

APHL Laboratory Alert: 2019-nCoV All PHL Lab Call

February 12, 2020

Call Summary

Main Contact Emails

CDC Emergency Operations Center (EOC) Contact: 770-488-7100

CDC Respiratory Virus inbox: respviro@cdc.gov

APHL EOC Contact: eoc@aphl.org

APHL Informatics Contact: informatics.support@aphl.org

Introduction (*Scott Becker, APHL*)

APHL received emails from members about the N3 showing sporadic aberrant activity, with fluorescent signal crossing at late Ct values. CDC has consulted with FDA on this issue. A replacement N3 component of the EUA assay is being manufactured and undergoing enhanced quality control. APHL appreciates public health laboratories (PHLs) efforts to begin verification and alert APHL and CDC of the issues they observed.

2019-nCoV Epidemiology Update (*Alicia Fry, CDC*)

Since the beginning of response, CDC has evaluated 420 PUIs. The number of daily PUIs that CDC is evaluating has been decreasing (only 4 in the last 24 hours). CDC still wants states to call CDC to report their PUI numbers. To date, there have been 13 cases in the US. The most recent case was from an individual from repatriation flight from China. Over 700 contacts of positive cases are being followed (two became cases via close, household contact).

2019-nCoV EUA Implementation at PHLs (*Steve Lindstrom, CDC; Julie Villanueva, CDC*)

Update on N3 manufacturing issue

CDC appreciates the communications from PHLs to the respviro@cdc.gov email inbox. Given the reports of the aberrant activity of N3 reported by some labs, CDC is manufacturing a replacement N3 component for the EUA assay, and FDA has approved the use of the replacement component for the kits. The shipment of the new N3 component will include instructions to destroy the current N3 assay and to process as indicated in the package insert. The replacement N3 component will be made available next week and will allow PHLs to proceed with verification.

For PHLs that have already completed verification with the existing N3 component, they may proceed with testing patient specimens. However, when the replacement N3 component arrives, it will need to be verified and the original N3 component will need to be destroyed. CDC suggests re-running the

verification on all nine samples with the new N3 component in order to have all the data in one dataset which will be easier for CMS inspectors to review.

Sputum processing guidelines

Sputum samples are an appropriate specimen for testing with the EUA. CDC posted a [recommended procedure for sputum processing](#) that PHLs may use if they do not already have an in-house procedure for this. If PHLs have questions about sputum processing, they can email respvirus@cdc.gov.

Confirmation of presumptive positives

According to the EUA, the interpretation of the results obtained by PHLs is presumptive positive. A presumptive positive result allows public health officials to act on the presumptive result while waiting for confirmation from CDC. The purpose for the presumptive positive requirement is that CDC needs to demonstrate to FDA that the test is performing as expected in the field, and for confirmation that results are accurate. CDC cannot say when or if the presumptive positive reporting will be changed in the future – it will depend on the evidence received from the field and FDA’s approval.

Other notes on the EUA assay

For PHLs onboarding QIAGEN EZ1 extraction methods, the carrier RNA does need to be added to column well, otherwise the machine will give an error and you will lose the extraction. The carrier RNA provided with the DSP kit and with the Buffer AVL are the same and either can be used.

Over the coming weeks CDC will look at updating the EUA with additional extraction methods, with a priority for adding higher throughput automated extractions.

There have been questions regarding use of caps vs films. The assay is cleared for caps in order to separate the process for the NTC, sample addition and positive control. This mitigates the risk of false positives. PHLs should follow the EUA instructions for use.

Coordination of PUIs with CDC (*Wendi Kuhnert-Tallman, CDC*)

On February 12, CDC revised their [Criteria to Guide Evaluation of Persons Under Investigation \(PUI\) for 2019-nCoV](#) shared PUI guidance. This guidance provides information on where PHLs should be putting the nCoV-ID (CDC PUI ID). Currently CDC assigns the nCoV-ID; however in the future this will be generated at the state level once PHLs can test.

CDC Specimen Submission (50.34) Form Reminders (*Wendi, CDC*)

On form 50.34 PHLs should include the lab patient ID and lab specimen ID in the appropriate boxes. The nCoV-ID and nCoV-ID specimen type identifier should be included in the “Alternative Patient ID” and “Alternative Specimen ID” boxes.

