Urgent Field Safety Notice

SBN-RDS-Molecular Lab-2021-005

RMD / **cobas® Liat®**
Version 1
17-Mar-2021

cobas® SARS-CoV-2 & Influenza A/B – Invalids and False Positive results

Product Name	**cobas®** SARS-CoV-2 & Influenza A/B Test for use on the **cobas® Liat®** System **cobas® Liat®** Analyzer
GMMI / Part No **Device Identifier**	**cobas®** SARS-CoV-2 & Influenza A/B Test for use on the **cobas® Liat®** System GMMI: 09211101190 Device Identifier : 00875197006360 **cobas® Liat®** Analyzer GMMI: 07341920190 Device Identifier : 07613336100097
Production Identifier **(Lot No./Serial No.)**	Not Applicable
SW Version	Not Applicable
Type of Action	Field Safety Corrective Action (FSCA)

Dear Valued Customer,

Description of Situation

Roche received complaints alleging invalid and/or false positive results with the **cobas®** SARS-CoV-2 & Influenza A/B Test for use on the **cobas® Liat®** System for one or more targets (SARS-CoV-2, Influenza A, Influenza B).

When reviewing the customer-provided data associated with the reported invalid and false positive results abnormal PCR growth curves were seen.

Root Cause Analysis
Our investigation is on-going; however, during the course of the investigation, Roche evaluated 115,524 runs gathered from 455 analyzers. This includes data gathered during post market surveillance, including the customer support process, and includes all data present on the analyzers regardless of the initial complaint reported. We identified 79 analyzers that generated abnormal PCR growth curves that gave false positive or invalid results:

- 393 results out of 115,524 runs generated curves associated with false positive results (0.34%)

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- 860 results out of 115,524 runs associated with the issues described below were invalid (0.74%)

Table 1 shows the total number of assay invalids and the false positives by target observed in the 115,524 evaluated runs from the complaint database and related to the specific conditions listed below. Our investigation and analysis is still ongoing.

Table 1: Summary of invalid and false positives observed

Flu A false positive	21 out of 115,524 (~0.02%)
Flu B false positive	182 out of 115,524 (~0.16%)
SARS-CoV-2 false positive	64 out of 115,524 (~0.06%)
Dual target false positive	51 out of 115,524 (~0.04%)
Triple target false positive	75 out of 115,524 (~0.06%)
Assay invalids (IC or all targets)	860 out of 115,524 (~0.74%)

Several potential causes for the abnormal PCR growth curves leading to invalids and false positives have been identified including tube leaks, abnormal PCR steps, and loose thermal sensor wiring.

Roche identified that the assay tubes may sporadically leak, causing an obstructed optical path in the **cobas® Liat®** Analyzer, producing abnormal PCR growth curves. This could lead to invalid or false positive results. If a tube leak occurs, subsequent runs may have an increased likelihood of invalid or false positive results.

- Twenty-one (21) analyzers out of 455 assessed have shown signs of optical path obstruction consistent with tube leaks through various complaint investigations. The investigation is still ongoing.
- Tube leakage in the analyzer does not lead to subsequent sample contamination.
- All 21 affected analyzers have yielded invalid results, but not all affected analyzers have yielded false positive results.
- The Flu B channel was the most impacted given the algorithm parameters.
- To date, all 21 affected analyzers reported through the associated cases have been replaced or repaired.

Roche determined that abnormal PCR curves may also result from abnormal PCR steps or loss of temperature control, leading to invalids or false positive results for multiple analytes (Influenza A, Influenza B and/or SARS-CoV-2) in a single testing run. Abnormal PCR steps may be run specific and caused by multiple factors happening at the same time, such as hardware positioning, volume movement, and curve interpretation. Abnormal PCR reaction steps were seen across fifty-three (53) analyzers and 34 assay lots and no clear pattern in the analyzer or tube lot has been identified.

In the case of temperature sensor control loss the message "Thermal runaway (disable)" is generated and the affected run is aborted (see Figure 1 and 2 below for screenshots of Thermal Runaway message).

