

# APHL Laboratory Alert: 2019-nCoV All PHL Lab Call

January 28, 2020

## Call Summary

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### Main Contact Emails

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

APHL EOC Contact: [eoc@aphl.org](mailto:eoc@aphl.org)

### Situational Update of 2019-nCoV (*Dr. Aron Hall, CDC*)

The 2019-nCoV situation is rapidly evolving and as of January 28, 2020 approximately 4,500 cases have been reported worldwide with approximately 100 deaths. The vast majority of cases are occurring in mainland China, specifically Hubei province and Wuhan city. There have been exported cases in at least 16 other countries. In the US there are approximately 100 patients under investigation (PUIs), five of which have tested positive and many others with pending test results.

CDC is trying to gather more information from epidemiological investigations to understand the infectiousness, scope and severity of illness as well as epidemiological parameters such as the reproductive number and serial interval to identify appropriate mitigation and control strategies. CDC continues to update travel advisories. There is currently a [Level 3 Alert for all of China](#), recommending US personnel avoid non-essential travel there.

### CDC 2019-nCoV Assay Deployment Update (*Dr. Wendi Kuhnert-Tallman, Dr. Steve Lindstrom and Dr. Julie Villanueva, CDC*)

#### General Description of the 2019-nCoV Assay

CDC is developing a real-time RT-PCR (rRT-PCR) assay to qualify for emergency use authorization (EUA) to deploy to public health laboratories (PHLs) for the detection of 2019-nCoV. The assay design includes three singleplex reactions run at the same time (different from the MERS-CoV assay). The protocol is designed to be run with manual QIAGEN QIAamp DSP Viral RNA Mini Kit (Cat # [61904](#)) or the QIAGEN EZ1 XL extraction system and the ABI 7500 Fast Dx thermocycler. The EUA assay kit will include 2019-nCoV primers and probes (combined into one tube per target), a human RNaseP (RP) set, and a transcript for a positive control. A human specimen control (HSC) will also be available to order separately as an extraction control. Acceptable specimens for the assay include upper and lower tract specimens. PHLs will be able to report presumptive positive results with this assay, but will need to submit specimens to CDC for confirmatory testing.

#### Food and Drug Administration (FDA) EUA

CDC is currently pursuing regulatory pathways with the FDA to receive EUA status for the rRT-PCR 2019-nCoV assay. CDC's goal is to get the EUA as quickly as possible and expects the assay will be ready to deploy within two weeks, possibly sooner. CDC is working to align the EUA and manufacturing timelines so there will not be a lag.

### Distribution Plan for CDC 2019-nCoV Assay Kits and Ancillary Reagents

The International Reagent Resource (IRR) is coordinating with CDC to get test kits into IRR inventory. As soon as the kits are released, there will be an announcement and the [IRR website](#) will be updated with a banner on the front page. Ancillary reagents will also be available to order in conjunction with the kits. The assay kit includes primers and probes including RP and a transcript for control. HSC will be available as a separate order from the IRR. PHLs (including state and local laboratories) that currently have access to order influenza tests will be given access to order the 2019-nCoV rRT-PCR kits. The IRR will automatically add the option to order these kits to the PHLs' views. The IRR will need to manage the initial inventory so there may be an initial order limit per lab in order to meet everyone's needs.

### Chemistries and Extraction Platforms that will be Qualified for the EUA

The QIAamp DSP Viral RNA Mini Kit for manual extraction and Qiagen EZ1 XL extraction platform will be qualified for the initial EUA. CDC has the intention to add additional platforms with future updates. CDC is not qualifying the test with Invitrogen Superscript III, but rather using Applied Biosystems Taqpath (a good manufacturing process [GMP] product that is more aligned for clinical testing).

### Intended Use of the rRT-PCR Protocol Posted to CDC's Website

CDC has posted a [protocol for an rRT-PCR Panel for detection of 2019-nCoV](#) on its website. However, this protocol is intended for researchers and international users. This protocol is **NOT** intended to be a provision of instructions to establish a laboratory developed test (LDT) at PHLs. Note that the EUA instructions for use will be different than this protocol; **PHLs should follow the instructions for use that will be sent with the EUA assay kit.** Under the EUA, PHLs will only be able to report positive results as "presumptive positive" and the specimen will need to be confirmed at CDC.

### Status of Verification Panels for the Assay

CDC is working with the Centers for Medicare and Medicaid Services (CMS) on a verification plan to assist PHLs with the verification process. The verification strategy and specimen(s) will be provided to ensure all PHLs are able to complete initial verification to begin testing and reporting. The goal is to facilitate onboarding at PHLs as quickly as possible. CDC has proposed a minimum level of verification to CMS that would involve the PHL spiking positive controls at a number of dilutions with replicates (negative and multiples of positives at different concentrations). There would be an expected Ct value provided for each concentration. In 2018, CMS [provided guidance on verification of assays authorized under emergency use](#). Additionally, since positive results will only be reportable as a "presumptive positive" and the specimen will be confirmed at CDC, laboratories can use the CDC results to strengthen their verification data.

