FIELD SAFETY CORRECTIVE ACTION

Number: **5742** Action: **Correction** Unit Name: **Microbiology**

Product Name: **MUELLER HINTON E AGAR - References : 413822 ; 413824 ; 413825 ; 417680 ; 421528**

Issue Date: **18-JAN-2023** Manufacturing Sites: Tres Cantos ; Combourg ; Rio de Janeiro ; Craponne

Required Actions

Section A: Details

Affected Product

- **System: see table 1**
- **REF: see table 1**
- **Lot/Serial: see annex 1**
- **Expiry: see annex 1**
- **Product: see table 1**
- **GMDN Code: see table 1**
- **Unique Device Identifier: see table 1**

System	REF #	Lot #	Expiry	Product	GMDN Code	Unique Device Identifier (UDI-DI)
PPM Clinical	413822	See annex 1	See annex 1	M HINTON E AGAR 90 20PL	58639	03573026406875
PPM Clinical	413824	See annex 1	See annex 1	M HINTON E AGAR 90 100PL	58639	03573026406899
PPM Clinical	413825	See annex 1	See annex 1	M HINTON E AGAR 120X120 20PL	58639	03573026406905
PPM Brazil Products	417680	See annex 1	See annex 1	M HINTON E AGAR 90 MM	58605	03573026463106
N/A	421528	See annex 1	See annex 1	MHE 145 LA BALME 20P	N/A	N/A

Table 1: list of product references affected by the issue.

Manufacturing Beginning & End Date: see annex 1

Distribution Beginning & End Dates: see annex 1

Quantity on hand: see annex 1

Date of Decision to take Action in the Field: 12-Jan-2023

Name and Address of Legal Manufacturer

Name & Address of Recalling Firm: BIOMERIEUX SA, 110 Allée Louis Pasteur, 69280 MARCY L'ETOILE
Name & Address of Manufacturing Sites : BIOMERIEUX Tres Cantos/Combourg/Rio de Janeiro/Craponne :

bioMérieux, TRES CANTOS
c/. Isaac Newton nº6
PTM 28760. Madrid (PTM) 28760 MADRID

bioMérieux, COMBOURG
2, Route de Dol,
35270 Combourg, France

bioMérieux, Brasil Industria e Comércio de Produtos Laboratoriais LTDA
Estrada do Mapuá, 491 – Lote 1 – Taquara – CEP : 22713-320 – RIO DE JANEIRO

bioMérieux, CRAPONNE
5 Rue des Aqueducs,
69290 Craponne

Product Intended Use

Mueller Hinton E Agar is a medium for disk diffusion antimicrobial susceptibility testing and the determination of Minimal Inhibitory Concentrations (MIC) using the ETEST® method.

The medium has been developed according to EUCAST (European Committee on Antimicrobial Susceptibility Testing) and CLSI (Clinical Laboratory and Standards Institute, Inc.) recommendations.

Description of the Issue

Is there a PSS associated with this FSCA? YES ☐ NO ■ PSS Number: N/A
Is this FSCA associated with a customer complaint? YES ■ NO ☐
Customer Complaint Number(s): CN-404976 ; CN-423139 ; CN-414596 ; CN-415553 ; CN-415556 ; CN-421962 ; CN-432950 ; CN-432951 ; CN-433486.
Investigation Reference Number: INV-13692

- Issue description:

• bioMérieux received nine (9) complaints from three (3) different customers, regarding MUELLER HINTON E AGAR 90 100PL (reference 413824 and 413822) as ATCC 27853 *Pseudomonas aeruginosa* and Gentamicin disk (Oxoid) and ETEST® method did not pass quality control (QC). Two customers reported smaller zones than expected for Gentamicin Oxoid disk (Expected results per EUCAST and CLSI for the combination ATCC 27853 *Pseudomonas aeruginosa* – Gentamicin are an inhibition diameter between 17-23 mm).

• After QC failure, the customer confirmed the issue via ETEST® method. A higher MIC was obtained (Expected results per EUCAST and CLSI for the combination ATCC 27853 *Pseudomonas aeruginosa* – Gentamicin is a MIC between 0,5-2 mg/L).

bioMérieux conducted an investigation (INV-13692) to identify the root cause and confirmed the customer issues.

