This content was published before guidance to change "monkeypox" to "mpox" was delivered to CDC programs in December 2022

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.

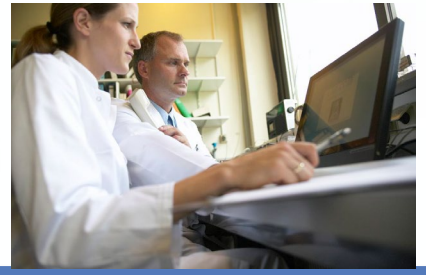
Four Goal Areas

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

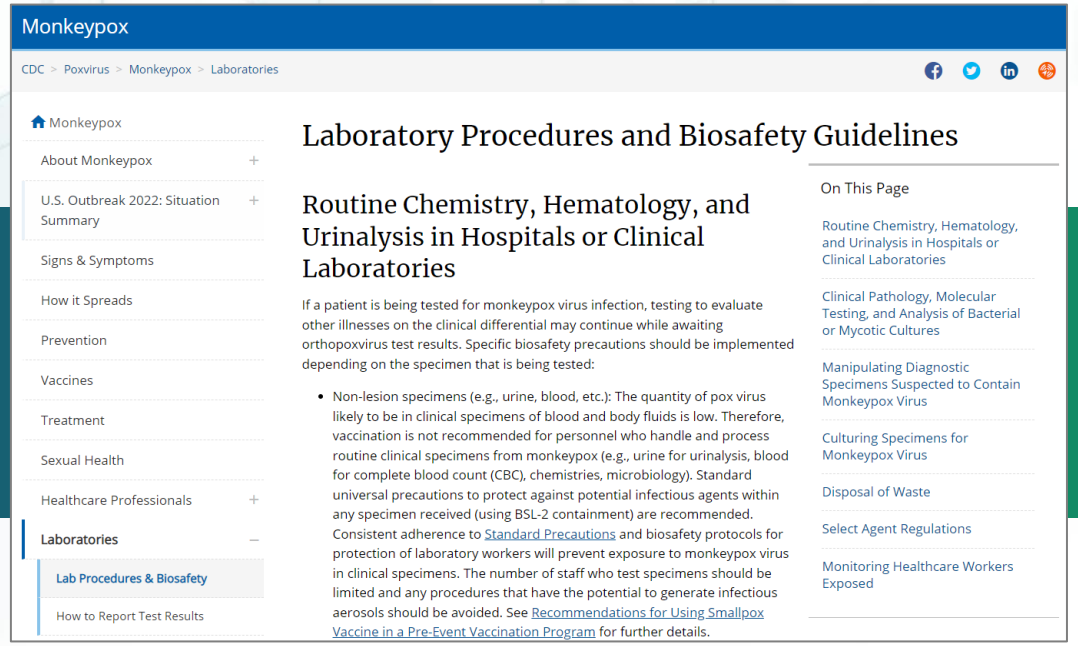
- Enhance the safety and response capabilities of clinical and public health laboratories

Accessible and Usable Laboratory Data

- Increase access and use of laboratory data to support response, surveillance, and patient care

