Corrective Action Report
FSCA Slidex Staph kit ref 73112 and 73113
28 NOV 2011

1. **Affected product:**
   Brand Name: Slidex Staph kit (50 Tests)
   Catalog number: 73112
   Lot Number: 1105104568
   Brand Name: Slidex Staph kit (250 Tests)
   Catalog number: 73113
   Lot Number: 1105104545

2. **Name and Address of manufacturer:**

   BioMerieux SA
   F-69280 Marcy l'Etoile, France

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3. **Product Classification:**

   FDA classification: -Class 1, 21CFR866.2660
   FDA Product Code: -JWX

   EU classification : -Directive 98/79/EC covering in vitro diagnostic medical devices
   -Conformity assessment procedure used to demonstrate compliance: Annex IIII (section 6 excluded)
   -GMDN Code: 30656

4. **Product Description and Intended Use:**
   The SLIDEX® Staph-Kit is a rapid latex and red blood cell agglutination test for the identification of *Staphylococcus aureus* strains from culture media.

5. **Description of Issue:**
   Customers noticed false negative results with patient samples and with reference strains. It is unknown whether false negative result was given to patient.

   Scope of the issue:
   At the date of this report, 53 complaints have been reported on the two following lots of Slidex Staph kit ref 73112 and 73113:

- 1105104545 (73113): 24 complaints
- 1105104568 (73112): 29 complaints

The lots 1105104545 and 1105104568 kept in house in Brazil were tested and gave positive results on 10 different strains (ATCC 51153, P18, 8915, S1, 431, ATCC 25923, 2122, 803, N21/7, Esp2). Simulation of aging of the product using the following thermal shocks confirmed the sensitivity issue : 3 days at 37°C, 8 days at 18 to 25°C, 2 days at 37°C, 4 days at 18 to 25°C and 1 day at 2-8°C.

The issue was also confirmed on the kit returned from customers (lot #1105104545).

The lots 1105104545 and 1105104568 comes from the same manufacturing lot which was released from manufacture on the 28/06/2011 and distributed from 4th july 2011 until the 27th of October 2011. The lots 1105104545 and 1105104568 were composed respectively of 1033 kits and 1016 kits.

The analysis of the batch history file showed that the two defective lots contained the same lot of raw material, the erythrocyte. This lot of raw material was different from lots of raw material used to manufacture products with correct performances. Therefore this lot of raw material is suspected to be linked to the issue. This hypothesis is currently being tested in internal investigation (results expected January 2012).

Although the symptoms of this issue are similar to the previous issue reported to Afssaps, the root cause is different (Afssaps #11DIV1415, FSCA0827). The lots for this issue were manufactured before the implementation of the corrective action for the previous FSCA.
The planned corrective action consisted in the implementation of thermal shocks before the quality control of the raw material and before the final quality control for release of the final products.

Investigations are currently ongoing in Research and Development department in order to confirm the root cause and to implement an action plan at that level.

Until the root cause is confirmed and the issue is corrected, the conformity of each lot of finished products will be tested after thermal shocks.

6. Health Hazard Assessment:

The SLIDEX Staph-Kit (ref 73112 and 73113) enables the identification of Staphylococcus aureus strains from culture media.

According to the instruction for use:

- After 18-24 hours of incubation at 33-37°C, suspect colonies should be tested with the classical methods of Gram stain, morphology and the catalase test, to confirm that they may be staphylococci.
- In the case of very weak agglutination with the anti- Staphylococcus aureus reagent, if the control reagent is agglutinated or if lumping occurs, further identification of the strain must be performed with the tube coagulase test or a biochemical range of tests.
- Interpretation of test results should be made taking into consideration the patient's history, the source of the specimen, colonial and microscopic morphology and, if necessary, the results of any other tests performed.
- Sensitivity was shown to be 95.4% for MRSA strains (confidence interval 93.2-97%) and 100% for MSSA strains (confidence interval 99-100%).

