Laboratory Outreach Communication System (LOCS) Call

Monday, May 15, 2023, at 3:00 P.M. EDT

- **Welcome**
  - Sean Courtney, CDC Division of Laboratory Systems
- **Avian Influenza Update**
  - Carrie Reed and John Barnes, CDC Influenza Division
- **Marburg Virus Disease Update**
  - Christine Kosmos, CDC Marburg Domestic Response
- **Aircraft Wastewater Surveillance for Early Detection of SARS-CoV-2 Variants**
  - Cindy Friedman, CDC Division of Global Migration and Quarantine
- **CLIA Post-PHE Guidance**
  - Sarah Bennett, Centers for Medicare and Medicaid Services
- **FDA Update**
  - Timothy Stenzel, U.S. Food and Drug Administration

About DLS

Vision

Exemplary laboratory science and practice advance clinical care, public health, and health equity.

Mission

Improve public health, patient outcomes, and health equity by advancing clinical and public health laboratory quality and safety, data and biorepository science, and workforce competency.

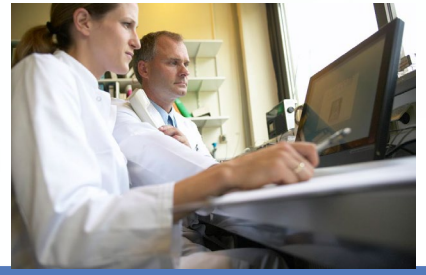
Four Goal Areas

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



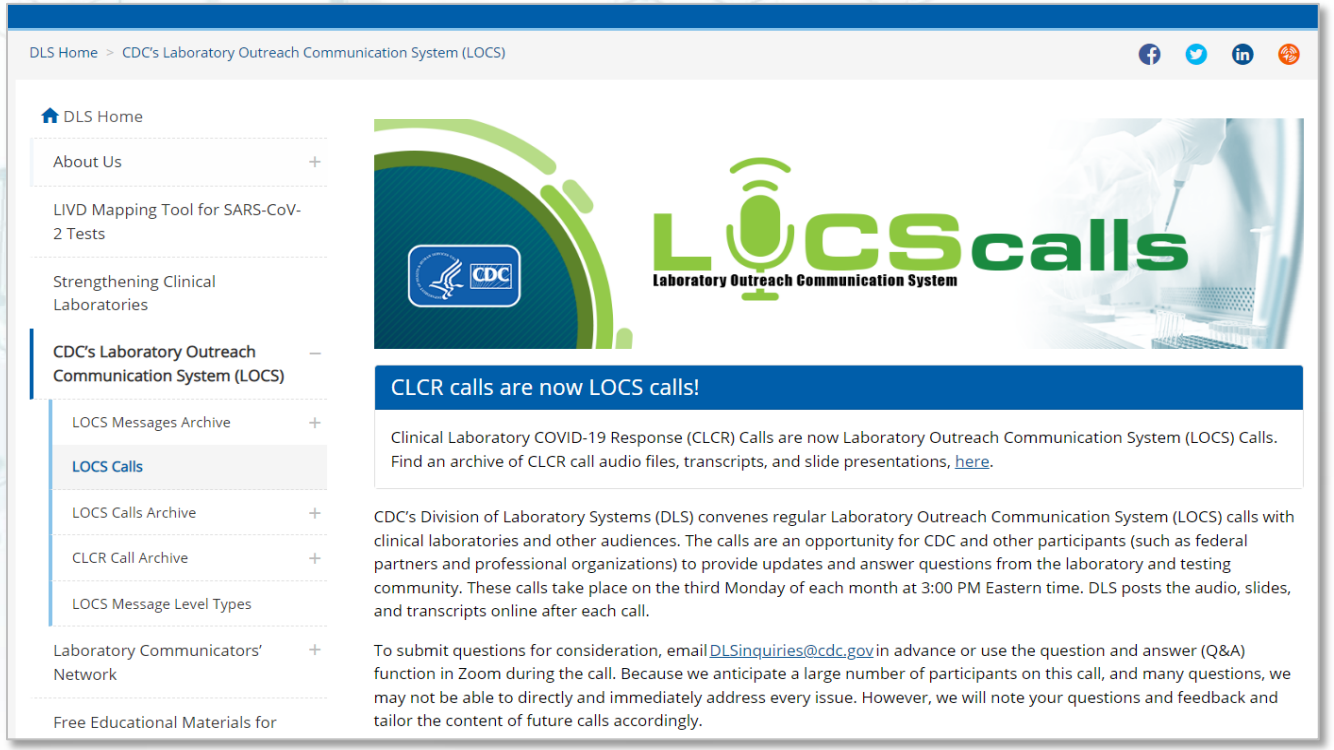
Safe and Prepared Laboratories

- 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

LOCS Calls



On this page, you can find:

- LOCS Call information
- Transcripts
- Slides
- Audio Recordings

https://www.cdc.gov/locs/calls

We Want to Hear From You!

