0	1	0	1	1	1	0	1	1	1	0
$8.5x10^5$	15	0	1	1	0	1	1	1	1	1	1	1	1
$8.5x10^5$	23	0	0	0	0	0	1	0	0	0	1	0	0
$8.5x10^5$	31	0	0	0	0	1	1	1	1	1	1	1	1
$8.5x10^5$	47	0	0	0	0	0	0	1	0	1	1	1	0
$8.5x10^5$	63	0	0	0	0	0	1	1	0	0	1	1	0
$8.5x10^5$	76	0	0	1	0	1	1	1	1	1	1	1	1
$8.5x10^5$	89	1	1	0	0	0	1	1	0	1	1	1	0
$8.5x10^5$	101	0	0	0	0	1	1	1	1	1	1	1	1
$8.5x10^5$	111	0	0	1	0	B	0	1	0	1	1	1	0
$8.5x10^5$	114	0	0	0	0	1	1	1	1	1	1	1	1
$8.5x10^5$	131	0	0	0	0	1	1	1	0	1	1	1	0
$8.5x10^5$	139	1	1	0	0	1	1	1	1	1	1	1	1
$8.5x10^5$	146	0	0	0	0	1	1	1	1	1	1	1	1
$8.5x10^5$	159	0	0	0	0	0	0	1	1	1	1	1	1
$8.5x10^5$	168	0	0	0	0	1	1	1	1	1	1	1	1
$8.5x10^6$	9	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	19	1	1	1	1	1	1	1	1	1	1	1	1

concentration	Prøve nr.	2 min	2 min	2 min	2 min	5 min	5 min	5 min	5 min	10 min	10 min	10 min	10 min
$8.5x10^6$	22	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	32	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	37	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	41	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	54	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	64	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	72	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	85	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	100	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	115	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	126	1	1	1	1	1	1	1	1	1	1	1	1
$8.5x10^6$	138	1	1	1	1	1	1	1	1	1	0	1	1
$8.5x10^6$	163	1	1	0	1	1	1	1	1	1	1	1	1
$8.5x10^6$	174	1	1	1	1	1	1	1	1	1	1	1	1
MIX	3	0	0	0	0	0	0	0	0	0	0	0	0
MIX	4	0	0	0	0	0	0	0	0	0	0	0	0
MIX	16	0	0	0	0	0	1	0	0	0	0	0	0
MIX	24	0	0	0	0	0	0	0	0	0	0	0	0
MIX	51					0	0	0	0	0	0	0	0
MIX	57	0	0	0	0	0	0	0	0	0	0	0	0
MIX	70	0	0	0	0	0	0	0	0	0	0	0	0
MIX	97	0	0	0	0	0	0	0	0	0	0	0	0
MIX	104	0	0	0	0	0	0	0	0	0	0	0	0
MIX	107	0	0	0	0	0	0	0	0	0	0	0	0
MIX	119	0	0	0	0	0	0	0	0	0	0	0	0
MIX	124	0	0	0	0	0	0	0	0	0	0	0	0
MIX	143	0	0	0	0	0	0	0	0	0	0	0	0
MIX	150	0	0	0	0	1	1	0	0	0	0	0	0
MIX	160	0	0	0	0	0	0	0	0	0	0	0	0
MIX	171	0	0	0	0	0	0	0	0	0	0	0	0
N	21	0	0	0	0	0	0	0	0	0	0	0	0
N	53					0	0	0	0	0	0	0	0
N	99	0	0	0	0	B	1	0	0	0	0	0	0
N	129	0	0	0	0	0	0	0	0	0	0	0	0
N	158	0	0	0	0	0	0	0	0	0	0	0	0
N	173	0	0	0	0	0	0	0	0	0	0	0	0
N	178	0	0	0	0	0	0	0	0	0	0	0	0
N	180	0	0	0	0	0	0	0	0	0	0	0	0
P	7	1	1	1	1	1	1	1	1	1	1	1	1
P	43	1	1	1	1	1	1	1	1	1	1	1	1
P	59	1	1	1	1	1	1	1	1	1	1	1	1
P	84	1	1	1	1	1	1	1	1	1	1	1	1
P	120	1	1	1	1	1	1	1	1	1	1	1	1
P	140	1	1	1	1	1	1	1	1	1	1	1	1
P	177	1	1	1	1	1	1	1	1	1	1	1	1
P	179	1	1	1	1	1	1	1	1	1	1	1	1
PBS	1	0	0	0	0	0	0	0	0	0	0	0	0
PBS	12	0	0	0	0	0	0	0	0	0	0	0	0
PBS	26	0	0	0	0	0	0	0	0	0	0	0	0
PBS	46	0	0	0	0	0	0	0	0	0	0	0	0
PBS	62	0	0	0	0	0	0	0	0	0	0	0	0
PBS	75	0	0	0	0	0	0	0	0	0	0	0	0
PBS	81	0	0	0	0	0	0	0	0	0	0	0	0
PBS	92	0	0	0	0	0	0	0	0	0	0	0	0
PBS	112	0	0	0	0	0	0	0	0	0	0	0	0