- Quality control of the reagents must be performed each time a new kit is opened, using the following strains: S. aureus ATCC® 25923 (agglutination with sensitized RBC) and ATCC® 51153 (agglutination with sensitized latex): deterioration of reagents should be suspected if the reagent R1 does not agglutinate with these strains.

Patient risk in case of false negative results:
In this instance the impact to the customer/patient is the potential for false negative results or delay in organism identification. As identified in the SLIDEX® Staph-Kit package insert, False negative reactions will occur if:

- an insufficient number of colonies is used for the test, In this case, the isolate should be subcultured and tested he there is sufficient growth;
- the strain does not produce clumping factor or protein A (blood agar);
- the specific antigen against which the monoclonal antibody is directed is not produced.

As a mitigating factor of the SLIDEX® Staph-Kit test, limitations of the test method is well documented in the package insert, and other mitigating test results should be used. In laboratory use, SLIDEX® Staph-Kit is not used as a single identification test method. SLIDEX® Staph-Kit is designed to aid in the identification of Staphylococcus aureus strains from culture media. Interpretation of test results should be made taking into consideration the patient's history, the source of the specimen, colonial and microscopic morphology and, if necessary, the results of any other tests performed.

Conclusion:

A false-negative result could cause a delay in organism identification and could potentially lead to a delay in starting treatment for 24 to 48 hours. The qualitative probability of the reported issue occurring is occasional; resulting in a few occurrences over the life of the product. The severity level is considered serious; with delayed or incorrect information resulting in no permanent deterioration or permanent impact because other diagnostic information is available on the patient state of health. Based on the severity level and probability of occurrence, the final risk to the patient is considered moderate. The reported issue does reflect that the use of the product may cause temporary or medically reversible adverse health consequences or the probability of serious adverse health consequence is remote.

7. **Notification to the Regulatory Authority required:**
   Afssaps (FR):
   According to the MEDDEV2.12-1 rev 6 part 5.1.1:
   - A: An event has occurred:
     - B) false negative test result falling outside the declared performance of the test.
   - B: The Manufacturer's device is suspected to be a contributory cause of the incident:
     - According to the results of the manufacturer's own preliminary assessment of the incident
   - C: The event led, or might have led, to one of the following outcomes:
     - A serious deterioration in state of health of a patient, user, or other person that can include any indirect harm as a consequence of an incorrect diagnostic or IVD test results when used within manufacturer's instruction for use
       - Indirect harm include delayed and inappropriate treatment (definition under 4.11)

Conclusion: Considering the positive answer to points , B and C, this incident is considered as a reportable event and should be reported to Afssaps.

According to the MEDDEV2.12-1 rev 6 part 4.6:
The device destruction will be implemented as a Field Safety Corrective Action in order to reduce a risk to serious deterioration in the state of health associated with the use of the affected medical device that is already placed on the market. The FSCA will be notified via a Field Safety Notice.

FDA (US):
According to 21CFR Part 806.10:

- Each device manufacturer or importer shall submit a written report to FDA of any correction or removal of a device initiated by such manufacturer or importer, if the correction or removal was initiated to reduce a risk to health posed by the device.

8. Product Distribution:

The countries concerned by this FSCA are the following: Argentina, Australia, Austria, Belarus, Belgium, Brazil, Chile, China, Dominican Republic, France, Germany, India, Italy, Ivory Coast, Kuwait, Lebanon, Netherlands, Panama, Poland, Portugal, Romania, Singapore, Slovenia, Spain, Sweden, Switzerland, Tunisia, United Arab Emirates, United Kingdom, United States of America.

9. Corrective Action Required:

9.1. <u>Short-term:</u>

- A Product Stop Shipment was implemented for both lots on the 21st of October 2011 (PSS1146)
- A Field Safety Corrective Action including a Field Safety Notice that request the destruction of the affected kits will be send to all subsidiaries and distributors concerned by this issue.

9.2. <u>Long-term:</u>

- CAPA 09/011
- A new lot of raw material are currently being validated following thermal shocks.
- A new lot of Slidex Staph will be manufactured with the validated raw material.
- The quality control techniques will be updated in order to include a test of the final products and of the raw material following thermal shocks.

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