PHLs must ensure that the nCoV-ID is where it needs to be on the 50.34 form. For CLIA compliance, a minimum of two patient identifiers are required. The 50.34 form has four sets of fields (patient name, DOB, a combination of sex and age, and a combination of patient ID and alternate patient ID). **At least**

two of these four need to be identified on 50.34 to ensure full CLIA compliance. Intermediate shippers can be included in the incoming 50.34 form, however it is unclear if the intermediate shippers are listed on the report when it goes back out to PHLs. CDC will check with their LIMS team. There may be a need for additional training on the 50.34 form for smaller PHLs - APHL's Infectious Disease Committee will be looking into this issue (i.e. job aids, webinars).

Community Based Surveillance Activities and Surveillance Testing (*Julie Villanueva, CDC*)

CDC's [PUI definition](#) was updated today (2/12/2020). The update includes a change to the footer of the table which now reads, "...For severely ill individuals, testing can be considered when exposure history is equivocal (e.g., uncertain travel or exposure, or no known exposure) and another etiology has not been identified."

CDC Lab Task Force is working with Epi Task Force to understand what community based surveillance activities they are interested in conducting. CDC has spoken with FDA about these activities and is waiting to hear back from FDA. PHLs must ensure that testing is being done in line with the EUA and guidance from the FDA.

IRR Update (*Erica Guthrie, CDC*)

Between Friday (February 7) and Monday (February 10), 99 US PHLs received EUA reagents from orders placed last week. CDC is in the process of ensuring that PHLs will get the replacement N3 component. PHLs do not need to do anything to get the new N3 component and PHLs should NOT order the N3 component from IRR; IRR will push the orders from their end. PHLs may receive an automated message from IRR as IRR places the orders on their behalf.

For some PHLs whose assay kits were shipped over the weekend, and if the order included extraction kits, they may have received notification that the extraction kit was removed. This is because the extraction kit is considered "dangerous goods" and some jurisdictions did not have airport agents available for clearing dangerous goods. IRR is working on re-sending the items that were removed.

nCoV Results Reporting Update (*Michelle Meigs, APHL*)

States received a [reporting FAQ and additional guidance](#) to support nCoV data messaging work. The guidance will show where to include nCoV-ID information in your message (optional). If PHLs are developing PHLIP messages, they need to get in contact with APHL informatics desk (informatics.support@aphl.org) when those messages are complete and ready to be reviewed.

APHL is monitoring which PHLs have been validated and which are ready to go into production. Forty-six states have requested technical assistance with validation, 16 states are in some stage of validation, and nine states are already approved for production. APHL is prioritizing funneling/repatriation sites, followed by sites that need LIMS vendor support. For PHLs that do not use HL7 2.3.1 or 2.5.1 and have not been contacted by APHL or CDC, please submit an APHL informatics desk ticket (informatics.support@aphl.org).

Reminder to complete online survey

Fifty-five states completed the online assessment (2-question survey). If PHLs have not already, please complete the [online survey](#).

Questions and Answers (Q&A)

Q: Is CDC aware that ThermoFisher has an nCoV assay available?

A: **CDC does not have a stance on commercial tests; this is a question for FDA. If companies are offering a test, they would have to be sold as research use only. Diagnostic testing must receive EUA through FDA.**

Q: Can CDC clarify what is meant by the note in the EUA assay SOP that states that positive specimens may be non-infectious viral particles?

A: **The assay is a molecular assay that detects nucleic acid, and CDC does not know yet how this relates to infectiousness. CDC will learn more as more tests are done. The current data is not sufficient to say that detection of RNA is reflective of infectious particles.**

Q: If PHLs get a presumptive positive, should this be called into the CDC EOC?

A: **PHLs are required to notify CDC of presumptive positive results. Follow the CDC guidance, which includes reporting to the CDC EOC phone number (770-488-7100) and respvirus@cdc.gov inbox.**

Q: When presumptive positive specimens are sent by PHLs to CDC, what testing is CDC doing to confirm the results?

A: **CDC will retest the specimen with the same EUA assay. This will verify both the result and the level of reactivity. This confirmation will help to further demonstrate to FDA the performance of the assay and hopefully enable the possibility for an eventual removal of 'presumptive' from the PHL result.**

Q: How long are reconstituted primers and probes good for in the freezer?

A: **The primers, as dried, are stable until the expiration on the kit. Primers reconstituted into working aliquots are stable for up to 4 months at 2-8°C. Frozen aliquots ($\leq -20^{\circ}\text{C}$) are stable until expiration of the kit.**

Q: Some PHLs are receiving an Excel spreadsheet of results back from the CDC EOC which are not CLIA compliant.

