Clinical Laboratory COVID-19 Response Call
Monday, July 18, 2022, at 3:00PM ET

- Welcome
  - Sean Courtney, Division of Laboratory Systems, CDC

- SARS-CoV-2 Variants Update
  - Clint Paden, Division of Viral Diseases, CDC

- A System for Early Detection and Monitoring of COVID Variants
  - Eric Lai, Rapid Acceleration of Diagnostics (RADx) Variant Task Force, National Institutes of Health (NIH)

- FDA Update
  - Tim Stenzel, US Food and Drug Administration (FDA)

- Monkeypox Update
  - Christina Hutson, Monkeypox Response, CDC
About DLS

Vision
Exemplary laboratory science and practice drive clinical care and public health.

Mission
Improve public health surveillance and practice as well as patient outcomes by advancing clinical laboratory quality and safety, data and biorepository science, and workforce competency.
Four Goal Areas

**Quality Laboratory Science**
- Improve the quality and value of laboratory medicine and biorepository science for better health outcomes and public health surveillance

**Highly Competent Laboratory Workforce**
- Strengthen the laboratory workforce to support clinical and public health laboratory practice

**Safe and Prepared Laboratories**
- Enhance the safety and response capabilities of clinical and public health laboratories

**Accessible and Usable Laboratory Data**
- Increase access and use of laboratory data to support response, surveillance, and patient care
Monkeppox Guidance

Laboratory Procedures & Biosafety Guidelines

Routine Chemistry, Hematology, and Urinalysis in Hospitals or Clinical Laboratories

- If a patient is being tested for monkeypox virus infection, testing to evaluate other illnesses as the clinical differential may continue while awaiting orthopoxvirus test results. Specific biosafety precautions should be implemented depending on the specimen that is being tested:
  - Non-lesion specimens (e.g., urine, blood, etc.) The quantity of pox virus likely to be in clinical specimens of blood and bodily fluids is low. Therefore, vaccination is not recommended for personnel who handle and process routine clinical specimens from monkeypox (e.g., cerebrospinal fluid, urine, blood for complete blood count (CBC), cholesterol, microbiology). Standard universal precautions to protect against potential infectious agents within any specimen received (using BSL-2 containment) are recommended. 
  - Lesion specimens (e.g., skin biopsy, cerebrospinal fluid, urine, body fluids)
  - Standard 4-layer lab coat, N95 or higher level mask, face shield, gloves, and plastic apron. 
  - Disinfectant present, sharps containers, transfer of specimens with minimal contamination, decontaminate when leaving isolation room.

https://www.cdc.gov/poxvirus/monkeypox/lab-personnel/report-results.html

How to Report Test Results

How to Report Results from Orthopoxvirus, Non-Variola Orthopoxvirus, and Monkeypox Virus Laboratory Diagnostic Testing

Introduction

The public health response to monkeypox depends on comprehensive laboratory testing and result reporting. These data will contribute to understanding the spread of the monkeypox virus and can contribute to predicting increases in testing demand and planning for potential supply chain issues for reagents and other testing materials. The information below outlines reporting requirements to laboratories.

Who should report

- Any laboratory that performs diagnostics testing for monkeypox should report results to the state, local, territorial, or tribal public health department(s). This includes nucleic acid testing for Orthopoxvirus non-variola Orthopoxvirus or Monkeypox virus.
- All results (positive, negative, equivocal) should be reported unless otherwise specified by the health department.
- Positive results should be reported within 24 hours of testing, or immediately by telephone to the appropriate public health department.
- Test results should be reported to the health department in the patient’s state or territory of residence.

https://www.cdc.gov/poxvirus/monkeypox/lab-personnel/lab-procedures.html
Communication strategies help simplify the process of translating complex information into meaningful messages for your audience.

OneLab’s Laboratory Communications toolkit helps laboratories develop plain language communication strategies.

This job aid is available at www.cdc.gov/labtraining/onelab/network.html.
Sensitivity and Specificity Job Aid

Understanding sensitivity and specificity helps determine test selection and whether retesting might be necessary.

OneLab’s Sensitivity and Specificity job aid helps public and clinical laboratory professionals understand how specificity and sensitivity performance characteristics affect test result interpretation.

This job aid is available at www.cdc.gov/labtraining/onelab/network.html.
NGS Quality Initiative Introduces Redesigned Page & New Resources

https://www.cdc.gov/labquality/qms-tools-and-resources.html
Clinical Laboratory COVID-19 Response Calls are now LOCS Calls
We Want to Hear From You!

