



October 2022

Important Note

therascreen[®] FGFR RGQ RT-PCR Kit (24), REF 874711 Version 1; Confirmatory retest of positive results might be required

Dear *therascreen* FGFR RGQ RT-PCR Kit customer,

QIAGEN has identified an increased occurrence rate of false positive results obtained with the *therascreen* FGFR RGQ RT-PCR Kit. For a proportion of samples with the Overall sample result "FGFR Alteration Detected", the result could be a false positive result.

For the continued use of REF 874711 *therascreen* FGFR RGQ RT-PCR Kit Version 1 with LOT number 172033373 or higher, use the following criteria for the interpretation of results:

- Review this notice with your laboratory/medical director.
- Forward this information to all individuals and departments within your organisation who are using REF 874711 *therascreen* FGFR RGQ RT-PCR Kit Version 1.
- In addition to the "Analysis Report", use the following criteria for the interpretation of results for "FGFR Alteration Detected" results:
 - All "FGFR Alteration Detected" results aside from "S249C Mutation Detected" (*i.e.*, detected targets other than p.S249C (c746C>G on Exon 7) should be disregarded and a retest for confirmatory positive result should be performed using the extracted RNA if available, or re-extracted if it is not. An overview of the affected results is provided in Table 1.

Table 1. Overview of affected results

| Overall sample result | Individual target result | Affected by the issue | Action to be taken by customer |
|--------------------------|--|-----------------------|---|
| No Alteration Detected | n/a | no | n/a (correct result) |
| FGFR Alteration Detected | S249C Mutation Detected | no | n/a (correct result) |
| FGFR Alteration Detected | S249C Mutation Detected and additional individual target results | no | n/a (correct result) |
| FGFR Alteration Detected | One or more individual target results that don't include S249C | yes | Disregard result for this sample. Retest for confirmatory positive result |

- The following results should be assigned to the affected samples after the retest:
 - **Retest result is positive for the same target(s)/ alteration(s):** Regard the result for the corresponding sample as positive.
 - **Retest result is positive for different target(s)/ alteration(s) in the retest compared to the initial result:** Regard the result as indeterminate.
 - **Retest is negative:** The result for the corresponding sample should be regarded as negative
 - **Retested sample is within an invalid run:** Repeat the run.
 - **Result for individual sample is invalid in the retest:** Regard the result as indeterminate.
 - An overview of the interpretation of retest results is provided in Table 2.

Table 2. Overview of interpretation of retest results

| Retest result | Individual target result in retest | Result to be assigned after retest |
|----------------------------------|---|---|
| FGFR Alteration Detected | Same target(s)/ alteration(s) as within initial test | FGFR Alteration Detected, "positive result" |
| FGFR Alteration Detected | Different target(s)/ alteration(s) as within initial test | Indeterminate result |
| No Alteration Detected | n/a | No Alteration Detected |
| Invalid run | n/a | n/a, repeat the run |
| Invalid individual sample result | n/a | Indeterminate result |

- Samples with the following results are not affected affected and thus no further actions required for such samples:
 - Overall sample result “No Alteration Detected”
 - Overall sample result “FGFR Alteration Detected” results with Individual target result S249C Mutation Detected. This includes samples with additional alterations detected.
- An overview of the affected results is provided in Table 1.

Detailed description of the issue

In the affected runs, the Run Controls pass correctly (leading to a valid result for the sample), while an artefact in one or more of the mutation assays might cause an incorrect valid mutation positive result for individual samples. The software for the interpretation of all mutations claimed in the assay does not distinguish such artefacts from a real amplification obtained with a valid mutation positive sample.

The investigation at QIAGEN demonstrated that all targets/Amino acid variants/Fusion IDs are affected, except for Amino acid variant p.S249C (c.746C>G on Exon 7).

As an interim solution, the newly manufactured batches with LOT number 172033373 and higher will undergo additional testing (until the issue is resolved or investigation is completed) to ensure a minimum specificity of 95%. If a positive sample result is obtained, a retest is required as described in this Important Note in order to mitigate the risk of a false positive result. Upon retest, the minimum specificity increases to 99%.

Potential risks associated with this issue

The issue can potentially lead to a false positive sample 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 experiencing side effects.

Actions taken by QIAGEN

QIAGEN is working on identifying and correcting the root cause of false positivity. Any update on mitigation measures will be promptly communicated. In the interim, we are providing kits with this Important Note.

Translations of this Important Note

QIAGEN provides the printed Important Note in the English language. Translations of the Important Note are electronically available in a portable document format (PDF). You may access the translated documents in the Product Resources tab of *therascreen*[®] FGFR RGQ RT-PCR Kit page on www.qiagen.com.

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

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

With kind regards,

QIAGEN

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