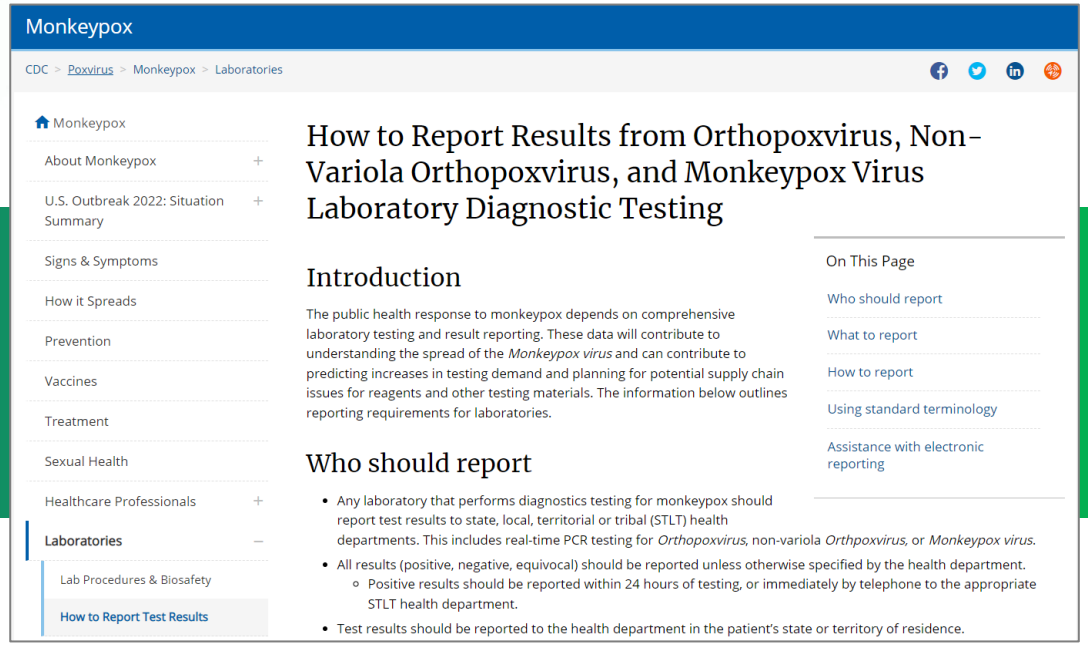
Monkeypox Guidance

Laboratory Procedures & Biosafety Guidelines



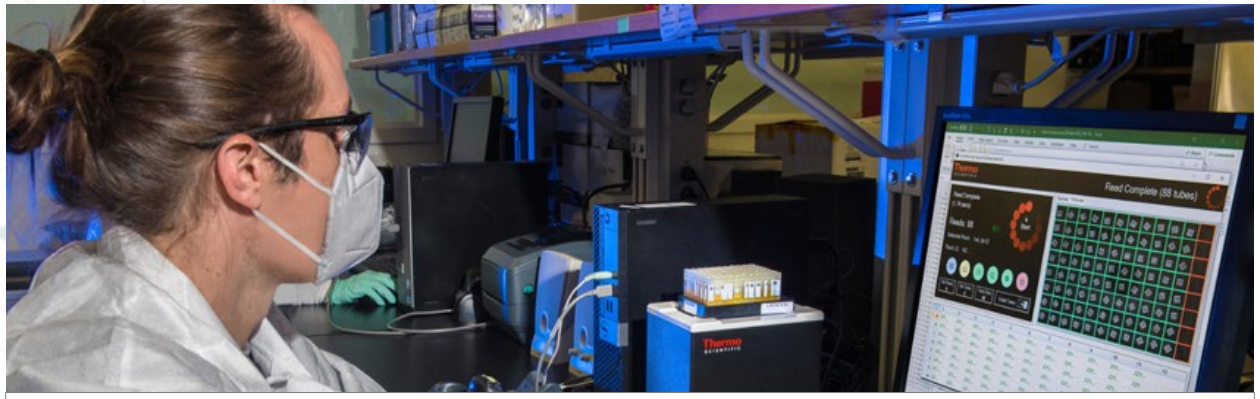
https://www.cdc.gov/poxvirus/monkeypox/lab-personnel/report-results.html

How to Report Test Results



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

Clinical Laboratory Biosafety Gaps: Lessons Learned



AMERICAN SOCIETY FOR MICROBIOLOGY | Clinical Microbiology Reviews®

REVIEW

Clinical Laboratory Biosafety Gaps: Lessons Learned from Past Outbreaks Reveal a Path to a Safer Future

Nancy E. Cornish,[a] Nancy L. Anderson,[a] Diego G. Arambula,[a] Matthew J. Arduino,[b] Andrew Bryan,[c] Nancy C. Burton,[d] Bin Chen,[a] Beverly A. Dickson,[e] Judith G. Giri,[f] Natasha K. Griffith,[g] Michael A. Pentella,[h] Reynolds M. Salerno,[a] Paramjit Sandhu,[a] James W. Snyder,[i] Christopher A. Tormey,[j,k] Elizabeth A. Wagar,[l] Elizabeth G. Weirich,[a] Sheldon Campbell[j,k]

https://stacks.cdc.gov/view/cdc/118337

Laboratory Communications Toolkit

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.

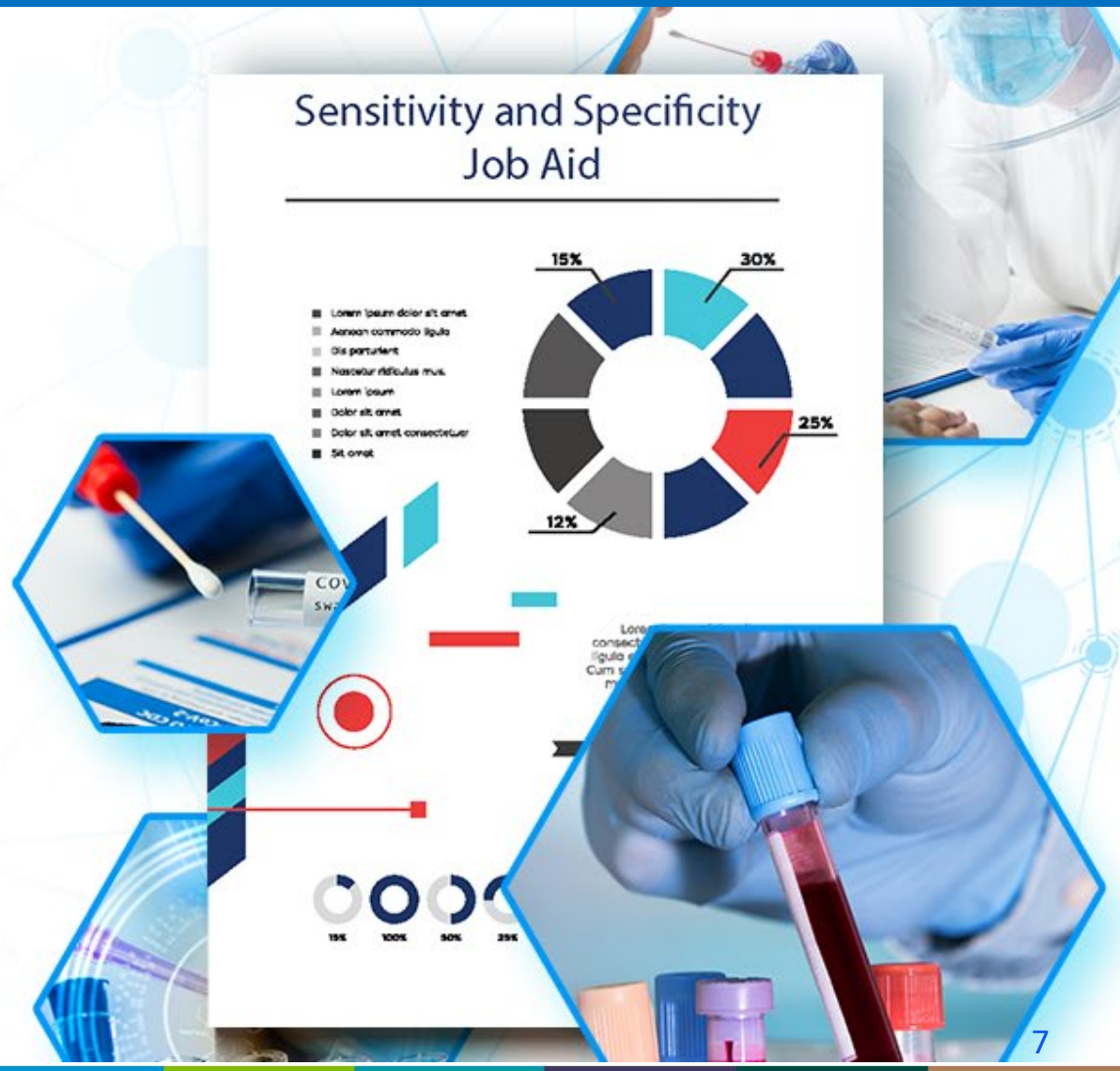
This job aid is available at www.cdc.gov/labtraining/onelab/network.html.

