Corrective Action Report
ChromID Strepto B agar (STRB), reference 43461, lot #1001508710
October 10, 2012

1. **Affected Product:**

Brand Name:	ChromID Strepto B agar (STRB)
Catalog Number:	43461
Lot/Serial Number:	# 1001508710
Expiry Date:	30 OCT 2012
Manufacturing Total:	1706 kits
On-Hand Total:	0 kits
Distribution Total:	1706 kits (included 86 kits blocked by the PSS at subs or distributor level)
Manufacturing date:	25 July 2012

2. **Name & Address of Legal Manufacturer:**

Legal Manufacturer:
bioMérieux SA
F-69280 Marcy l'Etoile, France

Regulatory Compliance contact:
Benjamin Smith
Director, Global Regulatory Compliance
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Manufacturing Site:
5 rue des Aqueducs
69290 – Craponne, France

3. **Product Classification:**

FDA Classification:	Not applicable (not sold in USA)
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: 33352

4. **Intended use of the device:**
chromID™ Strepto B agar is a selective chromogenic medium for the screening of S. agalactiae carriage in pregnant women and newborns using clinical specimens. S. agalactiae are responsible for serious infections in newborns (meningitis). Their detection is particularly important for the prevention, treatment, and monitoring of infections.

5. **Description of Issue:**
bioMérieux decided to implement a Product Stop Shipment (PSS-1488) on 10 SEP 2012 as a result of 26 customer complaints being received for lot #1001508710 of chromID Strepto B agar (ref 43461). An internal investigation was started to determine if there is a product performance issue with this lot.

The investigation observed a sensitivity issue (uncolored colonies) during QC of Streptococcus agalactiae colonies at 24 hours and 48 hours with the lot #1001508710 of chromID Strepto B agar (ref 43461). In the packaging insert, the QC strain required (Streptococcus agalactiae ATCC 12386) growths after 24 hours at

33-37°C and the color must be "pale pink to red colonies". Seven (7) customers observed uncolored colonies of their QC strain ATCC 12386 at 24 hours. Three (3) of them observed uncolored colonies of their QC strain ATCC 12386 at 48 hours. For the other complaints, we don't have the information.

For specimen collections, the package insert defines the appearance of the colonies: typical Streptococcus agalactiae colonies are pale pink to red, round and pearly. They must be confirmed using a biochemical or immunological test. The growth of micro-organisms belonging to other species is either inhibited or the colonies produced are a different color (e.g.: violet, blue, colorless etc.). Three (3) customer complaints were received alleging they observed uncolored colonies from specimen collections at 24 hours. Four (4) of them observed uncolored colonies from specimen collections at 48 hours. For the other complaints, we don't have the information.

During the initial Quality Control, the lot #1001508710 was conform according to the QC specifications. The lot (1706 kits) was accepted by QC on 25 July 2012. Expiry date : 30 OCT 2012

During the investigation, 10 lots were tested including the lot #1001508710. Four (4) strains were tested :

- 2 QC strains Streptococcus agalactiae ATCC 12386 and NCTC 8190
- 2 strains from R&D (B1424 and B1839)

As described in the Instruction for use of the packaging insert, "the incubation is at 37°C for 18-24 hours in aerobic conditions in the dark. If no typical colonies are observed after 24 hours, prolong incubation up to 48 hours."

The investigation concluded, 2 of 4 strains of Streptococcus agalactiae tested on the lot #1001508710 do not conform at 24H and do conform at 48H. The nine (9) other lots all conformed to product specification. The QC labs didn't confirm the product performance issue at 48H. The same results were observed when using specific temperature conditions (thermal shock during 4 hours at 33-37°C).

Additionally, the QC labs performed tests from 2 customer return strains (vaginal sampling from Italia). One of the strains was sent on the media chromID Strepto B agar (ref 43461), lot #1001508710 and the QC labs observed that colonies were not colored upon receipt confirming the issue upon receipt. The two (2) return strains were also tested according to the QC method. 1 of 2 strains of Streptococcus agalactiae tested on the lot #1001508710 did not conform at 24H and did conform at 48H. The second strain was conform at 24H and 48H.

The customer strain observed uncolored by the QC labs has been tested according to the QC control. The investigation results indicate the product conforms because the pink coloration at 48H. However these results contradict with the no-color observed upon receipt of the customer strain which, requiring further investigation.

The lot #1001508710 was manufactured between 15H50 and 22H06. All the tests done as part of the QC investigation used plates manufactured at the end of the batch (≅ 22H). However, all the customer complaints concerns the plates manufactured between 16H30 and 18H05. The investigation and production information suggest that product performance issue is with the plates manufacturing in the middle of the batch and not at the end of the batch. Which is why the QC lab investigation didn't observe a non-conforming result of "no color" like the customer obtained on the same customer strains when using plates from the end of the batch.

The investigation confirmed the failure of the product to meet performance specifications due to the strain returned from the customer on the ChromID Strepto B plate, REF 43461, lot #1001508710. However, the root cause has not been identified and a CAPA will be opened to track the issue.

6. **Risk Assessment / Health Hazard Assessment:**

As described in the Instruction for use of the packaging insert, "the incubation is at 37°C for 18-24 hours in aerobic conditions in the dark. If no typical colonies are observed after 24 hours, prolong incubation up to 48 hours."

The product risk analysis file (RAR000091-01 revision 2) defines the risk to have false negative results at 48 hours as critical because the S. agalactiae are responsible for screening of serious infections in newborns (meningitis).

The customers observed a sensitivity issue at 48H and the issue has been confirmed the issue at 24H but we don't have confirm the issue at 48H as part of the QC investigation that tested strains on retain samples.

Field Action board recommends to implement a FSCA to inform the subs, distributors and customers about the issue and ask them to destroy the lot #1001508710. We recommend the customers to confirm the identification of all negative results obtained with the lot #1001508710 if they didn't use an additional media or an other method in parallel.

The action required is a FSCA because there is a risk to have an incorrect diagnostic that could led to a serious deterioration in state of health of patients. According to the guideline on Medical devices Vigilance System, MEDDEV 2.12-1, rev. 7, we will inform ANSM because the issue is a reportable event. The lot #1001508710 was not sold in US so notification to FDA is not required.

7. **Notification to the Regulatory Authorities:**

Europe
The removal will be reported to ANSM per MEDDEV 2.12-01 rev 7 and the French regulation (Code de la Santé Publique, article L5522-3), because the identified hazard results in an increased risk to health for the device user. Based on the impact to the customer, taking corrective action in the field will reduce that risk and therefore notification to the ANSM is required.

FDA
The product is not sold in USA, so notification to FDA is not required.

8. **Product Distribution:**
Canada, France, Japan, Netherlands, Germany, Poland, Italia, Portugal, Australia, Austria, Sweden, Slovenia, Colombia, China, Guyana, Switzerland, Croatia, Macedonia, Czech republic, Hungary

9. **Corrective Actions Required:**
Following the Product Stop Shipment (PSS-1488), the following corrective actions will be implemented:
- To inform the customer about the issue and to ask them to destroy the lot #1001508710 of chromID Strepto B agar (ref 43461) and to recommend them to confirm the identification of all negative results obtained with the lot #1001508710 if they didn't use an additional media or an other method in parallel.

10. **Attachments:**
Not applicable

10 OCT 2012		10-Oct-2012	
Anne-Sophie AUBERTY Regulatory Compliance Specialist	Date	Benjamin SMITH Director, Global Regulatory Compliance	Date