



Please distribute the attached customer letter.
To the Laboratory Manager
To the attention of the Healthcare center Chairman

Address
City, Date

Our reference: FSCA#5124

IMPORTANT:

URGENT FIELD SAFETY NOTICE

**SARS-COV-2 R-GENE® Ref. 423720 and SARS-COV-2
RESPI R-GENE® 423732**

False positive results for RdRp gene PCR

Dear bioMérieux Customer,

Our records indicate that your laboratory received products listed in table 1 below:

Table 1: Impacted references

Product Ref. Number	Description	Lot Number	Expiry date
423720	SARS-COV-2 R-GENE®	1008394240	13/DEC/2021
		1008402290	13/DEC/2021
		1008441950	13/DEC/2021
		1008446610	28/DEC/2021
		1008458080	30/SEP/2022
423732	SARS-COV-2 RESPI R-GENE®	1008443900	12/NOV/2021
		1008444240	20/NOV/2021

Description of the issue

bioMérieux received complaints from customers who observed positive PCR signals for RdRp gene at 670 nm for negative samples and negative controls when using SARS-COV-2 R-GENE® kit (Ref.423720) lots: #1008402290 and #1008394240. These false positive results correspond to abnormal curves above the threshold of the PCR. These false positive samples result in detected Ct (between 35 to 45 CT, most of them are above 40).

bioMérieux initiated a complaint investigation to confirm product issue and determine root cause.

While the investigation is still ongoing the following have been identified:

Subsidiary name (if applicable) / Nom de la filiale (si approprié)



- ⇒ The customer's issue has been confirmed at least on the two compliant lots SARS-COV-2 R-GENE® kit (Ref.423720) lots: #1008402290 and #1008394240 listed in Table 1.
- ⇒ The premix reagent tube part of the SARS-COV-2 R GENE® kit (Ref.423720) and SARS-COV-2 RESPI R-GENE® kit (Ref. 423732) contains different RdRp oligonucleotide references. Each RdRp oligonucleotide reference can be composed of several oligonucleotides lots.
- ⇒ An analysis of critical raw materials (TAQ enzyme, RT enzyme, oligonucleotides) and cross reagent experiments allows to identify that the root cause of the issue comes from instability over time of one or several RdRp oligonucleotides lots.
- ⇒ The investigation confirmed that two RdRp oligonucleotide lots of a specific oligonucleotide reference present a shift over product shelf life that triggered the potential false positive results for RdRp gene PCR.
- ⇒ Those two lots of RdRp oligonucleotides were used for the manufacturing of the impacted products SARS-COV-2 R-GENE® (Ref. 423720) and SARS-COV-2 RESPI R-GENE® (Ref. 423732) listed in Table 1
- ⇒ Also, the issue could appear over the product shelf-life, therefore we cannot exclude that all lots listed table 1 could be impacted by the issue.

Impact to customer:

Based on the investigation results, there is a potential of false positive result when using lots of SARS-COV-2 R-GENE® (Ref. 423720) and SARS-COV-2 RESPI R-GENE® (Ref. 423732) listed in Table 1.

Required actions:

We request you to take the following actions at this time:

- 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.
- Stop using and destroy any stock of lots SARS-COV-2 R-GENE® (Ref. 423720) and SARS-COV-2 RESPI R-GENE® (Ref. 423732) mentioned in Table 1 remaining in your inventory
- Complete the Acknowledgement Form in Attachment A and return it to your local bioMérieux representative to confirm receipt of this notice.
- Discuss any concerns you may have regarding previously reported patient results obtained with your Laboratory Medical Director to determine the appropriate course of action.
- In case of you would like to perform a retrospective analysis of previous results, bioMérieux suggest you the following:



⇒ For retrospective analysis on SARS-COV-2 R-GENE® (Ref. 423720) results:

Previous results should be checked in order to consider as positive :

- Only samples detecting both N and RdRp positive genes.
- Or sample detecting only N positive gene with Ct < 40.

To avoid false positive status, the interpretation of samples status must be updated according to the following table.

A positive sample cannot be positive only with RdRp target but with N + RdRp positive:

Results Interpretation for PCR1 (SARS-COV-2 R-GENE®) for complaints batches

N Gene(530 nm)	Ct target or ΔCt [IC1sample – IC1W0]				
	Ct < 40		- or Ct ≥ 40		
IC1sample – IC1W0 (560 nm)	Any difference in Ct value is acceptable		<table border="1" style="width: 100%;"> <tr> <td style="width: 50%; text-align: center;">≤ 3 Ct</td> <td style="width: 50%; text-align: center;">> 3 Ct</td> </tr> </table>	≤ 3 Ct	> 3 Ct
≤ 3 Ct	> 3 Ct				
RdRp Gene (670 nm)	+(1)	-	- or +(1)		
INTERPRETATION					
	SARS-CoV-2 detected	SARS-CoV-2 NOT detected ⁽²⁾	Invalid result ⁽³⁾		

(1) Any Ct value is considered as positive result.

(2) SARS-COV-2 not present or below Limit of Detection. In case if unexpected negative result, sample eluates can be tested with PCR2 to check sample quality (presence of cells).

(3) Invalid due to extraction issue or inhibition effect. Recommendation to test new sample.

Results should be reviewed and interpreted in the context of the overall clinical picture

⇒ For retrospective analysis on SARS-COV-2 RESPI R-GENE® (Ref. 423732) results, the advice would be to position the threshold above negative control and at 10 % of maximal fluorescence of positive control PC03.

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 faithfully,

Customer Service



Attachment A: Acknowledgement Form.

URGENT FIELD SAFETY NOTICE

**FSCA 5124- SARS-COV-2 R-GENE® Ref. 423720 and SARS-COV-2 RESPI R-GENE® Ref. 423732
– False positive results with RdRp gene PCR**

**TO BE RETURNED TO YOUR BIO-MERIEUX CUSTOMER SERVICE AT THE FOLLOWING
FAX NUMBER : XXXXXXXX**

Name of the laboratory:

City:

Customer number:

- I acknowledge receipt of the bioMérieux letter regarding the “SARS-COV-2 R-GENE® Ref. 423720 and SARS-COV-2 RESPI R-GENE® Ref. 423732 – False positive results with RdRp gene PCR”
- I will implement the required actions, stop using and destroy the affected lots listed in Table 1 as indicated in the Urgent Field Safety Notice.
- Have you encountered impact on patients’ results, or reports of illness or injury related to the identified issue ?
 - Yes No

REF #	Product Name	Lot #	Quantity received	Quantity discarded
423720	SARS-COV-2 R-GENE®	1008394240		
423720	SARS-COV-2 R-GENE®	1008402290		
423720	SARS-COV2-R-GENE®	1008441950		
423720	SARS-COV-2 R-GENE®	1008446610		
423720	SARS-COV-2 R-GENE®	1008458080		
423732	SARS-COV-2 RESPI R-GENE®	1008443900		
423732	SARS-COV-2 RESPI R-GENE®	1008444240		

DATE

SIGNATURE :