### How should PHLs report results back to CDC?

CDC is in the process of developing guidance on reporting including HL7, LOINC and mechanisms for reporting back to CDC. PHLs will be required to report presumptive results to CDC and forward specimens to CDC for confirmatory testing. CDC is working towards putting electronic systems (e.g., PHLIP) or other systems test result reporting. There may be manual solutions such as leveraging the PUI reporting system made available as well.

### **CDC Testing Workflow (Steve Lindstrom, CDC)**

#### Guidance for PUI specimen shipments to CDC:

**CDC can receive specimens on weekends through coordination of shipment with EOC.** Regardless of the day, it is important that jurisdictions work with the CDC EOC PUI team (Tel. 770-488-7100) to coordinate the shipment. The PUI team can help identify the best shipping method and it gives CDC notice on what to expect and allows them to prioritize specimens coming in appropriately. For shipping during the weekdays INCLUDING Friday shipments for delivery on Saturdays, PHLs can use FedEx or their regular shipping agent. For shipping outside of regular hours or on weekends (beyond FedEx Saturday delivery), PHLs should work with the CDC EOC PUI team to identify the most appropriate carrier. The CDC EOC PUI team will also advise on support for shipping expenses.

#### What Specimen Types should PHLs Send to CDC?

PHLs should send three specimen types - lower respiratory, upper respiratory and serum specimens. To maintain timely throughput, the CDC is only testing respiratory specimens; serum will be tested only if there is a positive result from the respiratory specimens. If possible, additional specimen types (e.g., stool, urine) should be collected and stored by the PHL until CDC determines whether additional specimen sources should be tested. PHLs should not send additional specimen types unless requested by CDC because they can slow down CDC's accessioning process. Whole blood is not an appropriate specimen type and will not be tested. Samples must be sent in universal transport media (UTM) or viral transport media (VTM). Specimens sent as dry swabs or in gel media are unacceptable.

#### What Testing is Occurring at CDC in Addition to the 2019-nCoV PCR?

CDC is not testing 2019-nCoV negative specimens for other respiratory diseases at this time. Positive cases are being sequenced; genome sequences of all five US cases have been made available publicly.

#### Expected Turnaround Time for Results from CDC

CDC is working to streamline their testing workflow including expediting accessioning for the increased volume of specimens. Currently, CDC is maintaining a 24-48 hour turnaround time with same day or next day reporting once testing is completed. To maintain throughput, CDC will only test and report results on respiratory specimens. If a specimen is positive, they will go back and test any other specimen types submitted for that patient.

#### Reporting Mechanism for Positive and Negative Results from CDC

Given that this is a new assay, CDC has been trying to get reports out as soon as possible, including via manual methods. There will be a change in how results are communicated from CDC once the ELIMS is activated. As a specimen is received, the CDC PUI team will input the public health laboratory that has jurisdiction over the case as the "submitter" in the ELIMS. ELIMS will automatically send results to the public health laboratory as a PDF attached to a secure email or available through CSTOR. City or state epidemiologists will be copied on the results.

Positive results are handled differently; CDC will reach out directly via phone to public health departments and PHLs to notify them of positive cases.

### **Questions and Answers (Q&A)**

#### **EUA Assay**

**Q:** Which manual extraction kits can be used on the 2019-nCoV rRT-PCR EUA assay?

**A: The manual extraction kit approved for this protocol is the QIAamp DSP Viral RNA Mini Kit (QI Catalog number 61904).**

**Q: Which extraction platforms will be in future EUA updates?**

**A: The Roche MagNA Pure 96 instrument is currently the only other extraction platform that CDC is looking to qualify in future amendments to the EUA. Inclusion of this platform would provide the EUA with low, medium and high throughput extraction options; all are GMP level diagnostic devices.**

**Q: Is the 2019-nCoV rRT-PCR EUA assay multiplex?**

**A: The 2019-nCoV rRT-PCR EUA assay is not a multiplex test; rather three singleplex assays. As CDC knows more about the detection of the virus, additional assay designs may be considered.**

**Q: Will the 2019-nCoV EUA assay be run on a fast cycle protocol?**

**A: No, the run is for use in standard mode on the ABI 7500 Fast Dx per the TaqPath manufacturer instructions. The standard mode will run in a little over an hour. (TaqPath saves some time as compared to Invitrogen Superscript III protocol.)**

**Q: Will the primer and probe set available in the 2019-nCoV EUA assay be the same as those posted in the protocol for research/international use?**

**A: The designs are similar, but the protocol will not be exactly same. CDC is looking at various quenching options based on manufacturing availability, so there may be a slight difference.**

**Q: Does CDC have any advice on risk assessment?**

**A: CDC is currently developing risk assessments internally (related to the PCR assay and growth of the virus). Once ready, CDC can share their risk assessments, however they will be based on the CDC laboratory environment. CDC would encourage PHLs to take their own laboratory environment into consideration (e.g. types of samples being tested, percent positive) to guide their own risk assessment.**