Sensitivity and Specificity Job Aid

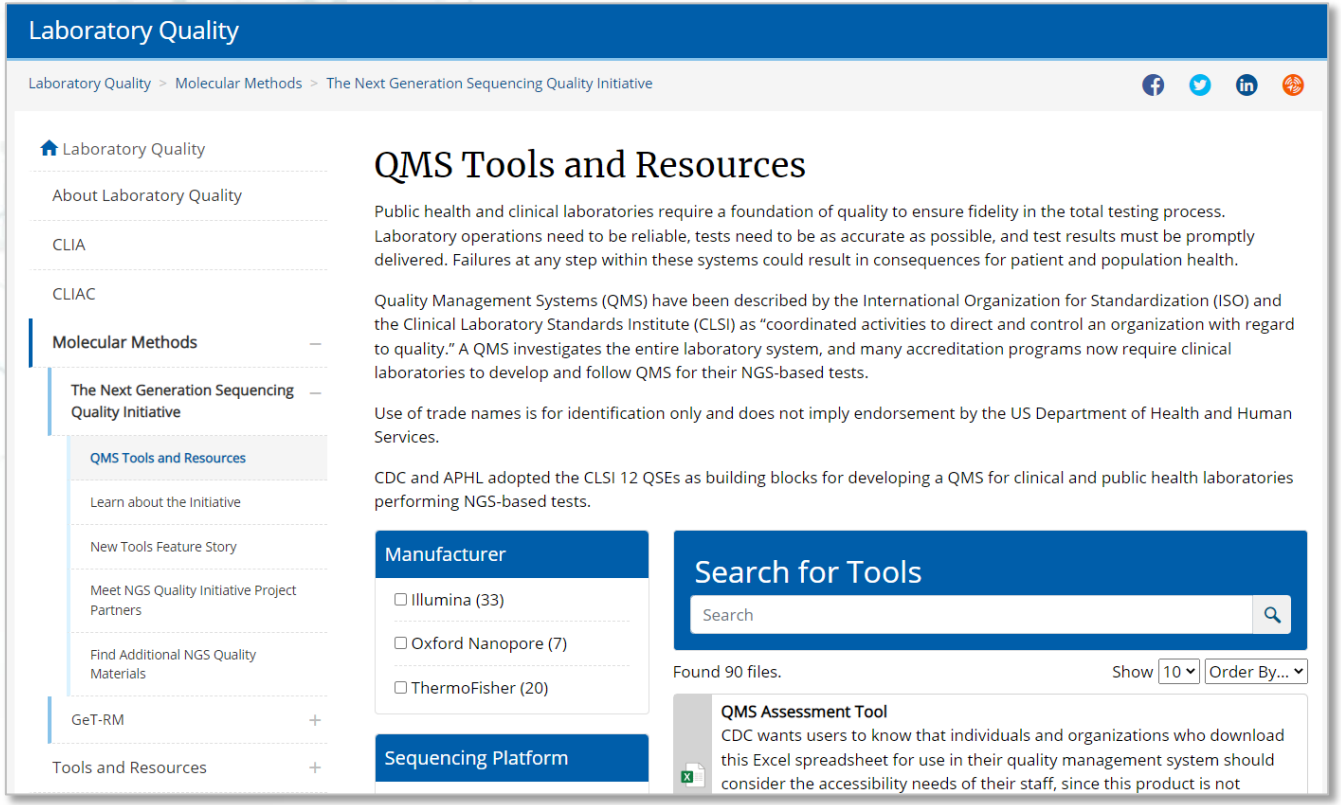
Understanding sensitivity and specificity helps determine test selection and whether retesting might be necessary.