- Investigation:

The batch records analysis indicated that the eight impacted batches, reference 413824 and 413822, complied with bioMérieux specifications and neither non-conformance or deviations were recorded during the manufacturing process.

Nevertheless, the reported issue (smaller zones than expected and a higher MIC) was reproduced during the investigation on 4 of the 8 batches claimed.

All the non-conforming batches were produced using the 33 formula of the dry media (8301143 reference). Being their only element in common, to date, investigators impact the dry media formula, since the problem is not confirmed on the batches produced using the 32 formula.

Conclusion: Product issue concerning the ATCC 27853 *Pseudomonas aeruginosa* has been confirmed on reference batch . The performance issue has been confirmed after additional investigation performed on wild strains of *Pseudomonas aeruginosa*.

In total, **97** batches were produced using this formula (33) dry media. See Annex 1 for details regarding impacted lots.

Root cause: the investigation is still ongoing to determine the root cause of the issue.

- Field action decision:

The Field Action Board determined that a Field Safety Corrective Action (FSCA) was necessary on **all lots produced using dry formula (33) (see Annex 1 – list of lots in the scope of the FSCA#5742).**

The customer letter will inform customers of the referenced performance issue, along with instructions to refrain from testing the combination *Pseudomonas aeruginosa* - Gentamicin on the associated lots of MUELLER HINTON E Agar.

All customers who have received the impacted products will be notified via customer letter notification.

* Actions required at subs/distributors levels:

bioMérieux will inform the Subsidiaries and Distributors and will require them to implement the following corrective actions:

- Translate and distribute the customer letter to all customers that have received and who may receive MUELLER HINTON E AGAR - References: 413822, 413824, 413825, 417680 impacted lots (listed in Annex 1).

* Actions required at customer level:

bioMérieux will require the customer to implement the following actions:

- Stop using MUELLER HINTON E AGAR – References: 413822, 413824, 413825, 417680 regarding batches mentioned in Annex 1 and non-expired at the time of FSCA/customer letter publication when testing the combination *Pseudomonas aeruginosa* – Gentamicin.

Note: for the reference 421528 (internal use only), an internal notification will be sent from VOT to La Balme site.

* Actions required at manufacturing site level:

The CAPA **PR#1796589** was initiated to investigate the root cause of the issue and to determine potential short term/long term actions.

- Authorization to produce/release the following batches produced with the F33 formulation mentioned below and in Annex 1. These batches will be part of the scope of the FSCA and will be accompanied by the customer letter.
  * Reference 413822 : 1009801610
  * Reference 413824 : 1009790420
  * Reference 413825 : 2190570 ; 2190840 ; 2191040 ; 2191280
  * Reference 417680 : 1009801280 ; 1009806430

- Destruction of the remaining stock of dry media F33.

Risk Assessment / Health Hazard Assessment

Immediate and Long Range Health Consequences

- Definition of the severity:

For the risk of **Delayed AST Result:** With QC being out of range, AST results for gentamicin would be delayed until retesting can occur and QC returns to the expected value. The timeframe for this would be at least 24 hours. This may impact the patient by delaying the administration of appropriate antibiotics due to the continued use of broad-spectrum empiric antimicrobial therapy. Unnecessary broad-spectrum antimicrobial usage may result in toxic side effects to the patients (e.g., damage to the kidneys), and may contribute to the development of antimicrobial resistance. Therefore, the severity is **SERIOUS**.

For the risk of **Erroneous AST result Overestimated MIC/Over-calling Resistance**: Gentamicin is truly susceptible, but the Etest result may be falsely resistant (ME: Major Error). The risk to the patient is that he/she may continue on inappropriate antimicrobial therapy. As Gentamicin can be considered a viable antimicrobial option for laboratories following CLSI AST reporting guidelines, a falsely resistant result may eliminate gentamicin as a choice for treatment and could have a negative impact on antimicrobial management, as resistant results limit the treatment options available to the clinician. Therefore, the severity is **SERIOUS**.