A: **CDC will need to follow up with the epi side and EOC to understand what aspects are not compliant. Reports sent from the CDC lab team are being sent under CDC's CLIA certificate. CDC is reporting to the email address that is registered for the state public health labs in the CDC ELIMS system, using information from the 50.34 form. APHL suggests that CDC re-verify the address for the ELIMS reports.**

Q: What is the timeline for CDC getting EUA amendments for community surveillance from FDA?

A: **CDC understands there is pressure from epidemiologists for community surveillance activities. CDC spoke with FDA today – nothing has been approved yet under the EUA. CDC needs clear guidance from FDA about what can and cannot be done with the EUA. APHL and CSTE can help push a joint message out to both memberships as soon as CDC gets more information from FDA.**

Q: How will CDC deal with discordant results on presumptive positive cases?

A: This will be dealt with on a case-by-case basis. For presumptive positive cases, it is likely that multiple specimen types would be collected, so additional specimens could be tested if the initial CDC confirmatory test is negative.

Q: Will the new N3 primer be a new sequence or the same sequence that has been newly manufactured?

A: The N3 primer will be the same sequence, just newly manufactured. It will meet all the same performance criteria detailed in the EUA.

Q: Are there any updates on the structure of the nCoV-ID number?

A: Updates are pending. CDC has heard from states that the original nCoV-ID structure was problematic. CDC will provide specific guidance shortly.

Q: For presumptive positive cases, should PHLs report the nCoV number assigned by CDC, or the ID number assigned by the PHL?

A: PHLs should use the nCoV-ID assigned by the jurisdiction when reporting presumptive positive cases. There is HL7 and mapping guidance coming out from APHL soon (post-teleconference update: see [Lab Alert #11](#)). The nCoV-ID assigned by jurisdictions will be the only case ID once PHLs are performing testing roll out the kits. At this time, CDC is still assigning the ID.

Q: For testing asymptomatic contacts of a case, does the testing need to be done at CDC?

A: CDC is waiting for guidance from FDA on this issue. Right now, please send these samples to CDC for testing until we know more.

Q: If a PHL has already validated with the current N3 primer, can the PHL begin testing PUIs?

A: If a PHL was able to successfully complete the verification, that is sufficient to continue testing and reporting. If PHLs later see aberrant N3 activity, please report it. All PHLs will receive the new N3 and PHLs will be instructed to destroy old N3. This will ensure all PHLs are using the same lot of reagents.

Q: For patient samples, should nasopharyngeal (NP) and oropharyngeal (OP) swabs be prioritized over sputum?

A: CDC does not have a prioritization scheme. CDC has observed that sputum will give positive results at a lower Ct than NP/OP swabs.

Q: Can CDC clarify the level of biosafety required for handling specimens? CDC's guidance on the website indicates BSL-2, however it also refers to the BMBL for SARS, which indicates BSL-2+.

A: CDC posted updated biosafety guidance yesterday and will follow up to see if clarifications need to be made on this point.

Q: How many PHLs have successfully verified the EUA assay to date?

A: CDC does not have an exact number. APHL has heard, anecdotally, of five PHLs that have successfully completed the verification. Please email eoc@aphl.org to share the status of your verification. APHL will start a more systematic effort to collection this information next week once the new N3 component is distributed to PHLs.

Q: Can CDC clarify what specimen types need to be sent to CDC for presumptive positive cases?

A: Respiratory specimens are the only specimen types authorized for testing on the EUA. For positive cases, there may be additional specimen types tested for clinical evaluations however not for diagnostic testing. CDC will work with PHLs for further investigation for positive cases. All samples

submitted should be used with the 50.34 form. For studies that involve multiple samples making use of the individual 50.34 form cumbersome, CDC may advise using the global file accessioning template (GFAT). This spreadsheet-based method is used for studies and can be used without PII if appropriate identifiers are included. Laboratories should use the 50.34 form unless otherwise advised by CDC.

Q: How many lots of N3 were original shipped out?

A: The N3 was from a single lot. Some PHLs observed sporadic reactivity at high Ct values (a weak response) for N3 during verification. CDC is investigating the reason and cause behind this aberrant activity. As labs receive the new N3 primer, they should destroy the current lot.

Q: Does CDC have recommendations for testing for other respiratory viruses for PUIs?

A: This is a state decision on what other respiratory viruses should be tested.

Q: Is there a plan to change the name of the assay to align with WHO's new name (COVID-19)?

A: The FDA EUA labeling will stand until another EUA is authorized. At that time, CDC may consider making changes to the name to align with WHO.