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

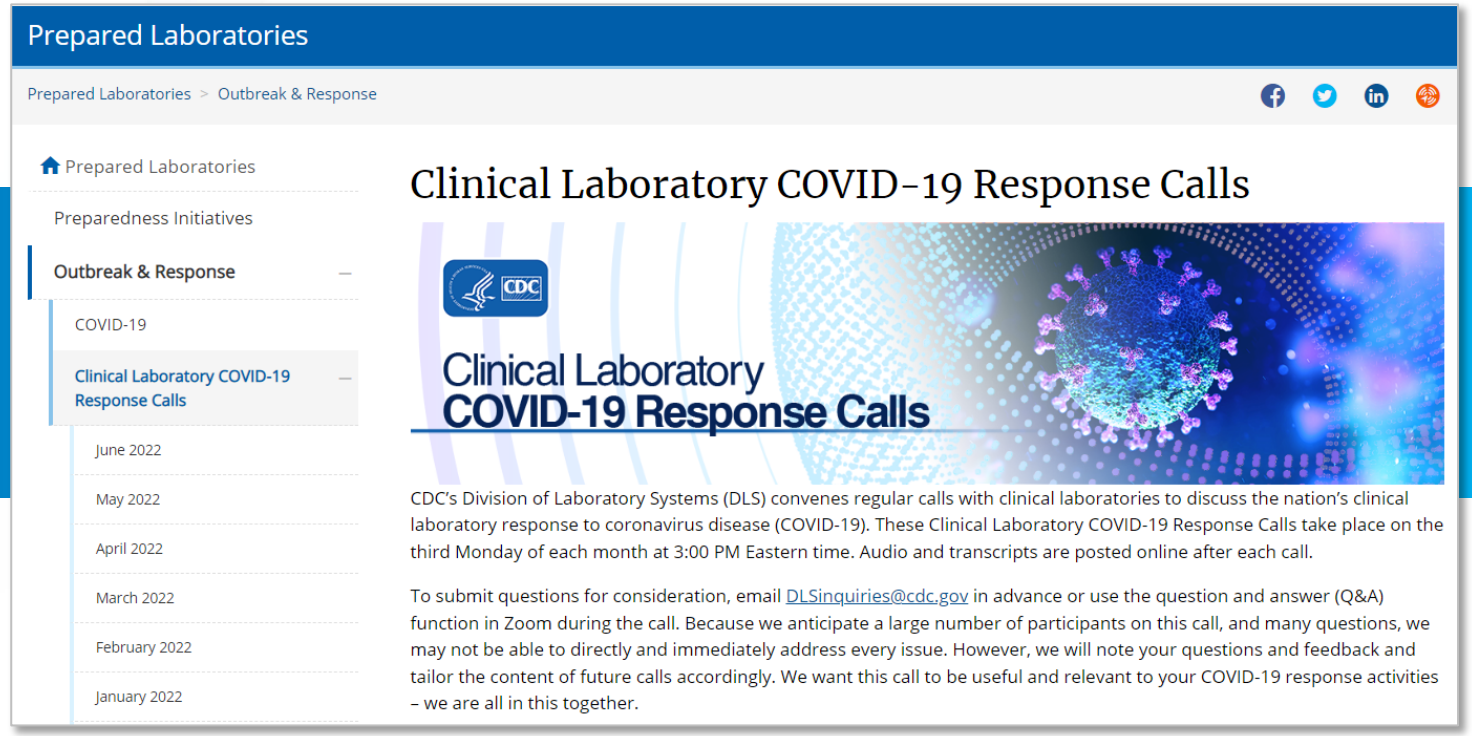
Questions about education and training?

Contact LabTrainingNeeds@cdc.gov

CDC Preparedness Portal

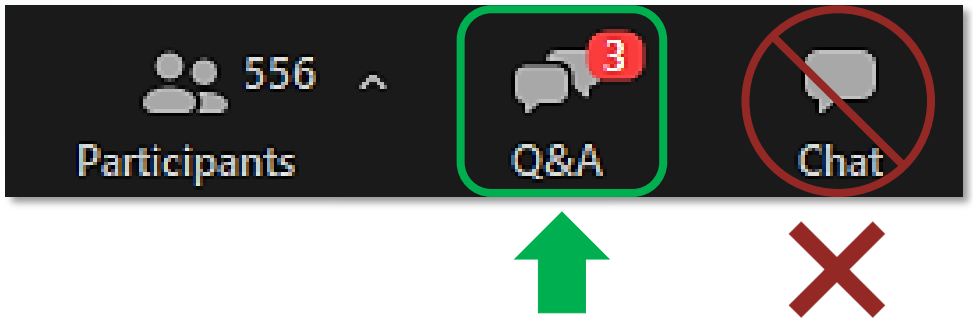
https://www.cdc.gov/csels/dls/preparedlabs/covid-19-clinical-calls.html

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
- 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