Training and Workforce Development

Questions about education and training?
Contact LabTrainingNeeds@cdc.gov
CDC Preparedness Portal


Find CLCR call information, slides, transcripts, and audio recordings on this page.
How to Ask a Question

• **Using the Zoom Webinar System**
  – Click the **Q&A button** in the Zoom webinar system
  – Type your question in the **Q&A box** and submit it
  – Please do not submit a question using the **chat button**

• For media questions, please contact CDC Media Relations at [media@cdc.gov](mailto:media@cdc.gov)

• If you are a patient, please direct any questions to your healthcare provider
Slide decks may contain presentation material from panelists who are not affiliated with CDC. Presentation content from external panelists may not necessarily reflect CDC’s official position on the topic(s) covered.
SARS-CoV-2 Variants Update

Clinton Paden
Division of Viral Diseases, CDC
Project Rosa: A system for early detection and monitoring of COVID variants

Eric Lai, Ph.D.,
Pharma-Dx, LLC
NIH RADx Variant Task Force
SAR-CoV-2 variant lineage prevalence in the US

Observations:
- New variants appeared in ex-US countries and migrated to the US
- There is a window of opportunity for the US to prepare for the appearance of new variants
- The duration of first appearance in the US and taking over the variant(s) is getting shorter and shorter
Specific Aims of Project ROSA

- **Specific Aim 1.** Can we develop a highly sensitive and specific assay that can detect all positive COVID samples and is not sensitive to variants?
  - All current COVID tests were designed using the original Wuhan COVID strain and have the potential of “missing/not detecting” new COVID variants. A lot of efforts are spent in determining whether any specific assay can detect all variants.

- **Specific Aim 2.** Can we develop a system to potentially identify new variant and to monitor known variants in a cost and time efficient manner to complement the CDC sequencing effort?
  - Variants are detected and monitored by random sequencing (i.e. surveillance sequencing up to 5%) of positive COVID samples. The process is labor intensive (i.e. picking of positive samples) and the procedure is time consuming (weeks) and expensive (hundred of $$) per sample.
Specific Aim 1: Develop a highly sensitive and specific variant agnostic assay

In collaboration with CDC and ThermoFisher, we have identified specific markers for the detection of most (>99%) COVID samples independent of variant lineage. S:D614G (VTF), N:SC2 region (CDC) and ORF1ab (ThermoFisher). The positivity rates have been confirmed bioinformatically and experimentally.

Testing of 1,024 COVID samples including Alpha, Beta, Gamma, Delta, Epsilon, Eta, Iota, Kappa, Lambda, Mu
### Specific Aim 2: Use of a panel of SNP markers/mutations to identify known PANGO variant VOC/I lineage

<table>
<thead>
<tr>
<th>Nucleotide Mutations</th>
<th>AA Mutation</th>
<th>Marker Set</th>
<th>Classification Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>nsp10 gene (position 13025-13441)</td>
<td>None</td>
<td>+</td>
<td>+</td>
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<tr>
<td>A23403G</td>
<td>S:D614G</td>
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<td>+</td>
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<tr>
<td>N gene SC2 (position 29461-29482)</td>
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<td>+</td>
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<tr>
<td>T16176C</td>
<td>None</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>A21801C</td>
<td>S:D80A</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>A22812C</td>
<td>S:K417T</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>C21618G</td>
<td>S:T19R</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>C22995A</td>
<td>S:T478K</td>
<td>+</td>
<td>+</td>
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<tr>
<td>T7424G</td>
<td>orf1ab:F2387V</td>
<td>+</td>
<td>+</td>
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<tr>
<td>A13057T</td>
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<td>+</td>
<td>+</td>
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<tr>
<td>G22018T</td>
<td>S:W152C</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>A16500C</td>
<td>orf1b:Q1011H</td>
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<td>+</td>
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<tr>
<td>T22917A</td>
<td>S:L452Q</td>
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<tr>
<td>A11456G</td>
<td>orf1ab:3731V</td>
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<td>TACATG21765----</td>
<td>S:V869-</td>
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<td>TTA21991---</td>
<td>S:Y144-</td>
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<td>G22132T</td>
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<td>C23604G</td>
<td>S:P681R</td>
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<td>Delta</td>
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<tr>
<td>C25489T</td>
<td>ORF3a:S26L</td>
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<td>Delta</td>
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Analytical performance of the variant specific panels

