To: `5.1.2e` `5.1.2e` [`5.1.2e` @rivm.nl]
Cc: `5.1.2e`, `5.1.2e` [`5.1.2e` @rki.de]; `5.1.2e`, `5.1.2e` [`5.1.2e` @rki.de]; `5.1.2e`, `5.1.2e` [`5.1.2e` @rki.de]
From: `5.1.2e` , `5.1.2e`
Sent: Tue 11/3/2020 3:02:02 PM
Subject: AW: RT-qPCR Ct cutoff values for positive/negative and highly likely infectious/less likely infectious in German labs
Received: Tue 11/3/2020 3:02:24 PM

20201020 INSTAND von RKI KLCoV INSTAND Ankündigung - quantitative Bezugsproben 1 und 2 - SARS-CoV-2.pdf

Dear `5.1.2e`

We don't know to which formal thresholds the lab is referring. It may be that the lab is dealing with the viral standards which are distributed currently in order to improve the comparison and evaluation of PCR results (file attached). For more details you can contact `5.1.2e` `5.1.2e` (`5.1.2e` @rki.de) who was involved in the preparation of these samples.

We agree with your considerations that an absolute cutoff cannot be given due to different workflows and methods used.

Best regards,

`5.1.2e`

-----Ursprüngliche Nachricht-----
Von: `5.1.2e` `5.1.2e` < `5.1.2e` @rivm.nl>
Gesendet: Montag, 2. November 2020 10:58
An: `5.1.2e`, `5.1.2e` < `5.1.2e` @rki.de>; `5.1.2e` , `5.1.2e` < `5.1.2e` @rki.de>; `5.1.2e`, `5.1.2e` < `5.1.2e` @rki.de>; `5.1.2e`, `5.1.2e` < `5.1.2e` @rki.de>
Betreff: RT-qPCR Ct cutoff values for positive/negative and highly likely infectious/less likely infectious in German labs
Priorität: Hoch

Dear colleagues at RKI,

Most of you know me from influenza surveillance.

In addition to influenza I have been involved in the Dutch COVID-19 laboratory response from January onwards. Part of that is an external quality assessment (EQA) that every lab has to perform and pass successfully to be included officially as COVID-19 testing laboratory in/for the Netherlands. Currently our MoH is including several German laboratories for testing specimens form Dutch patients. Because we have a sensitivity check with final interpretation of the PCR result in the EQA, we have learned from the German laboratories about guidelines for German labs how to deal especially with Ct values in the higher range. I have checked the RKI website (https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Vorl_Testung_nCoV.html;jsessionid=3BFA69A9452368F99D1761F9872 46B16.internet052 <https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Vorl_Testung_nCoV.html;jsessionid=3BFA69A9452368F99D1761F9872 46B16.internet052>), and that does not differ that much from the Dutch standpoint that Ct's in the higher range can be interpreted as that the patient at the moment of sampling is less likely infectious, but that an absolute Ct cutoff cannot be given as workflows between and within labs differ.

One of the German labs send last week an email to us saying:

Our technical analysis classifies everything up to 39 which has a sigmoidal curve as positive. Up to Cp 42, we classify as ambiguous. Above 42 the result is negative. This analysis is usually followed by a medical analysis that defines the final medical result. The medical team at ... for example uses much lower Cut-Offs than the ones mentioned above.

In addition, there is now more literature available that links viral load in the PCR test with infectiosity. We are currently preparing a validation of our kit with the thresholds published by the German Robert-Koch-Institute. This will most likely adjust the Cut-Offs for positive and negative results in the near future.

Is it possible to provide us with the formal thresholds published by RKI and your recommendations for laboratories? This is important for us because a large number of Dutch patients are tested in German labs and if criteria for positive/negative differ significantly from our guidelines for Dutch labs this might impact our control strategies. Ideally, the Dutch guidelines should be used by German labs for Dutch patients. Currently we consider to establish a cutoff for RT-qPCR based on Ct distribution from the large testing streets and using the Ct at 90th percentile (P90) to establish for each workflow independently as cutoff to distinguish positive from weakly positive. Negative is technical/analytical interpretation of the PCR result as absence of SARS-CoV-2 RNA, whereas positive/weakly positive can be used as a surrogate marker for level of being infectious in the control of COVID-19 by municipal health services.

Many thanks in advance for your answer and considerations how to deal with this. Highly appreciated!

Best regards,

5.1.2e

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5.1.2e 5.1.2e , PhD.

5.1.2e

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Together with ErasmusMC, Rotterdam, being the National Influenza Centre (NIC) in the Netherlands

WHO COVID-19 reference laboratory

Want to know more about surveillance of influenza in the Netherlands? See (click or scan):

 <https://www.rivm.nl/griep>

For COVID-19 see (click or scan):

 <https://www.rivm.nl/coronavirus-covid-19>