- Definition of P2 (Probability of hazardous situation leading to harm):

For the risk of **Delayed AST Result**, empiric therapy would be prescribed based on standard of care. However, full AST results would be available in parallel with the gentamicin result, and clinicians can tailor specific therapy based on full AST results. Additionally, while gentamicin has activity against *P. aeruginosa*, it is not recommended for use as monotherapy for severe infections (tobramycin is the aminoglycoside of choice for treatment of *P. aeruginosa* infections). Finally, EUCAST lists gentamicin as a drug having insufficient evidence (IE) that *P. aeruginosa* is a good target for the drug. This would lead laboratories that use EUCAST interpretive criteria for AST results to avoid reporting it, and clinicians who use EUCAST criteria to avoid its use as therapy. However, CLSI recommends reporting AST results for Gentamicin against *P. aeruginosa*. Based on this, the probability P2 is **OCCASIONAL** for the normal population and the most at risk.

For the risk of **Erroneous AST Result Overestimated MIC/Over-calling Resistance,** empiric therapy would be prescribed based on standard of care. However, full AST results would be available in parallel with the gentamicin result, and clinicians can tailor specific therapy based on full AST results. Additionally, while gentamicin has activity against *P. aeruginosa*, it is not recommended for use as monotherapy for severe infections (tobramycin is the aminoglycoside of choice for treatment of *P. aeruginosa* infections). Based on this, the probability P2 is **REMOTE** for the normal population and the most at risk.

P1 (Probability of hazardous situation occurring)	P2 (Probability of hazardous situation leading to harm)	P (Overall probability)	Severity	OVERALL RISK
Occasional	Occasional	REMOTE	Serious	Minor

Notification to the Regulatory Authority

Recipients of this notification must assess the product issue and any associated patient risk in accordance with local regulations to determine if it is reportable to their local regulatory authority. Notification to your regulatory authority must include device classification when required.

Product Distribution

Type	Sold-to pt	Sold to Party Name	Country name	Country code
Subsidiaries	AR01	BIOMERIEUX ARGENTINA	Argentina	AR
	AU01	Biomerieux Australia Pty Ltd	Australia	AU
	AT01	BIOMERIEUX AUSTRIA GMBH	Austria	AT
	BE01	bioMerieux Benelux SA/NV	Belgium	BE
	BR01	BIOMERIEUX BRASIL INDUSTRIA E	Brazil	BR
	CA01	BIOMERIEUX CANADA INC	Canada	CA
	CL01	BIOMERIEUX CHILE SpA	Chile	CL
	CN01	BIOMERIEUX SHANGHAI	China	CN
	CO01	BIOMERIEUX COLOMBIA S.A.S	Colombia	CO
	CZ01	BIOMERIEUX CZ S.R.O.	Czech Republic	CZ
	EG01	BIOMERIEUX EGYPT LIMITED	Egypt	EG
	FR01	BIOMERIEUX S.A	France	FR
	DE01	BIOMERIEUX DEUTSCHLAND GMBH	Germany	DE
	GR01	BIOMERIEUX HELLAS S.A.	Greece	GR
	HK01	BIOMERIEUX CHINA LIMITED	Hong Kong	HK
	HU01	BIOMERIEUX HUNGARIA KFT.	Hungary	HU
	IN01	BIOMERIEUX INDIA PVT. LTD	India	IN
	IT01	BIOMERIEUX ITALIA S.P.A.	Italy	IT
	JP01	bioMerieux Japan LTD	Japan	JP
	MX01	BIOMERIEUX MEXICO SA DE CV	Mexico	MX
	NL01	BIOMERIEUX BENELUX BV	Netherlands	NL
	PH01	BIOMERIEUX PHILIPPINES CORPORATION	Philippines	PH
	PL01	bioMerieux Polska Sp. z o.o.	Poland	PL
	PT01	BIOMERIEUX PORTUGAL, LDA	Portugal	PT
	RU02	BIOMERIEUX RUSS LLC,	Russian Fed.	RU
	RS01	BIOMERIEUX SRB DOO	Serbia	RS
	SG01	BIOMERIEUX SINGAPORE Pte LTD	Singapore	SG
	ZA01	BIOMERIEUX SOUTH AFRICA PTY	South Africa	ZA
	KR01	BIOMERIEUX KOREA CO., LTD	South Korea	KR
	ES01	BIOMERIEUX ESPAÑA, S.A.	Spain	ES
	SE01	BIOMERIEUX SWEDEN AB	Sweden	SE
	CH01	BIOMERIEUX SUISSE S.A.	Switzerland	CH
	TH01	BIOMERIEUX THAILAND LTD	Thailand	TH
	TR01	BIOMERIEUX DIAGNOSTIK A.S.	Turkey	TR
	GB01	BIOMERIEUX UK LTD	United Kingdom	GB
	US01	BIOMERIEUX US	United States	US
Distributors	1093315	Vi Sole FZC	Afghanistan	AF
	1126205	LABOPHARMA LTD	Albania	AL
	1126202	BIOCHEM NRP LTD	Albania	AL
	1039376	INDUSTRIES MEDICO-CHIRURGICALES	Algeria	DZ
	1038835	PERINO LDA	Angola	AO
	1063040	ORGANIZACOES MAURO RUI, LDA	Angola	AO
	1043099	ISLA LAB CARIBBEAN LLC	Anguilla	AI
	1038425	CONCERN-ENERGOMASH CJSC	Armenia	AM