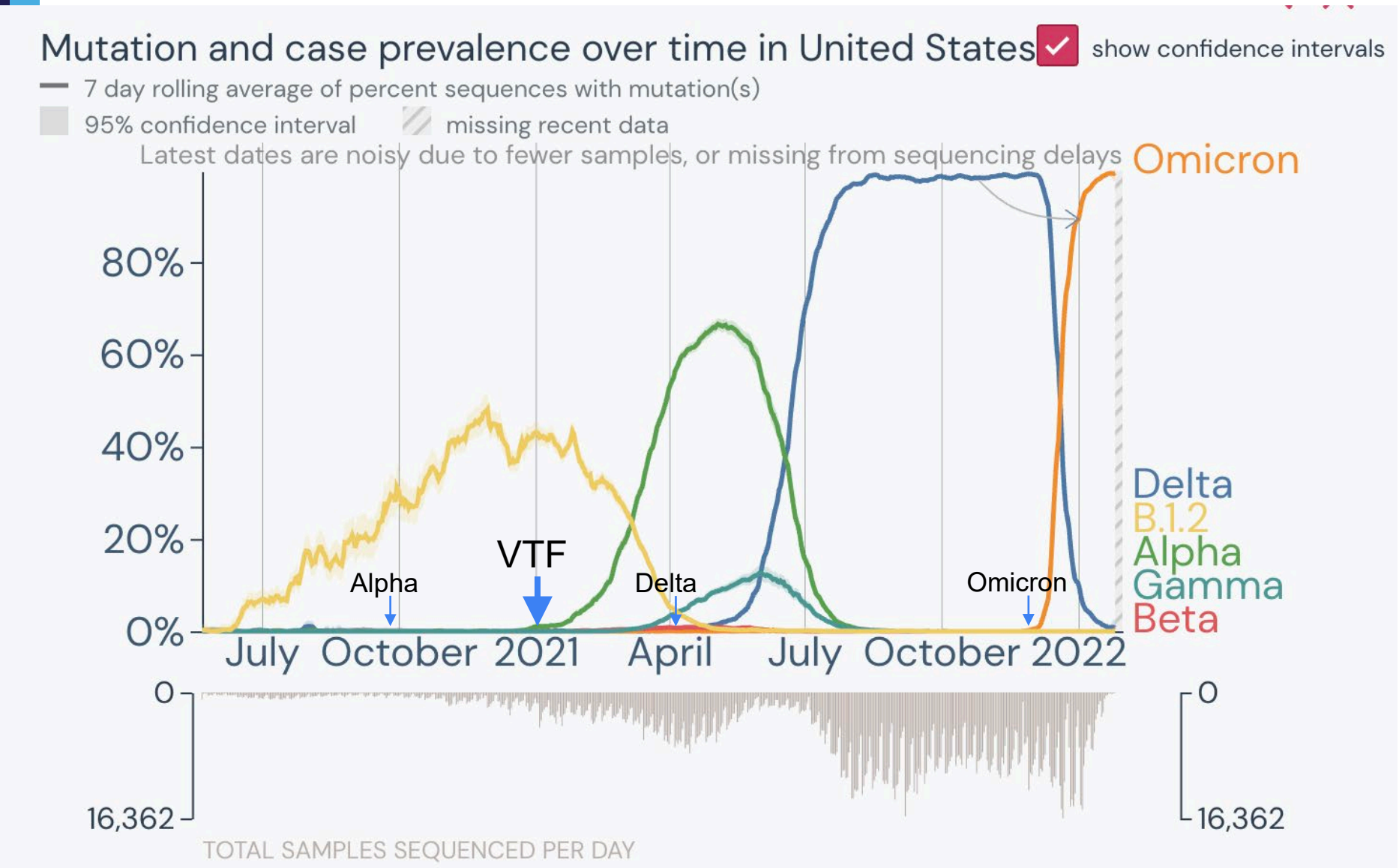
Clinton Paden
Division of Viral Diseases, CDC

Project Rosa: A system for early detection and monitoring of COVID variants

Eric Lai, Ph.D.,
Pharma-Dx, LLC
NIH RADx Variant Task Force

7/18/22

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.

	Variant Agnostic Marker				
Number of Markers	S:D614G	nsp10 gene	N gene SC2	Positive Calls	PPA (%)
3	+	+	+	1,024	99.3
2	+	+		1,020	98.9
	+		+	1,021	99
		+	+	1,023	99.2
1	+			993	96.3
		+		1,018	98.7
			+	990	96
0				7	0.7
Total SARS-CoV-2 positive samples				1,031	

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

Nucleotide Mutations	AA Mutation	Marker Set					Classification Outcome
		48	24	16	12	8	
nsp10 gene (position 13025-13441)	None	+	+	+	+	+	
A23403G	S:D614G	+	+	+	+		SARS-CoV-2 detected
N gene SC2 (position 29461-29482)	None	+					
T16176C	None	+	+	+	+	+	Alpha
A21801C	S:D80A	+	+	+	+	+	Beta
A22812C	S:K417T	+	+	+	+	+	Gamma
C21618G	S:T19R	+	+	+	+	+	Delta
C22995A	S:T478K	+	+	+	+	+	Delta
T7424G	orf1ab:F2387V	+	+	+	+	+	Lambda
A13057T	None	+	+	+	+	+	Mu
G22018T	S:W152C	+	+	+	+		Epsilon
A16500C	orf1b:Q1011H	+	+	+	+		Iota
T22917A	S:L452Q	+	+	+	+		Lambda
A11456G	orf1ab:I3731V	+	+	+			Delta
A28699G	None	+	+	+			Eta
G23593C	S:Q677H	+	+	+			Eta
A24775T	S:Q1071H	+	+	+			Kappa
TACATG21765------	S:HV69--	+	+				Alpha
TTA21991---	S:Y144-	+	+				Alpha (when combined with T16176C)
CTTTACTTG22281---------	S:LLA241---	+	+				Beta (when combined with A21801C)
T733C	None	+	+				Gamma
T22917G	S:L452R	+	+				Delta (or Epsilon when combined with G22018T)
A22320G	S:D253G	+	+				Iota (when combined with A16500C)
G23012C	S:E484Q	+	+				Kappa (when combined with A24775T)
C27925A	ORF8:T11K	+	+				Mu
G22132T	S:R190S	+					Gamma
C23604G	S:P681R	+					Delta
C25469T	ORF3a:S26L	+					Delta