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<tr>
<th></th>
<th>48 Markers</th>
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<th>24 Markers</th>
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<th>16 Markers</th>
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<th>12 Markers</th>
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<tbody>
<tr>
<td></td>
<td>PPA (%)</td>
<td>NPA (%)</td>
<td>PPA (%)</td>
<td>NPA (%)</td>
<td>PPA (%)</td>
<td>NPA (%)</td>
<td>PPA (%)</td>
<td>NPA (%)</td>
<td>PPA (%)</td>
<td>NPA (%)</td>
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<tr>
<td>Alpha</td>
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<td>99.2</td>
<td>99.2</td>
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<td>Gamma</td>
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<td>Delta</td>
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<td>98.7</td>
<td>99.6</td>
<td>98.7</td>
<td>99.6</td>
<td>98.7</td>
<td>99.6</td>
<td>98.9</td>
<td>99.8</td>
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<tr>
<td>Epsilon</td>
<td>96.3</td>
<td>99.7</td>
<td>96.3</td>
<td>99.7</td>
<td>96.3</td>
<td>99.7</td>
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<td>99.7</td>
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<tr>
<td>Eta</td>
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<td>97.3</td>
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<td>Kappa</td>
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<td>100</td>
<td>100</td>
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<td>99.9</td>
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<td>Mu</td>
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</tr>
</tbody>
</table>

*Cannot call

Genotyping of 1,024 COVID samples including Alpha, Beta, Gamma, Delta, Epsilon, Eta, Iota, Kappa, Lambda, Mu
Number of “undetermined” calls
What would we have seen if we had ROSA before Delta appeared in the US?

Here are the steps taken to evaluate how ROSA would have worked for Delta:

- Remove from the 12 markers classifier config file any mutation linked to Delta resulting in a list of 10 markers including the 2 positivity ones.
- Run the simulation using as data the first week of each month in GISAID for North America from November 2020 to July 2021.

With no prior knowledge of Delta, the ROSA classifier would have categorized 99.93% of Delta sequences as “Undetermined” and therefore recommended for sequencing.
ROSA Tracker: https://tracker.rosalind.bio/dashboard

## Value proposition – NGS Surveillance vs Project Rosa

<table>
<thead>
<tr>
<th>Metrics</th>
<th>Project Rosa</th>
<th>Next Generation Sequencing (NGS)</th>
<th>Project Rosa Compared to NGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cap-Ex Cost (List Price) per set</td>
<td>$125K</td>
<td>$850K-$1M</td>
<td>5x-8x Lower Cost</td>
</tr>
<tr>
<td>Cost Per Sample</td>
<td>$50</td>
<td>$125-$500</td>
<td>5x-20x Lower Cost</td>
</tr>
<tr>
<td>Turn-Around Time</td>
<td>&lt;5 hours</td>
<td>7 - 10 Days</td>
<td>Up to 30x Faster</td>
</tr>
<tr>
<td>Number of Technicians Required</td>
<td>1 FTE</td>
<td>2-3 FTE</td>
<td>2x Less Labor Required</td>
</tr>
<tr>
<td>Lab Resource Proficiency</td>
<td>Standard PCR Experience</td>
<td>High-End Bio-Informatics</td>
<td></td>
</tr>
<tr>
<td>Sample coverage</td>
<td>~100% of COVID samples</td>
<td>5% of random positive samples</td>
<td>20x increase in coverage</td>
</tr>
</tbody>
</table>

Proposal: Use of genotyping to monitor known variants and focus the use of NGS for detection of new variants.
Wide spread adaption plan and long-term implementation plan

- FDA: discussion on approval path for the genotyping assay
- CDC: collaborative path for CLIA lab adaption
- CMS: discussion on reimbursement/pricing model(s)
- Long Term Implementation:
  - Informatic automated monitoring of new variants
    - Proactive monitoring of the variants prevalence globally and in the US
    - Monitoring of the rate of increase in prevalence
    - Monitoring of US regional prevalence
    - Predictive modelling of biological significance mutation(s)
  - Establish an expert panel to review marker panel composition and update marker panel at a regular basis (similar to Flu vaccine committee).
U.S. Food and Drug Administration

- COVID-19 Emergency Use Authorization (EUA) Information for Medical Devices

- COVID-19 In Vitro Diagnostic EUAs

- COVID-19 Frequently Asked Questions

- COVID-19 Updates

- FDA Townhall Meetings

- Independent Evaluations of COVID-19 Serological Tests
  https://open.fda.gov/apis/device/covid19serology/
COVID-19 Diagnostic Development
CDRH-EUA-Templates@fda.hhs.gov

Spot Shortages of Testing Supplies: 24-Hour Support Available
1. Call 1-888-INFO-FDA (1-888-463-6332)
2. Then press star (*)

FDA MedWatch
Monkeypox Update

Christina Hutson
Monkeypox Response, CDC
These slides were shared during the call but are not available for public distribution.
Next Scheduled Call

The next call will be on

Monday, August 15 @ 3:00 PM to 4:00 PM ET
Thank You For Your Time!

Photo submitted by the Microbiology Laboratory at The University of Pittsburgh Medical Center