1049008	OZEL NESIL	Azerbaijan	AZ
1038802	GULF PHARMACY AND GENERAL STORE	Bahrain	BH
1071059	TECHNOWORTH ASSOCIATES LTD	Bangladesh	BD
1144693	NOVAMEDAS UAB	Belarus	BY
1032146	BGL SYSMET	Benin	BJ
1148694	INTERSALUD SRL	Bolivia	BO
1032570	TUZLA FARM	Bosnia-Herz.	BA
1039252	BROMA BEL D.O.O.	Bosnia-Herz.	BA
1054909	MC QUIPP TECHNISELL	Brunei Daruss.	BN
1107336	MEDICLIM EOOD	Bulgaria	BG
1107059	MEDIC BURKINA	Burkina Faso	BF
1035066	BIOFASO SARL	Burkina Faso	BF
1115675	DYNAMIC PHARMA CO., LTD	Cambodia	KH
1034910	MEDICALEX SARL	Cameroon	CM
1037237	PERINO	Cape Verde	CV
1038371	SLEM MEDICAL	Chad	TD
1035388	TECNO DIAGNOSTICA S.A.	Costa Rica	CR
1055441	TYM MEDICAL	Cote d'Ivoire	CI
1035919	A & B d.o.o.	Croatia	HR
1126196	TCC - T.C.CHRISTOFOROU LTD	Cyprus	CY
1036110	WAGENIA SARL	Dem. Rep. Congo	CD
1043329	BGL SYSMET	Dem. Rep. Congo	CD
1037462	SAHA DIAGNOSTICS	Djibouti	DJ
1035835	SUED & FARGESA S. R. L.	Dominican Rep/	DO
1039487	ISED N.V.	Dutch Antilles	AN
1037316	FARMINPEX N.V.	Dutch Antilles	AN
1089884	SIMED S.A. (CL)	Ecuador	EC
1039305	TECNO DIAGNOSTICA DE EL SALVADOR,	El Salvador	SV
1036446	DIAMEDICA OÜ	Estonia	EE
1032990	SETEMA LIMITED PLC	Ethiopia	ET
1030189	MEDILAB	Gabon	GA
1038050	PRIMA MEDI LTD	Georgia	GE
1107853	PHYLLYPS MEDICAL DIAGNOSTICS Co.	Ghana	GH
1054907	MEDPHARM	Guam	GU
1076188	LABYMED S.A.	Guatemala	GT
1039100	LABONET	Guinea	GN
1103797	PRODYLAB, PRODUCTOS DE DIAGNOSTICO	Honduras	HN
1085804	PT. DIPA PUSPA LABSAINS	Indonesia	ID
1029326	PT. ENSEVAL MEDIKA PRIMA	Indonesia	ID
1039948	PISHRO TASHKHIS FARD AVAR	Iran	IR
1039792	ISMAILIYA TRADING AGENCIES &	Iraq	IQ
1038017	ILEX MEDICAL LTD	Israel	IL
1038737	ISMAILCO MEDICAL COMPANY	Jordan	JO
1149814	ARAB MEDICAL & SCIENTIFIC ALLIANCE	Jordan	JO
1030286	SPF MEDILAND LTD	Kazakhstan	KZ
1114155	VISION SCIENTIFIC AND ENGINEERING	Kenya	KE
1030908	HASS SCIENTIFIC & MEDICAL SUPPLIES	Kenya	KE
1040989	BIOTEK Kosova L.L.C.	Kosovo	XK

