Urgent Field Safety Notice

Notice Ref No:	**PAN_SB_RPD_2014_06: White Deposits cobas b 221 Update 1**
Document Date:	**xx-Dec-2014**

PRODUCT AFFECTED:	**cobas b 221** system <6> Roche OMNI S6 instruments **cobas b 221** system <5> Roche OMNI S5 instruments
SYSTEM AFFECTED:	**cobas b 221** system <6> Roche OMNI S6 instruments **cobas b 221** system <5> Roche OMNI S5 instruments
MATERIAL NUMBERS:	**03337154001** **03337146001**
LOT NO (IF APPLICABLE):	**N/A**
SUMMARY OF ISSUE:	• "White deposits" in the fluidic system of the **cobas b** 221 <5>/<6> Roche OMNI S5/S6 may cause a reduced lifetime of metabolite sensor cartridges. • The cause of the "white deposit" has been identified as a chemical component of the S3 Fluid Pack solutions, as well as bacterial contamination, and is not lot specific. • In the presence of "white deposits", patient results may be affected. Therefore regular customer visits will be required for **cobas b** 221 <5>/<6> Roche OMNI S5/S6. • Version 1.0 of this Field Safety Note was published along with PAN_SB_RPD_2014_06. The present version is published along with an update of the PAN_SB_RPD_2014_06.
ACTION REQUIRED:	• Run and maintain the **cobas b** 221/ OMNI S systems as per manufacturer instructions for use. • Initial and follow-up customer visits on a 4-weekly basis will be done by the FSRs in order to execute a maintenance procedure.
CONTACTS:	**Technical Services:** **Country:**

Dear valued **cobas b** 221 system/OMNI S customer,

As communicated in the first version of this Field Safety Notice in July 2014 we would like to give you an update of the situation and want to inform you that regular visits by Field Service Representatives (FSRs) will be required for **cobas b** 221 <5>/<6> Roche OMNI S5/S6 systems.

We have been receiving complaints for **cobas b** 221 <5> and <6> Roche OMNI S6 systems related to issues with the calibration and QC stability of MSS parameters.
First investigations identified the formation of "white deposits" in the fluidic system, especially in the SD cartridge tubing, as the cause for the reported premature failure of the MSS parameters. Whereas until recently, contamination was only known to affect the Standby solution fluidic pathway, latest investigations revealed that the pathways of calibration solutions Cal1 to Cal4 (from the S3 Fluid Pack) can be affected as well. However, this has the potential to affect patient results.
We want to point out that a retrospective case review confirmed that there was no complaint from a customer, in which a wrong patient result was generated due to the influence of bacterial contamination of the MSS calibration solutions.

Initially, the underlying failure was identified within the Standby solution of the S3 Fluid pack. Since the problem is not lot specific, all currently available S3 Fluid Packs can potentially contribute to the problem. In spite of this, not all instruments are affected by this issue as the environment an instrument is placed in plays an important role.

It has been found that the root cause is the preservative component Kathon® 893. Analysis confirmed decay products of the preservative compound Kathon® 893 in those "white deposits" found in tubes of affected instruments. In addition, bacteriological examination of several affected tube samples from various customers showed that the "white deposits" also contain Gram-negative bacteria. Analysis revealed that the current Kathon® 893 concentration is not sufficient to fully suppress the externally triggered Gram-negative bacterial contamination, existent in the various environments our instruments are used in. We want to state that these **bacteria are not introduced to the system via contaminated Fluid Packs**.

For instruments affected by "white deposits", issues with the calibration and stability of QC measurements of the parameters glucose and lactate have been observed. As already communicated, the lifetime of metabolite sensor cassettes may be reduced in the presence of "white deposits".
We performed studies regarding the system reliability, in the presence of "white deposits" in the Standby solution fluidic pathway compared to instruments without "white deposits". Data from this initial study and comparison with a reference system (Hitachi c501) confirmed that affected instruments were fully within specifications regarding measurement results for all sample types.

Recently, we received complaint data and material from the field indicating that this bacterial contamination can also affect the MSS calibration solutions fluid paths (Ca1, Cal2, Cal3 and Cal4) from the S3 Fluid Pack, even if there are no "white deposits" visible.

An instantaneously started new provocative performance study, with instruments received back from customers, revealed that the effect on the calibration of the parameters glucose and lactate may lead to patient results being affected as well. This is because calibration drifts are not certain to be detected by the existing calibration and QC regime currently in place.

We want to point out that a retrospective case review confirmed that there was no complaint from a customer, in which a wrong patient result was generated due to the influence of bacterial contamination of the MSS calibration solutions. We observed this in our internal provocative study only, involving heavy duty use of severely contaminated instruments.

However, as the detection of calibration drifts by the software cannot be guaranteed, we regret to inform you that it will be required to monitor all active instruments with activated glucose and/or lactate parameters, by visiting you as a customer on a regular basis. During these visits, the instruments need to be checked for

indicators of beginning contamination and need to be cleaned in case bacterial contamination has been identified.

As a consequence, for each **cobas b** 221 <5> and <6> Roche OMNI S5/S6 system, with activated parameters glucose and/or lactate, an initial and follow-up customer visits on a 4-weekly basis are mandatory to exclude an effect on patient results.

We clearly want to state that this above described activity is an interim corrective action. In order to make these regular customer visits obsolete in the near future, a software based solution to automatically detect contamination and act accordingly is currently being developed. We expect this update to be available end of Q2/2015 for first customer monitoring.

As communicated earlier, the final solution to this issue is the implementation of changes to the reagents. In October, we received the results of the feasibility study aiming at increased concentrations of Kathon® 893 in the Standby solution. The outcome of this study indicated that the increase of the Kathon® 893 concentration was effective against some, but not all bacteria found in affected instruments from the field and thus would not significantly improve the situation. Therefore, a reformulation of Standby and calibration solutions of the S3 Fluid Pack is required to eliminate the root cause. Currently we expect this to be available end of 2016.

Action Required:

1. Run and maintain the **cobas b** 221 system/ OMNI S as per manufacturer instructions for use.
2. Initial and follow-up customer visits on a 4-weekly basis will be done by the FSRs in order to execute a maintenance procedure.

This issue is taken very seriously and our organization is making every effort to provide you with a resolution as soon as possible.

We sincerely apologize for any inconvenience caused by this issue.

Yours faithfully,

Roche Diagnostics GmbH

<Signature(s) according to guidelines>

The undersign confirms that this notice has been notified to the appropriate Regulatory Agency.

(Closing paragraph) Signature