# Urgent Field Safety Notice

*SBN-RMD-2016-024*

RMD / **cobas**® 4800
Version 1
31-Jan-2017

# Potential False Negative Results with cobas® HIV-1 and HBV Tests for use on the cobas® 4800 system

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| **Product Name** | **cobas**® HIV-1 Test for use on the **cobas**® 4800 system<br><br>**cobas**® HBV Test for use on the **cobas**® 4800 system |
| **GMMI / Part No**<br>**Device Identifier** | **cobas**® HIV-1 Test for use on the **cobas**® 4800 system<br>(GMMI: 06979599190; Device identifier: 00875197005547)<br><br>**cobas**® HBV Test for use on the **cobas**® 4800 system<br>(GMMI: 06979564190; Device Identifier: 00875197005585) |
| **Production Identifier**<br>**(Lot No./Serial No.)** | Not Applicable |
| **SW Version** | Not Applicable |
| **Type of Action** | Field Safety Corrective Action (FSCA) |

Dear Valued Customer,

## Description of Situation

In extremely rare circumstances, the algorithm for the **cobas**® HIV-1 and HBV Tests for use on the **cobas**® 4800 system may inappropriately call an extraordinarily high viral load sample as negative (i.e., false negative result). This situation occurs when the positive PCR growth curve for the target has a Ct value below the Ct minimum for the test, resulting in the kinetic algorithm calling the curve "negative" instead of "invalid".

Clinical specimens containing extremely high viral loads above the aforementioned tests' Upper Limits of Quantitation (ULoQ) are affected. Such high viral loads are rarely seen in clinical specimens and as a consequence have not been utilized during Development or internal testing. The estimated titers impacted by the situation are:

- HIV-1: >/= 2.3E+08 copies/mL (Test ULoQ: 1.00E+07 copies/mL)
- HBV: >/= 4.05E+10 IU/mL (Test ULoQ: 1.00E+09 IU/mL)

# Potential False Negative Results with cobas® HIV-1 and HBV Tests for use on the cobas® 4800 system

For the HIV-1 and HBV viral load assays described above, false negative results could occur in samples with extremely high titers. These high titers would rarely or never be seen in clinical samples. While adverse health consequences can be severe in worst case scenarios, the probability of occurrence of such adverse health consequences due to false negative results is remote for both the HIV-1 and HBV testing setting.

For HIV-1, extremely high viral loads would only be seen in a very small minority of patients undergoing testing, such as those with acute HIV-1 infection or end-stage AIDS patients not taking antiretroviral therapy. As newly diagnosed patients with HIV-1 are all recommended to start antiretroviral therapy, and patients with late stage disease may be on other medications to prevent certain opportunistic infections and may receive additional testing, the probability that a false negative result could cause adverse health consequences is remote. Additionally, from an overall medical perspective, the benefits of access to HIV-1 viral load testing far outweigh the risks in this situation.

For HBV, extremely high viral loads may rarely be seen in the immune tolerant phase and with perinatal transmission. Such viral loads would only be seen in patients not receiving anti-viral therapy. (Even in the case of drug-resistance, therapy will still result in lower viral loads due to decreased viral fitness. Therefore, false negatives are not a concern for treatment monitoring). A false negative result in such patients would raise suspicion of a wrong result because of the discordance between a positive HBeAg and the undetectable HBV DNA viral load. Other clinical and laboratory findings which are not consistent with a false negative viral load result would likely prompt additional testing and investigation to clarify the discordance between serological and molecular markers. In the worst case scenario, a false negative result could lead to a delay in treatment initiation, with a remote probability of adverse health consequences due to progression to end-stage liver disease or hepatocellular carcinoma. Again, the benefits of HBV viral load testing far outweigh the risks.

## Actions taken by Roche Diagnostics

This situation represents a safety concern for the **cobas**® HIV-1 and HBV Tests for use on the **cobas**® 4800 system. There are no safety concerns for other tests on this platform.

The root cause is currently under investigation and is related to the kinetic algorithm associated with the impacted tests.

Updated Assay Specific Analysis Packages (ASAPs) for the **cobas**® HIV-1 and HBV Tests for use on the **cobas**® 4800 system will be available 1Q2017. Users are reminded that the impacted tests are intended to be used in conjunction with clinical and laboratory findings.

## Actions to be taken by the customer/user

In the vast majority of cases, there is no need to review previously generated viral load results as patients receiving an initial false negative result on the **cobas**® HIV-1 test would eventually receive an HIV-1 diagnosis, either due to subsequent **cobas**® HIV-1 testing of a sample with a viral load below the threshold affecting the test, or else detected through other clinical and laboratory findings.

In a very rare scenario, a patient with acute HIV-1 infection might not be diagnosed with HIV-1 if the patient had a positive HIV-1 4th generation screening test (due to HIV-1 antigen), a negative antibody-based confirmation test, and then a false negative **cobas**® HIV-1 Test result, with no further laboratory testing performed. Labs that are concerned that they may have had cases fitting this rare scenario should review those cases to ascertain if further action is needed.

Retesting can be considered to be performed for any patients generating Target Not Detected results who, based on other clinical and laboratory findings, might be expected to have extremely high viral loads. For HIV-1, this

would be patients clinically suspected to have acute HIV-1 infection or patients with end-stage HIV-1 infection. For HBV, this would be patients with positive Hepatitis B e antigen (HBeAg) and in the immune tolerant phase or in cases of perinatal transmission.

## 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
Tel. +xx-xxx-xxxx xxxx
Email name@roche.com