1100455	Gulf Integrated Security Solutions	Kuwait	KW
1099346	LEADER MEDICAL LTD	Kyrgyzstan	KG
1036944	SIA DIAMEDICA	Latvia	LV
1031376	BIOTECK MEDICAL AND HOSPITAL SUPPLI	Lebanon	LB
1103306	Medsystems Liberia Limited	Liberia	LR
1036359	DIAR ASSLAM	Libya	LY
1034890	UAB DIAMEDICA	Lithuania	LT
1031183	BIOTEK D.O.O.	Macedonia	MK
1054442	DIAGNOSTIC SYSTEMS (M) SDN BHD	Malaysia	MY
1054476	MEDIGENE SDN BHD	Malaysia	MY
1071118	BioMali	Mali	ML
1038728	CHERUBINO LTD	Malta	MT
1042815	KOTHAR MEDICAL	Mauretania	MR
1033132	SRL MEDICLIM AM	Moldova	MD
1092723	Lifetronik LLC	Mongolia	MN
1042795	I.M. ALLIANCE SARL	Morocco	MA
1037064	PERINO	Mozambique	MZ
1030694	OKKAR THIRI COMPANY LIMITED	Myanmar	MM
1117060	Nepal Meditech and Surgitech	Nepal	NP
1037710	TECNO DIAGNOSTICA NICARAGUA SA	Nicaragua	NI
1031035	BIO-PLUS	Niger	NE
1103997	DCL LABORATORY PRODUCTS LTD	Nigeria	NG
1032696	AL HASHAR PHARMACY	Oman	OM
1038615	GMS GLOBAL MARKETING SERVICES	Pakistan	PK
1038067	AL-WALID MEDICAL TRADING CO.LTD	Palestine	PS
1035981	INVERSIONES SAGRAV S.A.	Panama	PA
1035801	TECNOFAST S.A	Paraguay	PY
1100291	SIMED PERU S.A.C.	Peru	PE
1043421	FAS DIAGNOSTIC GROUP, INC.	Philippines	PH
1116673	Horeca Plus Distribution Corporation	Philippines	PH
1035279	ALI ALSUWAIDI TRADING ESTABLISHMENT	Qatar	QA
1130525	Innovation Scientific Company	Qatar	QA
1031779	S.C. MEDICLIM S.R.L.	Romania	RO
1030057	AL JEEL MEDICAL TRADING COMPANY	Saudi Arabia	SA
1055815	SENEGALAISE DES SYSTEMES MEDICAUX	Senegal	SN
1030995	YUNYCOM DOO	Serbia	RS
1035226	MIKRO + POLO d.o.o.	Slovenia	SI
1118111	MODERN MEDICAL LABORATORY SUPPLIES	Somalia	SO
1090591	LABLINK LABORATORY SERVICES	Sudan	SD
1038018	ABDALLAH SAADE	Syria	SY
1097357	PYRAMID PHARMA LIMITED	Tanzania	TZ
1031022	MAGHREB MEDICAL MAINTENANCE	Tunisia	TN
1054863	SEDA ES	Turkmenistan	TM
1063022	INTERNATIONAL MEDICAL DEVICES / UKRBIO	Ukraine	UA
1033969	TRESUL S.A.	Uruguay	UY
1034755	AL HAYAT PHARMACEUTICALS	Utd/Arab Emir/	AE
1095680	OSIYOMEDIKA LTD	Uzbekistan	UZ

