

11th December 2020

Urgent Field Safety Notice

therascreen[®] PIK3CA RGQ PCR Kit, REF 873111

Dear valued *therascreen* PIK3CA RGQ PCR Kit user,

As part of our ongoing market surveillance process, QIAGEN has identified that the *therascreen* PIK3CA RGQ PCR Kit may generate false Q546R mutation positive results caused by non-specific molecular interactions within the Q546R reaction.

In these cases, the run controls for the Q546R reaction pass validity checks correctly. The software for the interpretation of PCR run data and identification of the Q546R mutation is currently not able to differentiate between the signal created by the non-specific interaction and that created by genuine amplification from a valid mutation positive sample. Consequently, Q546R false positive results are reported to the system operator.

As a result of the preliminary investigation performed at QIAGEN, the likelihood for any Q546R false mutation positive result was evaluated as higher than previously observed and described within the Instructions For Use.

The performance of other mutation detection assays within the kit is not affected.

Potential risks associated by this issue

The issue can potentially lead to a false positive *PIK3CA* Q546R mutation detected result, which could subsequently be reported by the laboratory. Receipt of such a false positive result by the clinician who ordered the test could lead to incorrect treatment decisions being made that could significantly impact patient health, including inappropriate treatment of a patient with PIQRAY[®] (alpelisib).

Actions to be taken by the customer/user

- For patient samples where a PIK3CA Mutation Detected Result is obtained, disregard the Q546R positive results.
- Cease to report patient samples where a Q546R mutation result is obtained as PIK3CA Mutation Detected. Information about individual target results is specifically obtained from the "Individual target result" column of the Rotor-Gene AssayManager v2.1 result table.

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- If multiple mutations including Q546R are detected, disregard the Q546R result only. Continue to consider all other results as valid and report them accordingly.
 - For the purpose of run validity, Q546R control data must still be produced. The *therascreen* PIK3CA RGQ PCR Kit software requires valid run control data from the Q546R reaction for the overall test to be valid. Therefore, continue to use all supplied reagents and perform testing as described in the kit handbook, but disregard Q546R positive results generated for patient samples as described in the previous bullet points.
 - Forward this information to all individuals and departments within your organization who are using the *therascreen* PIK3CA RGQ PCR Kit REF 873111. If you are not the end-user, please forward this notice to the product end-user.
 - Review this notice with your laboratory/medical director.
 - Complete the Acknowledgement or Receipt Form attached to this letter by December 22, 2020 and email it to quality.communications@qiagen.com.

For commercial partners:

- Forward this notice to your customers.
- Follow-up on the Acknowledgement of Receipt with all of your customers.
- Confirm the completion of the follow-up of the Acknowledgement of Receipt of your customers to quality.communications@qiagen.com.

Actions taken by QIAGEN

QIAGEN is now revising the Instructions for Use for the *therascreen* PIK3CA RGQ PCR Kit, as described in this notice, to reduce any risk resulting from non-specific molecular interactions within the Q546R reaction leading to the generation of Q546R false mutation positive results.

QIAGEN is also updating the *therascreen* PIK3CA FFPE and Plasma Assay Profile software packages to resolve this issue. You will be informed as soon as the updated software is available, and provided with instructions for updating the *therascreen* PIK3CA assay profiles. Until then, we advise you to disregard and cease to report mutation detected results generated by the *PIK3CA* Q546R reaction, as outlined above.

If you have any questions or concerns, please contact your local QIAGEN Technical Service Department. For contact information, visit the following webpages:

QIAGEN Subsidiaries

www.qiagen.com/de/about-us-old/contact/global-contacts/subsidiaries

QIAGEN Commercial Partners and Importers

www.qiagen.com/de/about-us-old/contact/global-contacts/distributors-and-importers

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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Acknowledgement of Receipt Form

Please complete this form using block letters and email it to **quality.communications@qiagen.com** by December 22, 2020.

Or (equivalently to your signature) reply via email to **quality.communications@qiagen.com** using the following acknowledgement text:

I hereby acknowledge that I have received, read, and understood the included Urgent Field Safety Notice dated December 11, 2020. We have taken the necessary actions as suggested by this notice.

We acknowledge that this document may be presented to regulatory or administrative bodies globally according to mandatory legislation.

Laboratory name:

Address:

Contact name:

Title:

E-mail address:

Phone number:

Date:

Signature: