

To: (10)(2e) <(10)(2e)@fhi.no>
From: (10)(2e)
Sent: Thur 2/6/2020 9:15:12 PM
Subject: FW: warning !! 2019-nCoV primers/probes contamination with synthetic controls

Dear (10)(2e)

Taking notice of the strong reaction from (10)(2e) I would propose to leave the issue to the EVD network..

Warm regards,
 And success in these busy times...

(10)(2e)

From: (10)(2e) <(10)(2e)@rivm.nl>
Sent: donderdag 6 februari 2020 12:18
To: (10)(2e) <(10)(2e)@fhi.no>; (10)(2e) <(10)(2e)@rivm.nl>
Cc: (10)(2e) <(10)(2e)@rivm.nl>
Subject: RE: warning !! 2019-nCoV primers/probes contamination with synthetic controls

Hi,

I'm completely against this for the following reason: expert labs know that they need to do entry QC for primers and probes. This was an internal warning from lab people to lab people: " please don't forget within the heat of things to do proper entry QC when you receive new primer/probe batches. It is a lab issue: labs need to do the proper QC and based on that they know what their results are worth. This e-mail was to remind them of that (what they already know) and to highlight that due to massive ordering of primers and probes and synthetic controls in Europe batches produced at several companies appeared to have contaminants. Because of the massive response this became apparent. But still nothing new: the need for proper entry QC when you start with new reagents.

Please don't make more of this then there is to it. It is a lab issue that the labs in the networks understand.

If the Norwegian lab is **absolutely sure** that it was indeed in the original primer/probe batches they bought and not a contamination due to own lab procedures it would be very useful if they could share that experience within the labnetwork. It is absolutely essential to not mix the issue in my e-mail to (10)(2e) with the issue of lab contaminations. That is something completely different, that's why it is important to really know for sure it is in the company order and not added afterward in the lab.

It is not worth an EWRS at this point as we do not know the extent of the problem and all relevant labs have been informed (both in (10)(2e) and ERLI-Net) It is most certainly not an EWRS involving the Netherlands. As indicated there were labs from a few different countries that experienced this problem.

So please don't make this bigger than it is, the labs should be aware and stick to proper entry QC which they should always do.

Best (10)(2e)

From: (10)(2e) <(10)(2e)@fhi.no>
Sent: donderdag 6 februari 2020 11:24
To: (10)(2e) <(10)(2e)@rivm.nl>
Cc: (10)(2e) <(10)(2e)@rivm.nl>; (10)(2e) <(10)(2e)@rivm.nl>
Subject: SV: warning !! 2019-nCoV primers/probes contamination with synthetic controls

Dear (10)(2e)

And thank you for your rapid reply!

The incident is only an internal issue, and is not public. However, we think it is sufficient to just inform about the risk of contamination and false positive, and the need for verification before a lot of measures are implemented.

What do you think?

(10)(2e)

Fra: (10)(2e) <(10)(2e)@rivm.nl>

Sendt: torsdag 6. februar 2020 10:46

Til: (10)(2e) <(10)(2e)@fhi.no>

Kopi: (10)(2e) <(10)(2e)@rivm.nl>; (10)(2e) <(10)(2e)@rivm.nl>

Emne: RE: warning !! 2019-nCoV primers/probes contamination with synthetic controls

Dear (10)(2e) thank you for letting me know.

(10)(2e) is member of our ResponseTeam and my colleague at the RIVM.

Maybe it is good to make a combined EWRS message from you and us/EVD, where you explain the incident, and we, (10)(2e) add the warning?

Kind regards,

(10)(2e)

From: (10)(2e) <(10)(2e)@fhi.no>

Sent: donderdag 6 februari 2020 10:38

To: (10)(2e) <(10)(2e)@rivm.nl>

Subject: VS: warning !! 2019-nCoV primers/probes contamination with synthetic controls

Dear (10)(2e)

Hope everything is fine with you! I guess you also is very busy☺

Our reflag just received this warning from the evdlabnet. We had an incident with a false positive that generated much work and concern during the weekend, and this was very useful in order to understand what happened. Have you considered sending this also in EWRS so that all are aware of this, not only the lab network?

I think that could be useful, but I guess you may have discussed this also.

Greetings from Oslo!

(10)(2e)

From: (10)(2e) <(10)(2e)@erasmusmc.nl>

Sent: Wednesday, February 5, 2020 5:30 PM

To: (10)(2e) <(10)(2e)@fhi.no>

Subject: warning !! 2019-nCoV primers/probes contamination with synthetic controls

Warning !: 2019-nCoV primer/probe batches might be contaminated with synthetic control

Dear all,

We would like to draw your attention to the following important issue:

We have understood from a few laboratories in different countries that primer and probe batches for molecular detection of 2019-nCoV involving different companies might be contaminated with synthetic positive control material for 2019-nCoV. Companies synthesize primers, probes as well as synthetic controls. Apparently QC at the company level is sometimes such that it might allow for cross-contamination to occur and delivery of contaminated batches.

To illustrate one specific case: batch of primers and probes for (10)(1c) et al., E-gene and RdRp-gene test were received two days ago. All primers and probes that were ordered appeared to be contaminated with the synthetic E-gene control (so both for the E-gene test as well as the RdRp test while the synthetic E-gene control was not ordered and had not been ordered before). The contamination gave a robust signal that started at Ct33 and it responded in a quantitative way in a dilution series (Δ Ct 3 for each 10-fold dilution in the E-gene PCR). Extensive testing and cross-testing proved beyond doubt that the delivered batches were contaminated.

We would like to advise you the following:

- to apply a thorough entrance QC before you implement ordered primers and probes.

- to strictly follow the advice for secondary confirmatory testing in case of positives, *targeting a different genomic region* before confirming an infection. In the case illustrated above, the RdRp-gene PCR did not give false positives results regardless of the presence of the contamination (E-gene synthetic control will not be amplified in the RdRp gene PCR).

Furthermore, we would welcome any feedback on this issue when you have experienced the same or when you experience this in the future. We would like to try to get a better insight in the extent of the problem.

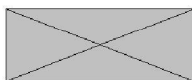
A great thank you to the laboratories who signaled this problem.

Best wishes (10)(2e)



(10)(2e)

(10)(2e)



Dit bericht kan informatie bevatten die niet voor u is bestemd. Indien u niet de geadresseerde bent of dit bericht abusievelijk aan u is verzonden, wordt u verzocht dat aan de afzender te melden en het bericht te verwijderen. Het RIVM aanvaardt geen aansprakelijkheid voor schade, van welke aard ook, die verband houdt met risico's verbonden aan het elektronisch verzenden van berichten.
www.rivm.nl *De zorg voor morgen begint vandaag*

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