

March 2022

Important Note

therascreen[®] KRAS Mutation Detection Kit RGQ 「QIAGEN」, REF 874052

Dear *therascreen* KRAS Mutation Detection Kit RGQ 「QIAGEN」 customer,

This Important Note is only relevant for the analysis of samples originating from non-small cell lung cancer (NSCLC) tissue.

QIAGEN has identified a risk for a false mutation result, in rare cases, resulting from Flags/Warnings. In these rare cases, the Run Controls pass correctly (leading to a valid result for the sample), while one or more Flag/Warning might invalidate the result for one or more individual mutation target of the kit. In combination with the cross-reactivity described in the Instructions for Use, this might lead to a false positive or false negative G12C (12CYS) result for the KRAS Mutation Status. The software for the interpretation of all mutations appeared in the Result Table of Analysis reports currently does not invalidate the results for samples with such Flags/Warnings.

Potential risks associated with the issue

The issue can potentially lead to a false positive or false negative G12C (12CYS) mutation result that could subsequently be incorrectly reported from the laboratory. A false positive result could lead to the risk of the patient being exposed to an inappropriate or suboptimal anti-cancer treatment and/or unnecessarily suffer from side effects. A false negative result may lead to a suboptimal treatment or loss of chance to get a tailored treatment (Sotorasib) for non-small cell lung cancer patients harboring a KRAS G12C mutation.

Detailed description of the issue

Affected samples can be identified by one or more of the following Flags/Warnings listed on the Sample Result table of the KRAS Analysis Report:

- SAMPLE_INT_CTRL_EARLY_CT
- SAMPLE_POSITIVE_AND_INVALID
- SAMPLE_INT_CTRL_FAIL
- MUTATION_EARLY_CT
- SAMPLE_INVALID_DATA

The likelihood for a G12C (12CYS) false positive result or false negative mutation result due to this issue was evaluated as a rare case.

Failure to follow the IFU with regards to reagent mixing at each mixing step during the assay setup may contribute to the occurrence of these Flags/Warnings.

The calling of a false G12C (12CYS) mutation result for samples due to the described Flags/Warnings can be avoided by interpreting sample results with the above listed Flags/Warnings as invalid. In the Sample result table, no KRAS Status and no KRAS Mutation Status should be taken for these samples.

Note:

- Sample Results with the KRAS Status "No Mutation Detected" are not affected by this issue.
 - Sample results with no Flags/Warnings (in the Sample Result table) are not affected by this issue.
 - Sample Results with other Flags/Warnings as listed in this notice are not affected by this issue. Follow the Instructions for Use in these cases.
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Actions to be taken by the customer:

- **For continued use of the *therascreen* KRAS Mutation Detection Kit RGQ 「QIAGEN」, check the Flags/Warnings in the Sample Result table for automated interpretation of results. Sample results with one or more of the Flags/Warnings listed in this notice should be regarded as invalid with respect to the KRAS status and KRAS Mutation status.**
- Setup a new PCR run to repeat the affected sample(s).
- To minimize Flags/Warnings for the controls and samples, strict compliance to the IFU guidance should be followed, including but not limited to:
 - Correct reagent mixing is required, and must be ensured at each mixing step during the assay setup.
 - Placement of the Rotor-Gene Q MDx according to Installation Procedures site requirements
- Forward this information to all individuals and departments within your organization who are using the *therascreen* KRAS Mutation Detection Kit RGQ 「QIAGEN」, REF. 874052.
- If you are not the end user, please forward this notice to the product end user.
- Review this Important Note with your laboratory/medical director.

Actions taken by QIAGEN

QIAGEN is revising the Instructions for Use, as described in this Important Note, to reduce any risk resulting from the calling of a false positive or false negative G12C (12CYS) mutation result for NSCLC samples due to the Flags/Warnings listed in this notice and to emphasize strict compliance to the IFU guidance to minimize Flags/Warnings.

If you have any questions or concerns, please contact your local QIAGEN Technical Service Department through any of the following:

Telephone: 03-6890-7300

Email: **techservice-jp@qiagen.com**

We sincerely apologize for any inconvenience this may cause and thank you in advance for your cooperation.

With kind regards,

QIAGEN

www.qiagen.com