Urgent Field Safety Notice
SBN-RMD-2016-006

RMD / **cobas**® 4800
Version 1
05-Apr-2016

Potential inhibition of plasma samples with the cobas® EGFR Mutation Test, v2 CE-IVD when used in conjunction with the cobas® cfDNA Sample Preparation Kit

Product Name	**cobas**® EGFR Mutation Test, v2 CE-IVD **cobas**® cfDNA Sample Preparation Kit IVD
GMMI / Part No **Device Identifier**	**cobas**® EGFR Mutation Test, v2 CE-IVD GMMI: 07248563190 UDI: 00875197005448 **cobas**® cfDNA Sample Preparation Kit IVD GMMI: 07247737190 UDI: 00875197005424
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

During internal studies using contrived plasma specimens, several mutations (L858R, Exon 19 deletion, T790M) inconsistently generated "No Mutation Detected" (i.e. False Negative) results with the **cobas**® EGFR Mutation Test, v2 when utilizing the **cobas**® cfDNA Sample Preparation kit.

There is no impact when using the **cobas**® DNA Sample Preparation Kit with the **cobas**® EGFR Mutation Test, v2 to test formalin-fixed paraffin-embedded tumor (FFPET) tissue samples.

For Exon 19 deletions and L858R, there is strong clinical validation of these mutations being sensitive to therapy with anti-EGFR tyrosine kinase inhibitor (TKI) therapy. Patients with either mutation would potentially be at risk and

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suffer temporary harm by not receiving anti-EGFR TKI therapy at diagnosis. Patients with a false negative result for either mutation may be denied the prospect of prolongation of disease control and survival (8-12 months), but may well receive anti-EGFR TKI therapy after failure of chemotherapy and derive some benefit.

Although T790M is considered a resistance mutation for 1st generation EGFR TKIs, there is now a 3rd generation EGFR TKI with activity against this mutation. As such, a patient with a false negative result for this mutation may be denied the prospect of prolongation of disease control and survival (8-12 months).

Actions taken by Roche Diagnostics (if applicable)

The Instructions for Use (DNA isolation procedures for plasma samples) for the **cobas**® EGFR Mutation Test, v2 and **cobas**® cfDNA Sample Preparation Kit will be updated to revise the handling of the eluate for plasma specimens prior to amplification and detection. The updated Instructions for Use will be available 29-Apr-2016.

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Actions to be taken by the customer/user

Until the updated Instructions for Use become available (29-Apr-2016), the following instructions must be followed when using **cobas®** EGFR Mutation Test, v2 and **cobas®** cfDNA Sample Preparation Kit:

Document	Original Instruction	Revised Instruction
cfDNA IFU EGFR IFU, Section B	Discard the FT. Close the caps on the elution tubes.	Discard the FT.
cfDNA IFU EGFR IFU, Section B	DNA stock is ready for PCR tests after vortexing. Store DNA stock according to instructions in **Sample transport storage and stability** section.	Slowly remove 80 µL of DNA stock, being careful not to disrupt the pellet (which may not be visible). Transfer removed DNA stock to a second elution tube (1.5-mL RNase/DNase-free microcentrifuge tube) pre-labeled with sample identification information. Close the caps on the elution tubes. DNA stock is ready for PCR tests. Store DNA stock according to instructions in Sample transport storage and stability section. Note: If the pellet is disrupted, return the DNA stock to the original elution tube, cap the tube, then pulse vortex the tube and, with the orientation mark facing outward, centrifuge the tube at 8,000 x g for 1 minute to collect eluate and repeat step 28 to remove 80 µL of DNA stock.

Instructions will be included for storage of extracted DNA stocks and for marking each elution tube with an orientation mark as well as how the mark should be oriented in the centrifuge in order to facilitate locating the pellet.

Additional revisions to the documents include:

- "Pipetting from the bottom of the elution tube may disrupt the pellet and adversely affect test results."

In the Instructions for Use for this assay, it is recommended that patients with a "No Mutation Detected" result for plasma samples should reflex to tissue testing to verify the result. As such, for previously generated results, in the case of a mutation not being detected in plasma, tissue should have been tested to evaluate for a mutation or confirm that no mutation was present.

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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