To: [redacted] @rivm.nl]; [redacted] @rivm.nl]; [redacted] @rivm.nl]
Sent: Wed 9/2/2020 3:13:27 PM
Subject: RE: SO signaal COVID-19 PCR
Received: Wed 9/2/2020 3:13:27 PM

Performance deficiencies observed in a commercial RT-PCR kit for detection of SARS-CoV-2 RNA

Announcement Displayed From :

Friday, August 28, 2020 - 16:28

Performance deficiencies observed in a commercial RT-PCR kit for detection of SARS-CoV-2 RNA

WHO was informed through the Early Warning and Response System of the European Commission (EWRS) on 24 August 2020 about false positive SARS-CoV-2 PCR results in Sweden, on a commercial manufactured test system. The artefact/false positive signal was initially observed in two different and independent laboratories (National Pandemic Centre [NPC], Department of Microbiology, Tumor and Cell biology, Karolinska Institutet and ABC labs) and was confirmed by third laboratory Karolinska University Hospital Laboratory (KUL).The artefact/ false positive results has occurred independently of lot, operator, instrument and time.

During systematic quality control procedures, the Swedish newly established SARS-CoV-2 laboratory at the Karolinska Institutet, Sweden has reported limitations of the diagnostic kit for PCR-detection of SARS-CoV-2 RNA marketed under the name "Real-time Fluorescent RT-PCR kit for detecting SARS-CoV-2", that is produced by BGI BIOTECHNOLOGY (WUHAN) Co., LTD. The evaluation has been conducted over a period of approximately six weeks (24 June to 4 August 2020).

The kit performance deficiency appears as an unspecific fluorescence signal that occurs at late CT-intervals. Although the fluorescence signal has high CT-values the amplification curve is sigmoidal and similar to a true amplifying curve but occurs at random, however within the threshold for PCR-positivity as specified in the manufacture provided kit product specification. There was no contaminating SARS-CoV-2 RNA identified. In total this artefact/false positive signal been observed in two separate lots in three different laboratories. The artefact/ false positive results has occurred independently of lot, operator, instrument and time.

The investigation of the kit's technical performance was conducted by serial dilution of SARS-CoV-2 RNA series and analyses of large numbers of true negative samples (water). The investigation shows that the fluorescence signal occurs with a frequency of approximately 14.9% (310/2088) in true negative samples. The false positive fluorescence signal occurs in the CT values of 34.77 – 39.47 (median 37.68). The analyses of the true-negative samples (nuclease-free H_2O) was performed as part of the technical investigation in the end of July/beginning of August. In order to ensure high specificity and to avoid false positive results, the threshold for PCR-positivity needed to be adjusted (fluorescence signal amplitude) compared to what is specified in the manufacture provided kit product specification on the cost of the sensitivity. As a consequence of the performance deficiencies, the test is unable to distinguish between low level positivity and false positive results.

As a result of this, a large number of test results (approximately 4000) have been re-evaluated in Sweden and now are defined as undetermined. A report has been filed to the Swedish Medical Product Agency, Member States of the European Union/European Economic Area and the United Kingdom (EU/EEA/UK), and the manufacturer.

From: [redacted] <[redacted] @rivm.nl>
Sent: woensdag 2 september 2020 09:32
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Subject: SO signaal COVID-19 PCR

Goedemorgen 5.1.2e, 5.1.2e en 5.1.2e

Gisteren in het RT is afgesproken een signaal op te nemen over de COVID-19 PCR die in Zweden ca 3.7000 vals positieve uitslagen gegeven heeft (periode tussen maart en augustus). Voor zover ik weet betreft het een self-test kit afkomstig uit 5.1.2a die in meerdere landen wereldwijd gebruikt wordt. In Nederland is deze test niet op de markt.
Tijdens routine kwaliteitschecks in 2 laboratoria is ontdekt dat de test geen onderscheid kan maken tussen negatieve samples en samples met een laag virusactiviteit De meeste mensen met een vals positieve uitslag hadden geen of milde symptomen. De vals positieve testuitslagen zijn opgemerkt in de regio's Stockholm, Västra Götaland, Gävleborg, Västerbotten, Västmanland, Dalarna, Västernorrland, Sörmland en Blekinge.

5.1.2e gaf aan dat de boodschap van het signaal zou moeten zijn dat een tweede test nodig is bij veel positieve uitslagen bij monsters met een lage load. Dit moet wel goed geformuleerd worden omdat de algemene boodschap is om geen tweede test te doen.

5.1.2e zouden jullie een voorzet voor dit signaal willen maken en dit afstemmen met 5.1.2e? Ik heb alleen maar berichten uit de media kunnen vinden en geen officiële bron en het is te microbiologisch voor mij.

Groet
5.1.2e