### **EUA Roll-out through the IRR**

**Q: Will the 2019-nCoV rRT-PCR EUA assay be rolled out to all PHLs?**

**A: The 2019-nCoV rRT-PCR EUA assay will not be provided proactively. If PHLs want to use assay, they will be able to order it through the IRR free of charge. It is the PHLs responsibility to place orders to the IRR. If PHLs place an order for the 2019-nCoV rRT-PCR EUA assay through the IRR, they can expect to receive it.**

**Q: Will CDC prioritize certain PHLs to receive the 2019-nCoV rRT-PCR EUA assay kits?**

**A: CDC is still determining if/how assays will be prioritized. Jurisdictions that are conducting airport screening will likely receive first prioritization if prioritization is determined to be necessary.**

**Q: Which reagents/consumables will be available through the IRR?**

**A: Through the IRR, PHLs can order the assay kit (primers and probes including RP and a transcript for control), HSC and ancillary reagents (e.g. extraction chemistries and master mix enzyme).**

### **Validation/Verification of the EUA Assay**

**Q: Can CDC provide verification panel information for the 2019-nCoV rRT-PCR EUA assay?**

**A:** CDC is working with the Centers for Medicare and Medicaid Services (CMS) on a verification plan to assist PHLs with the verification process. The verification strategy and specimen(s) will be provided to ensure all PHLs are able to complete initial verification to begin testing and reporting. The goal is to facilitate onboarding at PHLs as quickly as possible. CDC has proposed a minimum level of verification to CMS that would involve the PHL spiking positive controls at a number of dilutions with replicates (negative and multiples of positives at different concentrations). There would be an expected Ct value provided for each concentration. In 2018, CMS [provided guidance on verification of assays authorized under emergency use](#). Additionally, since positive results will only be reportable as a “presumptive positive” and the specimen will be confirmed at CDC, laboratories can use the CDC results to strengthen their verification data.

**Q:** Is CDC able to send out the verification plan for the 2019-nCoV rRT-PCR EUA assay ahead of the CMS approval?

**A:** CDC is unable to send anything before the plan receives full clearance.

**Q:** Will CDC be providing proficiency panels for CLIA?

**A:** CDC will be working on proficiency panels at a later time.

### **Shipping & Sample types**

**Q:** How should PHLs ship sample on weekends and is M4 an acceptable specimen type to ship to CDC?

**A:** CDC encourages PHLs to work with the CDC EOC PUI team to coordinate shipments on weekends (e.g. using World Courier). It is best to utilize the CDC EOC PUI team so that everyone knows what specimens are coming and what the priority level is. During the week, PHLs can use FedEx or their standard shipper. **Correction post call: Fedex can be used for Friday shipments set for Saturday delivery. M4 is an acceptable transport media.**

**Q:** Should presumptive positive specimens from the 2019-nCoV EUA test be shipped to CDC as Category A or Category B substance?

**A:** Currently, presumptive positive specimens should be shipped as Category B substances. This is subject to change. Isolates and amplified material would be a different question, and this issue is currently being discussed with a number of partners including the World Health Organization (WHO).

**Q:** Can PHLs send lung tissue from autopsies. If so, how should specimens be sent?

**A:** For autopsies from positive cases, PHLs should contact the CDC EOC PUI team who will coordinate testing with CDC’s pathology lab. Lung tissue must be shipped fresh or fixed, NOT frozen. CDC plans to develop additional guidance on this.

**Q:** For jurisdictions with positive patients, how should sequential/multiple specimens be sent to CDC?

**A:** Once a positive case is identified, there is proactive engagement from CDC with the PHL and health department to initiate investigation and conduct follow-up testing. CDC is still working out protocols for this.

**Q:** Can nasopharyngeal (NP) and oropharyngeal (OP) swabs be combined into the same tube?

**A:** Combined NP/OP swabs are not acceptable sample types for commercial diagnostic tests. CDC is currently seeing 2019-CoV in both NP and OP specimens but at varying concentrations. The CDC is trying to collect as much information as possible so they are requesting them to be kept as separate specimen types.

**Q:** Are upper or lower respiratory specimens better for diagnostics?

**A:** The CDC does not know yet, however the upper respiratory specimens that were tested were strongly positive. It will likely depend on the progression of the disease; as it progresses, lower respiratory tract specimens may become more positive.

## **Reporting**

**Q:** For results reported from CDC, is it possible to include the testing status for all specimens received in one report (e.g. including pending tests)?

**A:** Currently the CDC is only including specimens with results in the reports. CDC will consider adding 'not tested' to reports.

**Q:** Will CDC be calling jurisdictions to report positive results? If so, whom will they be contacting?

**A:** CDC will be calling multiple numbers – including the Health Department, epidemiologists and laboratorians.

**Q:** Is the 2019-nCoV rRT-PCR EUA assay a Laboratory Response Network (LRN) assay? Will LRN messenger be used?

**A:** The 2019-nCoV rRT-PCR EUA assay is not an LRN assay. It will be deployed via the IRR from the CDC Division of Viral Diseases (NCIRD). Result reporting is still being worked out – it could be manual or more automated like influenza PHLIP reporting.