concentration	Prøve nr.	2 min	2 min	2 min	2 min	5 min	5 min	5 min	5 min	10 min	10 min	10 min	10 min
PBS	133	0	0	0	0	0	0	0	0	0	0	0	0
PBS	141	0	0	0	0	1	1	0	0	0	0	0	0
PBS	145	0	0	0	0	0	0	0	0	0	0	0	0
PBS	153	0	0	0	0	0	0	0	0	0	0	0	0
PBS	157	0	0	0	0	0	0	0	0	0	0	0	0
PBS	167	0	0	0	0	0	0	0	0	0	0	0	0
PBS	176	0	0	0	0	0	0	0	0	0	0	0	0

Signatur : 1 = positive, 0 = negative, B = not valid

Grey (dark colour) = unexpected result, yellow: positive, orange: result can be positive and negative

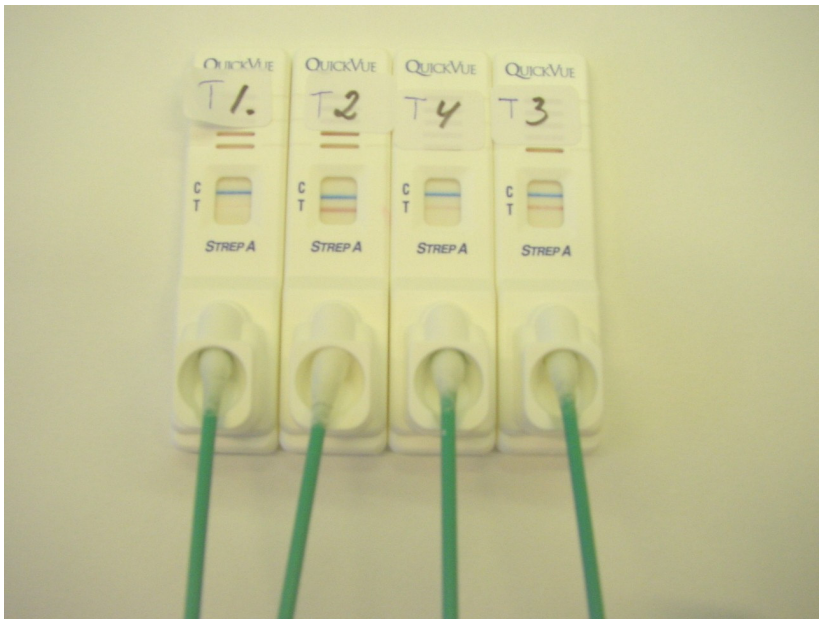
Table B

Hæm Strep A				
	antal	cfu	koncentration	applicering
direkte måling,	n=5	39	$3.9x10^{-8}$	Kulpodepind
< minut i Stuart medium	n=5	49	$4.9x10^{-7}$	Kulpodepind
24 h i Stuart medium	n=5	45	$4.5x10^{-6}$	Kulpodepind