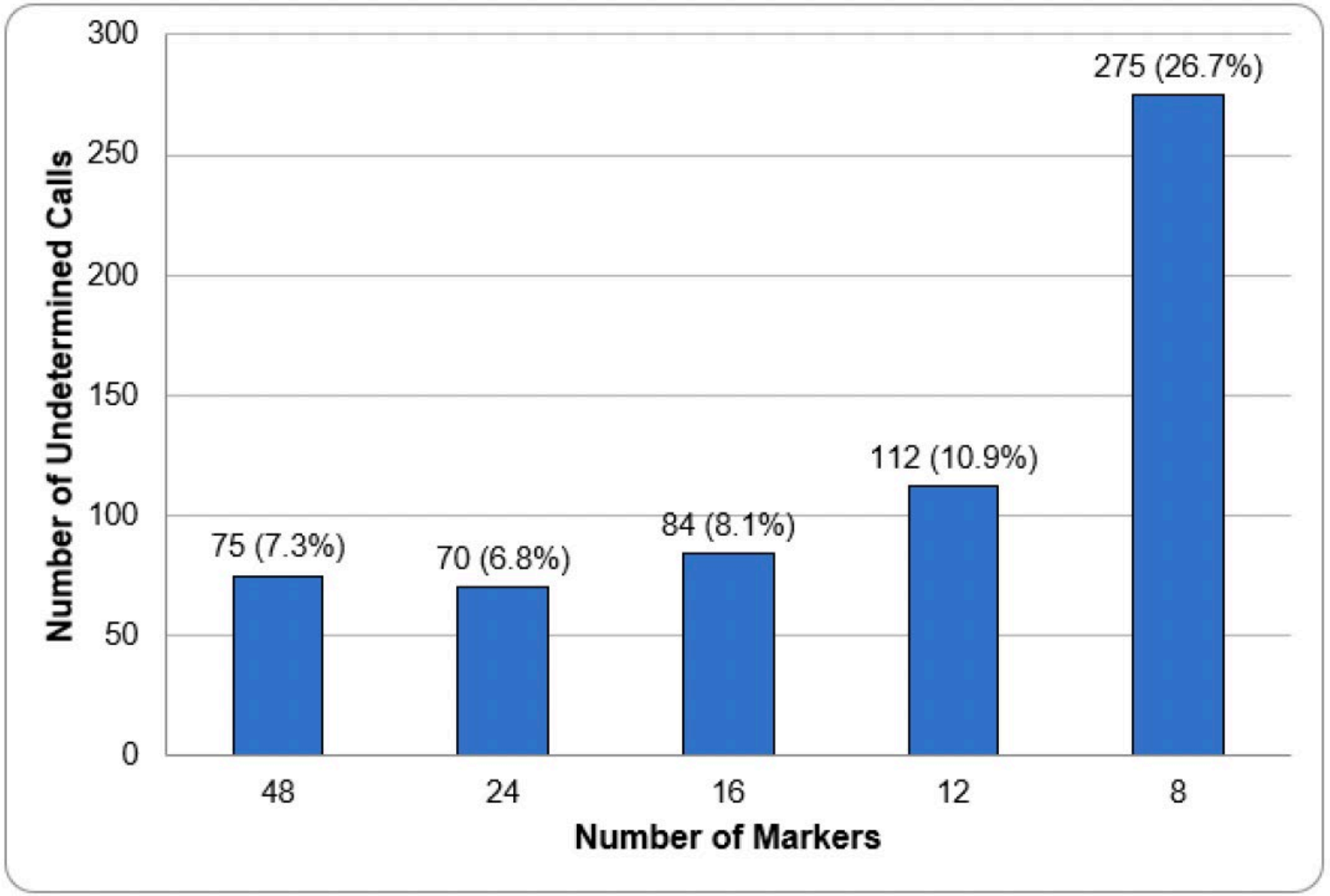
Analytical performance of the variant specific panels

	48 Markers		24 Markers		16 Markers		12 Markers		8 Markers	
	PPA (%)	NPA (%)	PPA (%)	NPA (%)	PPA (%)	NPA (%)	PPA (%)	NPA (%)	PPA (%)	NPA (%)
Alpha	99.2	99.2	99.2	99.2	98.4	99.1	98.4	99.1	98.4	99.1
Beta	100	100	100	100	100	100	100	100	100	100
Gamma	100	100	100	100	100	100	100	100	100	100
Delta	98.9	99.8	98.7	99.6	98.7	99.6	98.7	99.6	98.9	99.8
Epsilon	96.3	99.7	96.3	99.7	96.3	99.7	96.3	99.7	*	91.5
Eta	100	100	100	100	100	100	*	97.3	*	97.3
Iota	100	99.9	100	99.9	100	99.9	100	99.9	*	91.3
Kappa	100	100	100	100	100	100	*	99.9	*	99.9
Lambda	100	100	100	100	100	100	100	100	100	100
Mu	100	100	100	100	100	100	100	100	100	100

*Cannot call

Genotyping of 1,024 COVID samples including Alpha, Beta, Gamma, Delta, Epsilon, Eta, Iota, Kappa, Lambda, Mu

Number of “undetermined” calls

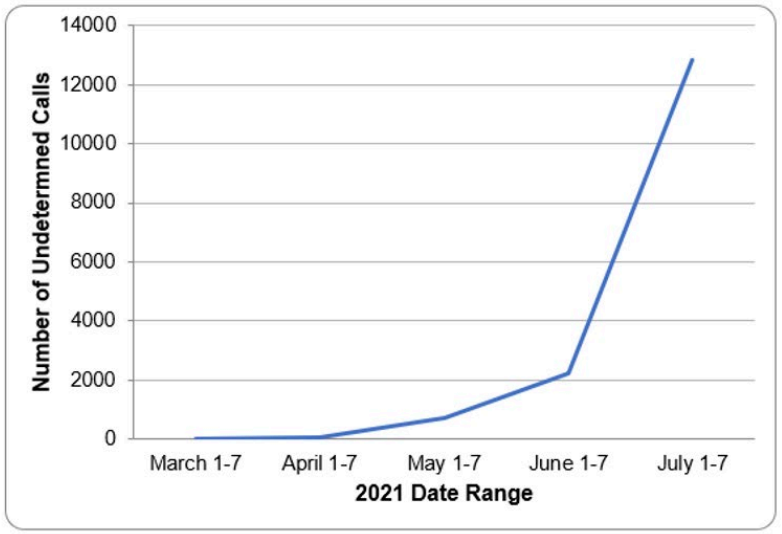


What would we have seen if we had ROSA before Delta appeared in the US?