1030805	GANBARO C.A.	Venezuela	VE
1097670	LAVITEC TECHNOLOGY JSC	Vietnam	VN
1070840	DKSH TECHNOLOGY CO LTD	Vietnam	VN
1071113	DKSH VIETNAM CO., LTD./VIMEDIMEX BINH DUONG	Vietnam	VN
1035989	MED-SOLUTIONS CORP	Yemen	YE
1040766	FLOW CYTOMETRY CENTRE	Zimbabwe	ZW

Customer Letter / Attachments

To access to the Urgent Field Safety Notice and the Annex 1 please click on the paper clip icons below:

Urgent Field Safety Notice	Annex 1 to be attached to the Urgent Field Safety Notice
📎	📎

Section B: Required Actions

1. Please immediately acknowledge receipt (**AR**) of this FSCA.
2. Identify all countries and customers for which you are responsible that are impacted by this FSCA.
3. Translate the Urgent Field Safety Notice and send it to all customers having received and may receive the impacted products lots listed in Annex 1.
   To see the impacted products and lots use the Excel file of Annex 1 attached herewith: 📎
4. After all actions above are complete, please return the acknowledgement of completion (**AC**) for this FSCA. The **due date** for completion of the required actions and submitting the AC is **18-FEB-2023**.

Subsidiaries

- Subsidiaries using SAP, please manage both the Acknowledgment of Receipt and the Acknowledgment of Completion within SAP.
- Subsidiaries not using SAP, to Acknowledge Receipt of this FSCA, please complete all of Sections D.1 and D.2, sign and date where indicated, then upload to LiveLink. To Acknowledge Completion of the required actions, complete Sections D.1 and D.3, sign and date, then upload to LiveLink. Please remember to complete all form sections. The Acknowledgement of Completion must be uploaded to LiveLink before the due date.

Distributors

- Please immediately Acknowledge Receipt of this FSCA by completing Sections D.1 and D.2 then send it by email to fieldactions@biomerieux.com or by fax to +33 4 78 87 21 79.
- To Acknowledge Completion, complete Sections D.1 and D.3 then send it by email to fieldactions@biomerieux.com or by fax to +33 4 78 87 21 79. This form must be must be completed, signed, then emailed or faxed before the due date.

Section C: Regulatory & Quality Compliance Recall Contact

Céline Strauel
Vigilance Operational Team Specialist
BIOMERIEUX SA, 5 Rue des Aqueducs, 69290 CRAPONNE – France

☎ **+33 4 26 69 78 06** 🖷 **+33 4 89 43 00 05** @ **celine.strauel@biomerieux.com**

Section D: Acknowledgement Form

Number: **5742**	Title: **FSCA - Mueller Hinton E Agar - AST Results Issue - P. aeruginosa - Gentamicin**	Deadline: **18-FEB-2023**

SECTION D.1

Location			
Group Company or Distributor Name(s)		Country	Account #
A			
B			
C			
D			

- -

SECTION D.2

Acknowledgement of Receipt (AR)	
Print Name	
Sign Name	
Position	
Date (dd/MMM/yyyy)	

- -

SECTION D.3

Check the appropriate box and follow the instructions for completion.

☐ **Field Action Not Applicable** (Complete the signature box below and return form.)

☐ **Field Action Applicable**

1. Complete the required information in the table below.
   a. Enter information only in the columns that are checked in the table below. Do not alter the column headers.
   b. Information must be completed for all group companies or distributors indicated in Section 1 of this form.
   c. Ensure that the column totals for Total Shipped, Total On Hand, and Total Destroyed equal the total number received. (Column 4 + Column 5 + Column 6 = Column 3).

Acknowledgement of Completion (AC)									
Group Company or Distributor (from Section 1)		**1.** REF #	**2.** LOT #	**3.** Total Received	**4.** Total Shipped	**5.** Total On Hand	**6.** Total Destroyed	**7.** Total Instruments Affected	**8.** Total Updates Completed
		☐	☐	☐	☐	☐	☐	☐	☐
A		N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
B		N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
C		N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
D		N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

2. Provide the date of issuance of the customer letter in the space below. Customer letters are always required for FCA and FSCA.

Customer Letter Issue date:	

3. Complete the signature box below and return Sections D.1 and D.3.

Print Name	
Sign Name	
Position	
Date (dd/MMM/yyyy)	