Please distribute the attached customer letter.

To the Laboratory Manager

To the attention of the Healthcare center Chairman

To the attention of the Reactovigilance correspondent

Address
City, Date

Our reference: FSCA 3303

IMPORTANT:

URGENT FIELD SAFETY NOTICE

ETEST® XM256 (Cefuroxime) Foam (Ref. 506958, 506918) and SPB (Ref. 412304, 412305)

Our records indicate that your laboratory has received the following products. This letter is intended for all ETEST® XM256 (Cefuroxime) Foam (Ref. 506958, 506918) and SPB (Ref. 412304, 412305) users (product reference and lot numbers included below).

Product References impacted:

Reference	Description	Lot Number	Expiry date
412304	**ETEST® XM256 (Cefuroxime)** US SPB	1004497830	02-DEC-2018
412305	**ETEST® XM256 (Cefuroxime)** WW SPB	1002884720	16-Jan-2017
412305	**ETEST® XM256 (Cefuroxime)** WW SPB	1003028270	20-Mar-2017
412305	**ETEST® XM256 (Cefuroxime)** WW SPB	1003075500	09-APR-2017
412305	**ETEST® XM256 (Cefuroxime)** WW SPB	1003383650	27-AUG-2017
412305	**ETEST® XM256 (Cefuroxime)** WW SPB	1004018820	19-MAY-2018
412305	**ETEST® XM256 (Cefuroxime)** WW SPB	1004497810	02-DEC-2018
412305	**ETEST® XM256 (Cefuroxime)** WW SPB	1005161160	15-Sep-2019
506918	**ETEST® XM256 (Cefuroxime)** WW Foam	1002884980	16-Jan-2017
506918	**ETEST® XM256 (Cefuroxime)** WW Foam	1003028290	20-Mar-2017
506918	**ETEST® XM256 (Cefuroxime)** WW Foam	1003075850	09-APR-2017
506918	**ETEST® XM256 (Cefuroxime)** WW Foam	1003385930	27-AUG-2017
506918	**ETEST® XM256 (Cefuroxime)** WW Foam	1003396150	2-Sep-2017
506918	**ETEST® XM256 (Cefuroxime)** WW Foam	1004022170	19-MAY-2018
506918	**ETEST® XM256 (Cefuroxime)** WW Foam	1004498100	02-DEC-2018
506918	**ETEST® XM256 (Cefuroxime)** WW Foam	1005161470	15-Sep-2019
506958	**ETEST® XM256 (Cefuroxime)** US Foam	1002885010	16-Jan-2017
506958	**ETEST® XM256 (Cefuroxime)** US Foam	1003075540	09-APR-2017
506958	**ETEST® XM256 (Cefuroxime)** US Foam	1003396550	2-Sep-2017
506958	**ETEST® XM256 (Cefuroxime)** US Foam	1004019050	19-MAY-2018

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506958	**ETEST® XM256 (Cefuroxime)** US Foam	1004501930	02-DEC-2018
506958	**ETEST® XM256 (Cefuroxime)** US Foam	1005161480	15-Sep-2019

Description of the issue

An analysis was performed on the Essential Agreement rate reflecting the MIC result obtained by the product for a significant strains kit including *Enterobacteriaceae, Haemophilus* and *S. pneumoniae*. Species. Then, an additional analysis was done on the clinical categorization of the strains based on CLSI guidance. The following have been identified:

⇨ The investigation confirmed a potential performance issue on strains categorization **for *Streptococcus pneumoniae* and for *Enterobacteriaceae* strains limited to oral cefuroxim breakpoints and based on 2016 CLSI clinical standards only:**

- **For *Streptococcus pneumoniae*** on ETEST® XM256 (Cefuroxime) FOAM and SPB that could lead to minor error on clinical strains :
  - False Susceptible result instead of Intermediate results with BMD (Broth Micro Dilution) reference method
  - False Intermediate result instead of Resistant results with BMD reference method

- **For Enterobacteriaceae** on ETEST® XM256 (Cefuroxime) FOAM and SPB that could lead to minor error on clinical strains:
  - False Susceptible result instead of Intermediate results with AD (Agar Dilution) reference method
  - False Intermediate result instead of Resistant results with AD reference method

⇨ Products perform within the specification when using the 2016 EUCAST guidelines.