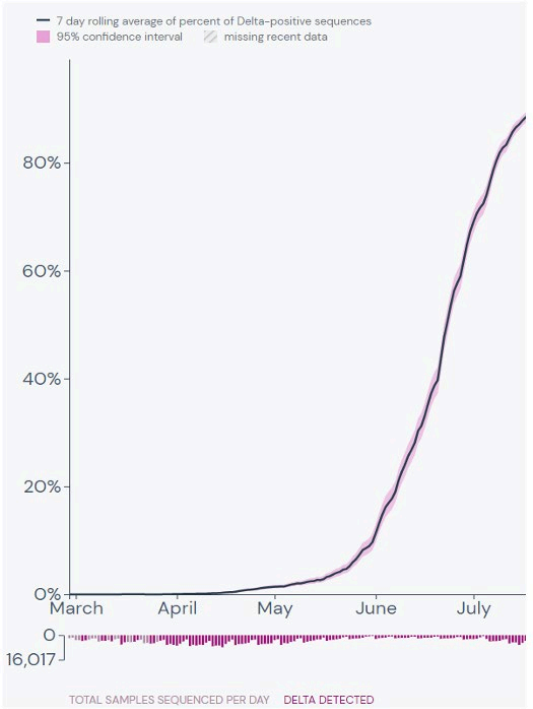
Here are the steps taken to evaluate how ROSA would have worked for Delta:

- 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**.

# of undetermined samples using 10 markers (without Delta)



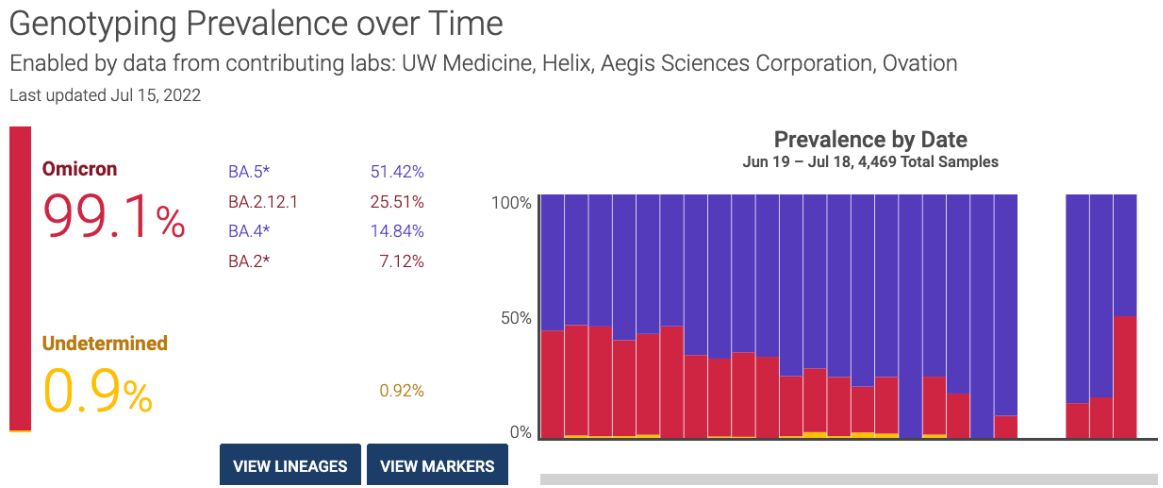
Appearance of Delta in the US



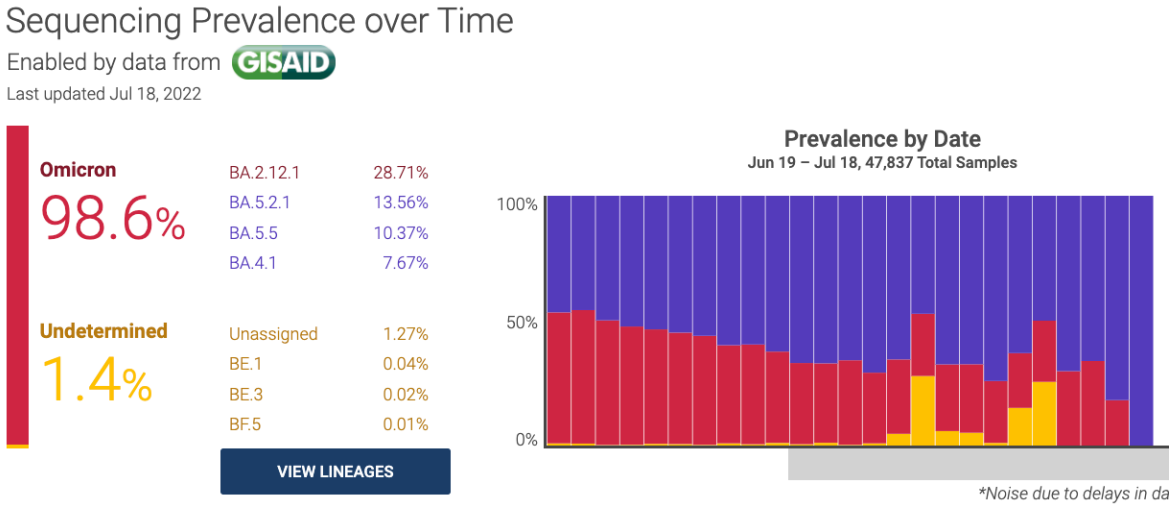
With no prior knowledge of Delta, the ROSA classifier would have categorized 99.93 % of Delta sequences as "Undetermined" and therefore recommended for sequencing

ROSA Tracker: https://tracker.rosalind.bio/dashboard

Genotyping



Sequencing



Reference: Lai E, et al., A Method for Variant Agnostic Detection of SARS-CoV-2, Rapid Monitoring of Circulating Variants, and Early Detection of Emergent Variants Such as Omicron. J Clin Microbiol. 2022 Jun 29:e0034222. doi: 10.1128/jcm.00342-22. Epub ahead of print. PMID: 35766514.