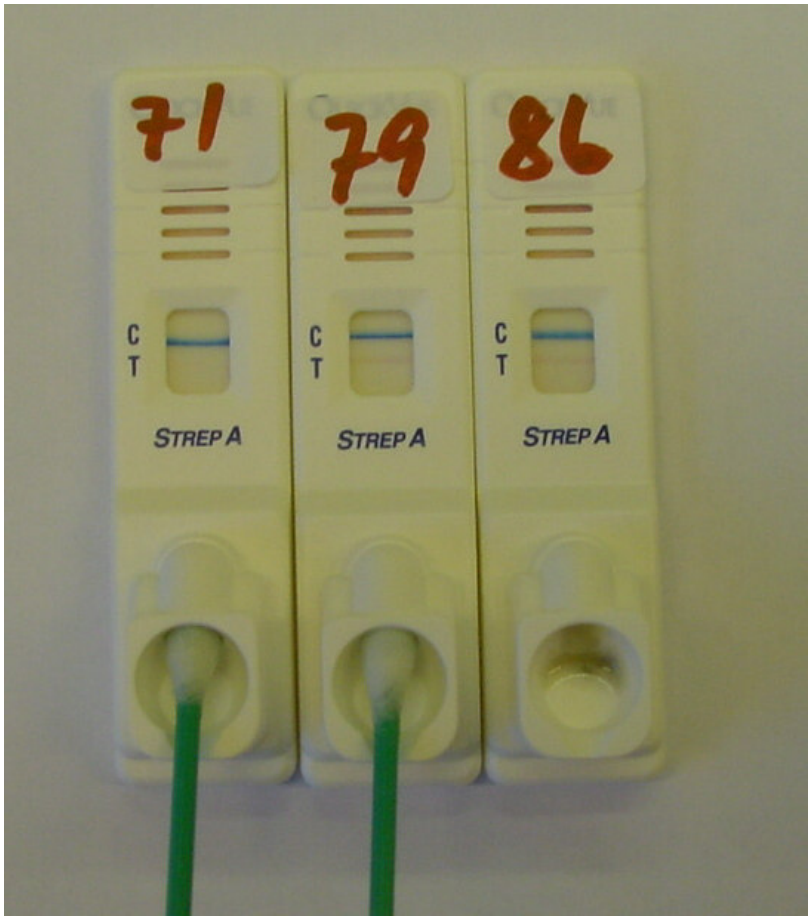
Figur 2

Figur 3

Figur 4



Figur 5



Figur 6

Figur 7

Figur 8

Figur 9

Figur 10

SKUP i Danmark
V/ Esther Jensen
KBA
Odense Universitetshospital
5000 Odense C

7. juni 2004

Vedr.: Quidel QuickVue® Strep A Inline.

Kære Esther

Vi har kun hørt fra Quidel, at de kan ikke kan genfinde jeres ellers veldokumenterede uregelmæssigheder ved Strep A InLine.

Vi har ingen forklaring på det observerede.

Resultaterne fra NOKLUS og EQUALIS kvalitetssikringsprogrammerne viser derimod at Strep A Inline ikke falder ud som upålideligt.
I de programmer anvendes en afmålt mængde vandig opslemning af bakterier som prøvemateriale.

I jeres forsøg har I dyppet swappen i opslemningen. Om dette forhold har nogen betydning kan vi kun gisne om. Da det tilmed har været et tilfældigt forekommende problem, vil det formodentligt ikke være videre oplysende at gentage forsøget endnu engang som en sammenligning mellem pådrypning af 50 µL på swappen og neddypning af swappen.

Vi må tage resultaterne til efterretning, som de er. Producenten QUIDEL har ikke ønsket at gøre noget ved sagen. De vil, hvis vi presser yderligere på, blot henvise til at man skal følge proceduren for InLine for at de kan stå inde for resultaterne.

Med venlig hilsen
Medinor A/S

Peter Albeck