Impact to Patient/User:

As the result of the referenced issue, the potential hazard is to obtain Minor error (**Susceptible instead of Intermediate or Intermediate instead of Resistant) on strain categorization for *Streptococcus pneumoniae* and for *Enterobacteriaceae* strains only when using the 2016 CLSI clinical breakpoints defined for cefuroxime oral forms.**

- For ***Streptococcus pneumoniae* strains and only when oral breakpoints are used** (not parenteral breakpoints) **for Cefuroxime**: **based on 2016 clinical CLSI guidelines**, a reduced MIC value could be obtained with ETEST® XM256 SPB and FOAM packaging that could lead to a susceptible categorization instead of intermediate categorization (Minor Error) or intermediate categorization instead of resistant categorization (minor Error) for clinical strains compared to broth microdilution (BMD) reference method.

- For ***Enterobacteriaceae* strains and only when oral breakpoints are used** (not parenteral breakpoints) **for Cefuroxime: based on 2016 CLSI clinical guidelines,** a reduced MIC value could be obtained with ETEST® XM256 SPB and FOAM that could lead to a susceptible categorization instead of intermediate categorization (Minor Error) or intermediate categorization instead of resistant categorization (minor Error) for clinical strains compared to Agar dilution (AD) reference method

Required actions:

- Please distribute this information to all appropriate personnel in your laboratory, retain a copy in your files, and forward this information to all parties that may use this product, including others to whom you may have transferred our product.

- **<u>Recommendations only for users under 2016 CLSI clinical guidelines</u>,:**

  Laboratories can continue to use ETEST® XM256 SPB and FOAM **<u>and can directly report the results</u>** for *Streptococcus pneumoniae* and Enterobacteriaceae **when oral breakpoints are used when applying the following recommendations**:

Cefuroxime oral breakpoints	
<u>Streptococcus pneumoniae</u>	**<u>Enterobacteriaceae</u>**
<u>→Cefuroxime Results can be directly reported for</u> ○ Isolate tests penicillin susceptible (MIC≤0.06 µg/ml) and cefuroxime susceptible (**ETEST® XM256** MIC ≤1 µg /ml) ○ Isolate tests penicillin resistant (MIC ≥0.12 µg/ml) and cefuroxime resistant (**ETEST® XM256** ≥ 4 µg /ml) ○ Isolate tests cefuroxime resistant (**ETEST® XM256** ≥ 4 µg /ml) **→ the cefuroxime MIC should be confirmed using an alternative MIC test method for** ○ isolates testing penicillin resistant (MIC ≥0.12 µg/ml) and cefuroxime susceptible (ETEST® XM256 MIC ≤1µg/ml) or intermediate (ETEST® XM256 MIC = 2µg/ml),	**<u>→Cefuroxime Results can be directly reported for</u>** ○ Isolate tests cefazolin **(*)** susceptible (MIC ≤16 µg/ml) and cefuroxime susceptible (**ETEST® XM256** MIC ≤4 µg /ml) ○ Isolate tests cefuroxime resistant (**ETEST® XM256** ≥ 32 µg /ml) **→the cefuroxime MIC should be confirmed using an alternative MIC test method** for ○ isolates testing cefazolin resistant (MIC ≥32 µg/ml) and cefuroxime susceptible (ETEST® XM256 MIC ≤4µg/ml) or intermediate (ETEST® XM256 MIC = 8 or 16 µg/ml) **(*) comment 19 of page 55 of CLSI M100 S26 – 2016**

- Among tests previously performed, we are asking you to identify any possible false Susceptible results, analyze the related risks and determine appropriate actions if relevant.

- Contact your local bioMérieux representative for product compensation.

- Complete and return the Acknowledgement Form in Attachment A by Fax to confirm receipt of this notice.

bioMérieux is committed to providing our customers with the highest quality product possible. We sincerely apologize for any inconvenience that this may have caused you. If you require additional assistance or have any questions, please contact your local bioMérieux Customer Service representative.

Yours sincerely,
Customer Service

Attachment A: Acknowledgement Form.

PLEASE RETURN TO YOUR CUSTOMER SERVICE

Fax : …….
Name of the laboratory:

City:

Customer number:

❑ I acknowledge the receipt of bioMérieux Urgent Field Safety Notice informing this laboratory on the ETEST® XM256 (Cefuroxime) Foam (Ref. 506958, 506918) and SPB (Ref. 412304, 412305) product issue.

❑ I have followed the instructions and implemented the actions as indicated in the Urgent Field Safety Notice.

Have you received reports of illness or injury related to the identified issue?
❑ Yes or ❑ No

DATE ..... **SIGNATURE :** .....

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