Value proposition – NGS Surveillance vs Project Rosa

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

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).

FDA Update

Tim Stenzel
US Food and Drug Administration (FDA)

U.S. Food and Drug Administration

- **COVID-19 Emergency Use Authorization (EUA) Information for Medical Devices**
  https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations-medical-devices
- **COVID-19 In Vitro Diagnostic EUAs**
  https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas
- **COVID-19 Frequently Asked Questions**
  https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-frequently-asked-questions
- **COVID-19 Updates**
  https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#2019-ncov
- **FDA Townhall Meetings**
  https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/virtual-town-hall-series-immediately-effect-guidance-coronavirus-covid-19-diagnostic-tests-06032020
- **Independent Evaluations of COVID-19 Serological Tests**
  https://open.fda.gov/apis/device/covid19serology/

U.S. Food and Drug Administration

- **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**
  https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program

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

CDC Social Media

https://www.facebook.com/CDC

https://twitter.com/cdcgov

https://www.instagram.com/cdcgov

https://www.linkedin.com/company/cdc

Thank You For Your Time!

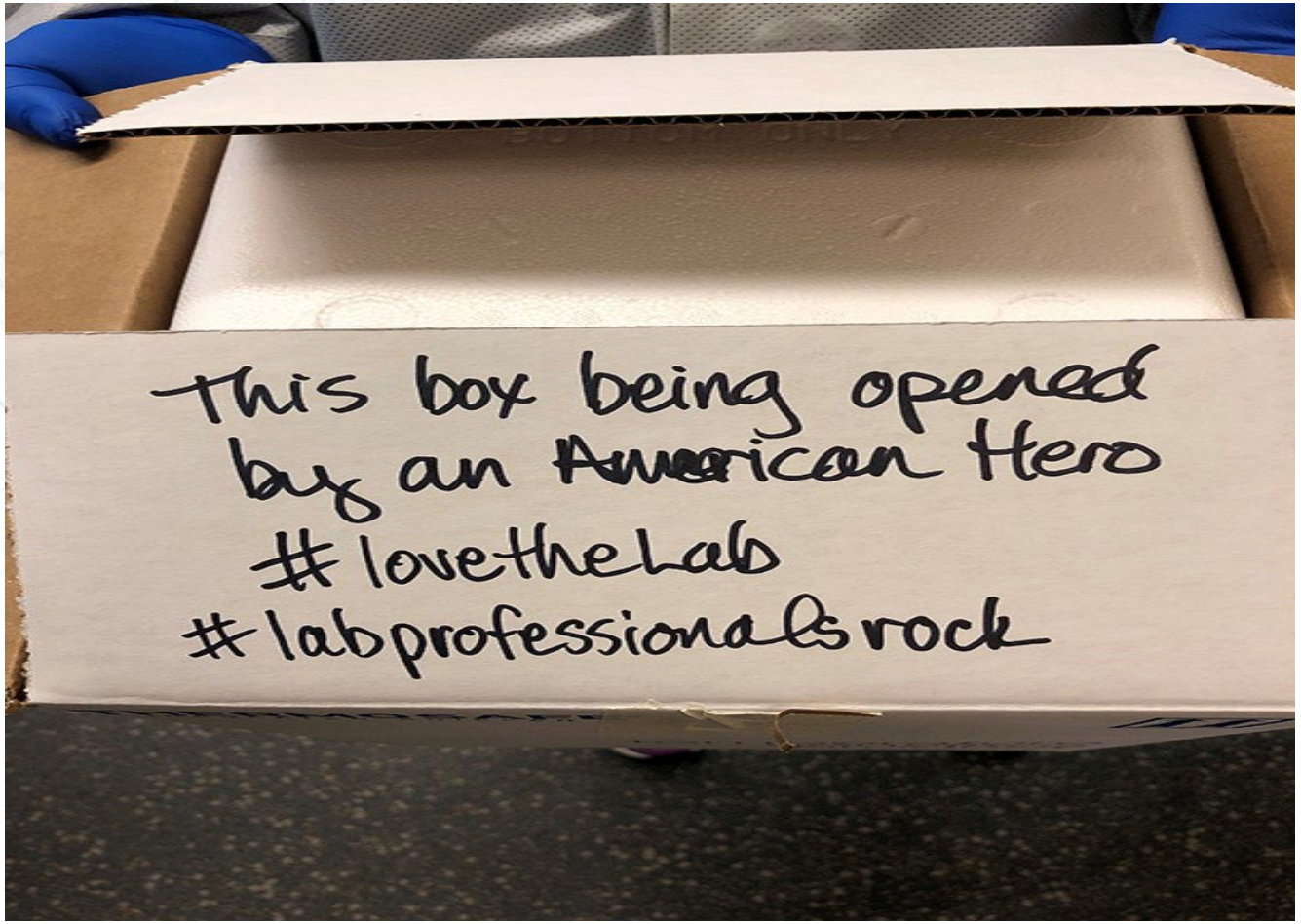


Photo submitted by the Microbiology Laboratory at The University of Pittsburgh Medical Center

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov