Urgent Field Safety Notice

SBN-RDS-MolecularLab-2022-008

RDS/**cobas**® 5800/6800/8800
Version 1
Dec-2022

Potential false negative Influenza A H1N1 Results with select Roche assays used on the cobas® 5800/6800/8800 systems

Product Name **GMMI / Part No** **Device Identifier**	**cobas**® SARS-CoV-2 & Influenza A/B Qualitative assay for use on the **cobas**® 6800/8800 Systems (CE-IVD) GMMI: 09233474190 UDI: 00875197006674 **cobas**® SARS-CoV-2 & Influenza A/B Qualitative nucleic acid test for use on the **cobas**® 5800/6800/8800 Systems (CE-IVD) GMMI: 09446125190 UDI: 00875197006827 **cobas**® Influenza A/B & RSV UC (Utility Channel) Qualitative nucleic acid test for use on the **cobas**® 6800/8800 Systems (CE-IVD) GMMI: 09233962190 UDI: 00875197006773
Production Identifier (Lot No./Serial No.)	Not kit lot specific
SW Version	N/A
Type of Action	Field Safety Corrective Action (FSCA)

Dear Valued Customer,

Description of Situation

Roche received customer complaints alleging the generation of false negative Influenza A (Flu A) results and late Flu A Target Ct values with the following Roche assays in relation to other platforms:

- **cobas**® SARS-CoV-2 & Influenza A/B Qualitative assay for use on the **cobas**® 5800/6800/8800 Systems;
- **cobas**® Influenza A/B & RSV UC Qualitative nucleic acid test for use on the **cobas**® 6800/8800 Systems.

These allegations are specific to recently circulating mutations (single or double mutation) in H1N1pdm09 pertinent to the region of interest to the aforementioned tests. The identified mismatches have been increasing among H1N1pdm09 sequences deposited to the GISAID database.

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Important: The detection of the SARS-CoV-2, Flu B, and RSV targets with the aforementioned tests is not affected by this situation.

In silico analysis performed by the Roche Global Surveillance team of available sequences within the GISAID database has identified two new single nucleotide polymorphisms (SNPs) within the region of interest of the **cobas®** SARS-CoV-2 & Influenza A/B test for use on **cobas®** 5800/6800/8800 Systems and **cobas®** Influenza A/B & RSV UC test on the **cobas®** 6800/8800 Systems.

Important: Roche's **cobas®** Liat® system solutions for Influenza were included in the *in silico* analysis and the performance of **cobas®** SARS-CoV-2 & Influenza A/B for use on the **cobas®** Liat® system and **cobas®** Influenza A/B and RSV for use on the **cobas®** Liat® system are not expected to be affected by the identified mutations in H1N1pdm09.

In vitro transcript model studies and testing cultured virus indicate there is impact on the tests' sensitivities. The root cause investigation is on-going.

In most cases, a false negative result will lead to additional testing (either a repeat test and/ or testing for additional respiratory viruses), psychological distress, and delayed access to targeted therapies for influenza. A false negative result may delay the detection of the true diagnosis. However, in most patients any serious adverse health consequences are not likely because 1) the influenza infection is typically mild and transient, 2) clinicians will make presumptive medical decisions regarding supportive care, treatment, and/or isolation based on the patient's clinical picture, and 3) results from concurrent ancillary tests, which may point to the true diagnosis. On the other hand, in at-risk patients, delayed or misdiagnosis of influenza may result in more severe consequences, especially if they live in a geographic setting where the occurrence of false negativity, and therefore the probability of harm, is higher (i.e., remote probability). A false negative result may also lead to lack of adequate isolation and potential spread of the disease to uninfected individuals. Finally, the severity of harm in the clinical routine is also highly dependent on the impact of the assay on common medical practices related to influenza. Since clinical practice and presumptive diagnosis and care of suspected influenza is not highly dependent on molecular testing results for the pathogen, the overall consequences of a false negative influenza A result is likely to be moderate for both common and at risk patients. In conclusion, there is a remote probability of transient adverse events in general and at-risk populations and of severe adverse events in at-risk patients due to false negative results with use of the affected assays with moderate impact on the clinical routine on the clinical management of patients with influenza.

Actions taken by Roche Diagnostics (if applicable)

CAPA investigation has been initiated and root cause investigation continues. As needed, corrective and preventive measures will be implemented after the completion of the root cause analysis.

Roche will continue to monitor the prevalence of circulating strains with one or both SNPs.

Actions to be taken by the customer/user

As a reminder, the "Procedural Limitations" sections of the corresponding Instructions for Use state "As with any molecular test, mutations within the target regions of **cobas®** SARS-CoV-2 & Influenza A/B could affect primer and/or probe binding resulting in failure to detect the presence of virus." or "As with any molecular test, mutations within the target regions of **cobas®** Influenza A/B & RSV UC could affect primer and/or probe binding resulting in failure to detect the presence of virus." Additionally, the "Intended Use" sections note "Negative results do not preclude infection from SARS-CoV-2, influenza A, influenza B, and/ or RSV and should not be used as the sole

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basis for treatment or other patient management decisions." Lastly, the "Intended Use" section within the **cobas**® SARS-CoV-2 & Influenza A/B Instructions for Use states "Negative results must be combined with clinical observations, patient history, and epidemiological information."

Customers should monitor for negative influenza A results that are inconsistent with clinical presentation and/or other clinical and epidemiological information. Authorized or licensed Influenza NAATs are available for confirmation if clinically indicated for at-risk patients. The following tests are known not to be affected by these variants:
cobas® Liat® System assays for influenza:

- **cobas**® SARS-CoV-2 & Influenza A/B (CE-IVD); GMMI: 09211101190
- **cobas**® Influenza A/B & RSV (CE-IVD); GMMI: 08160104190

In the case of testing for Influenza, uncovering false results more than 1 day old would be unlikely to change patient management due to the acute nature of influenza and the short time period for therapeutic intervention. Therefore, reviewing of previously generated influenza A negative results is not recommended.

Communication of this Field Safety Notice (if appropriate)

<If the recipient needs to forward the FSN to additional organizations/individuals then one or more of the following statements may be included:

This notice must be passed on to all those who need to be aware within your organization or to any organization/individual where the potentially affected devices have been distributed/supplied. (If appropriate).

Please transfer this notice to other organizations/individuals on which this action has an impact. (If appropriate).

Please maintain awareness of this notice and resulting action for an appropriate period to ensure the effectiveness of the corrective action. (If appropriate).>

The following statement is mandatory in FSNs for EEA countries but is not required for the rest of the World:

Include if applicable: The undersigned confirms that this notice has been notified to the appropriate Regulatory Agency.

We apologize for any inconvenience this may cause and hope for your understanding and your support.

<closing salutations>,

Contact Details

To be completed locally:
Name
Title
Company Name
Address

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