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Figure 1: Error Message displayed in SW 3.3

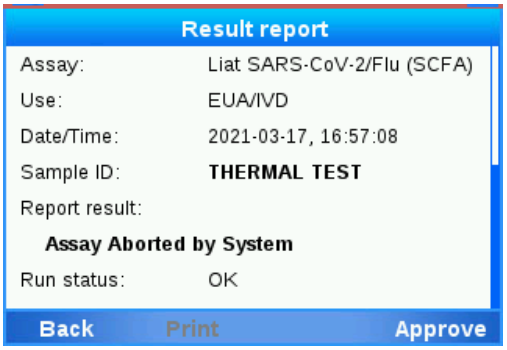
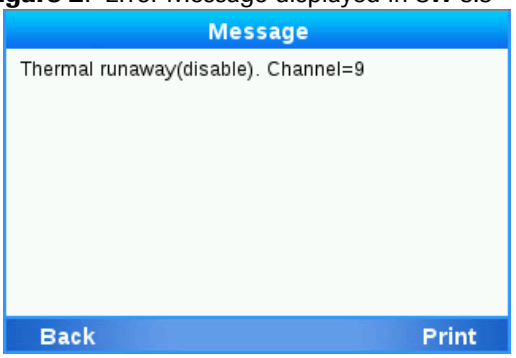


Figure 2: Error Message displayed in SW 3.3



With **cobas® Liat®** Software v3.3.0, this error occurs at the first instance of thermal runaway. If the instrument is not powered off using the 'shut down' option located on the log on screen followed by pressing the power button, subsequent runs will not show the error message and may not abort, and a high rate of assay invalids and/or some false positives may occur.

- Five (5) analyzers (5/455) assessed thus far have experienced the thermal runaway defect that generated false positives and/or invalid results in one or more target channels.

Risk Assessment

Overall across the install base, these issues from product use may occur sporadically. For invalid or false positive influenza results, adverse health consequences are not likely. For invalid SARS-CoV-2, adverse health consequences are not likely since detectability is high and testing can be performed on alternative platforms. For false positive SARS-CoV-2 results, there is a remote probability of adverse health consequences in high risk individuals:

- A false positive SARS-CoV-2 result may lead to a decision to cohort the tested individual with other COVID-19 positive individuals. If infection control measures are not comprehensive and progressive, cohorting may lead to SARS-CoV-2 exposure, that could then further result in COVID-19 with harmful sequelae. Effective infection control programs should; however, be associated with an overall low risk of hospital-acquired COVID-19 infection (Rhea et al. PMID: 32902653)
- Inappropriate treatment for COVID-19 could lead to worse outcomes from the true underlying cause of disease, such as could be the case with the administration of immune-suppressing medications in an individual with an underlying bacterial respiratory infection. Targeted COVID-19 treatments are generally well-tolerated and clinicians are likely to keep a high suspicion for alternative etiologies or even treat empirically (such as with antibiotics) in cases of severe illness. As per the Instructions for Use, Clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. The agent detected may not be the definite cause of disease.

Actions taken by Roche Diagnostics (if applicable)

This situation represents a potential safety concern.

A **cobas® Liat®** software update (v3.3.1) and a new SCFA script to better identify errors and detect abnormal PCR curves will be made available April-June 2021.

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Actions to be taken by the customer/user

The following actions must be performed:

- If customers observe an increase in Flu B positive results that does not match community rates of infection, the customer must discontinue testing on the analyzer and contact Roche to determine if a tube leak or other issue has occurred.
- If customers observe dual- and/or triple-positive results for a particular sample, they should retest the sample with **cobas®** SARS-CoV-2 & Influenza A/B test for use with the **cobas® Liat®** System using a different **cobas® Liat®** Analyzer. In the event that an additional **cobas® Liat®** Analyzer is not available for testing or in case of discordant results, discontinue testing on the analyzer and contact Roche.
- Customers should monitor their invalid rates, and if there is a sudden increase in invalid results or invalids are observed repeatedly on a specific **cobas® Liat®** Analyzer, the customer must discontinue testing on the analyzer and contact Roche.
- When the Thermal Runaway message appears on a customer's **cobas® Liat®** Analyzer running SW v3.3.0, customers must discontinue testing on the analyzer and contact Roche. Affiliate organizations are instructed to escalate global cases in these situations for further instructions.

For handling previous positive results generated with the **cobas®** SARS-CoV-2 & Influenza A/B Test for use on the **cobas® Liat®** System, customers should follow their laboratory standard operating procedures to investigate the potential for false positive results.

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>,

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Contact Details

To be completed locally:
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