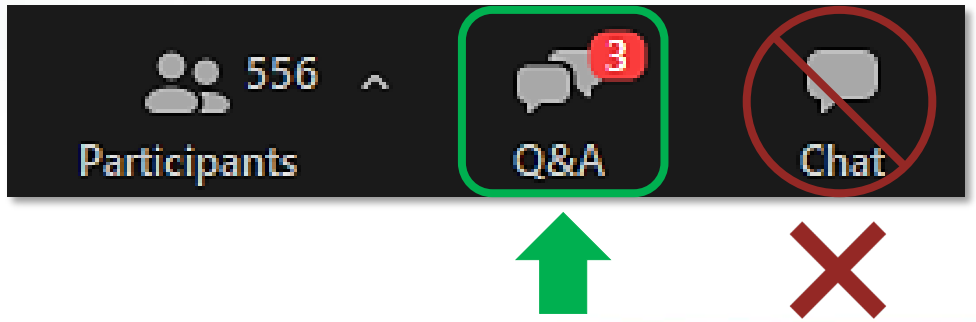
Training and Workforce Development

Questions about education and training?

Contact LabTrainingNeeds@cdc.gov

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

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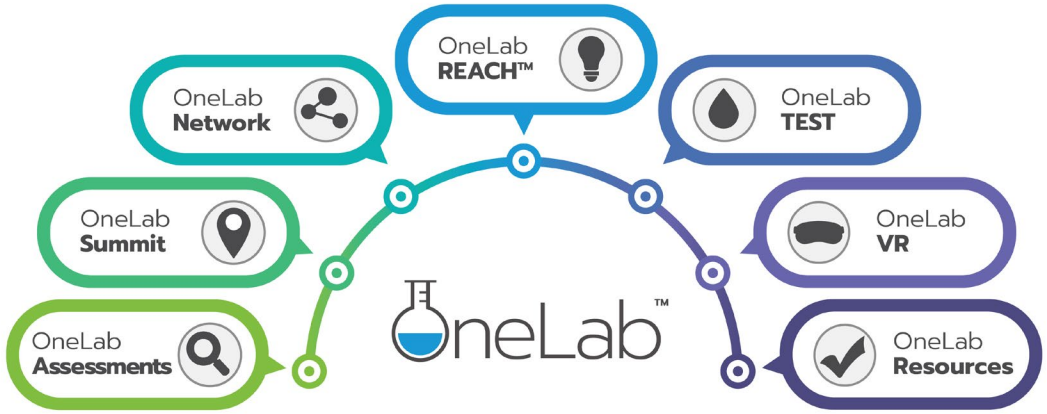


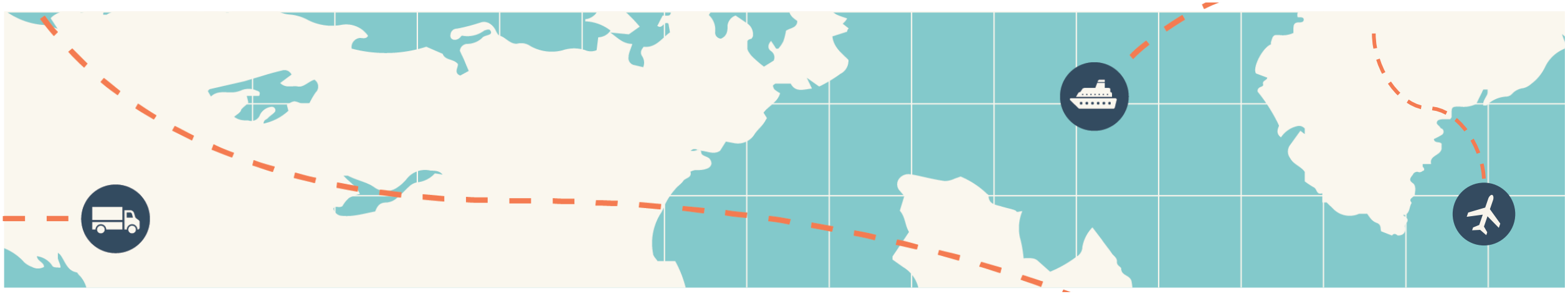
Slide decks may contain presentation material from panelists who are not affiliated with CDC. Presentation content from external panelists may not necessarily reflect CDC's official position on the topic(s) covered.

Avian Influenza Update

Carrie Reed, PhD
John Barnes, PhD
CDC Influenza Division

Marburg Virus Disease Update

Christine Kosmos, RN, BSN, MS
CDC Marburg Domestic Response



Multimodal Surveillance in the Global Transportation Network

CDC's Traveler-based Genomic Surveillance Program

Cindy R. Friedman, MD
Travelers' Health Branch
Division of Global Migration and Quarantine

Traveler-based Genomic Surveillance (TGS) plays an important role in U.S. national surveillance

- Enhance early detection of new SARS-CoV-2 variants
- Fill gaps in global SARS-CoV-2 surveillance using travelers as sentinels

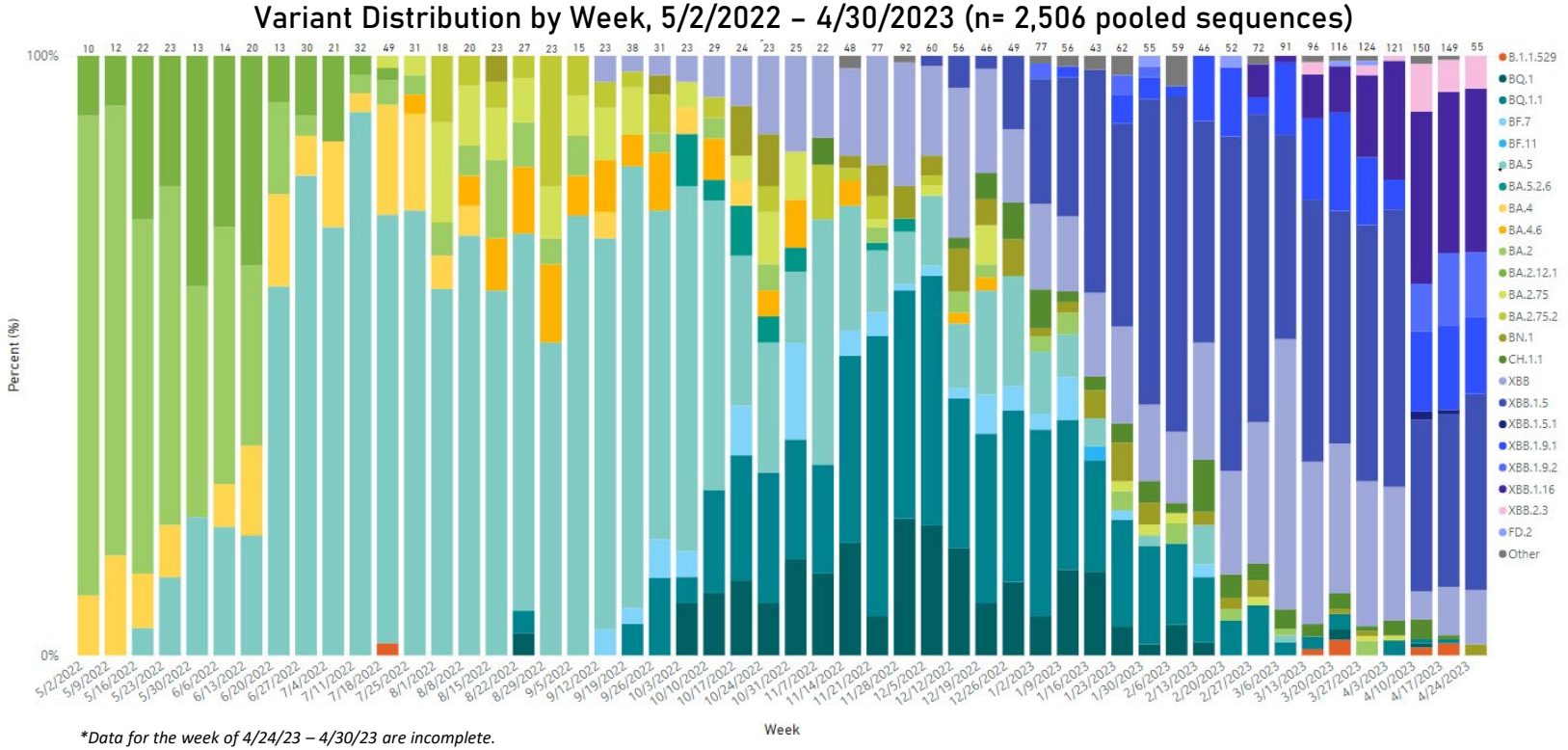
- September 2021 (3 airports), November 2021 (4 airports), January 2023 (7 airports)

The New York Times

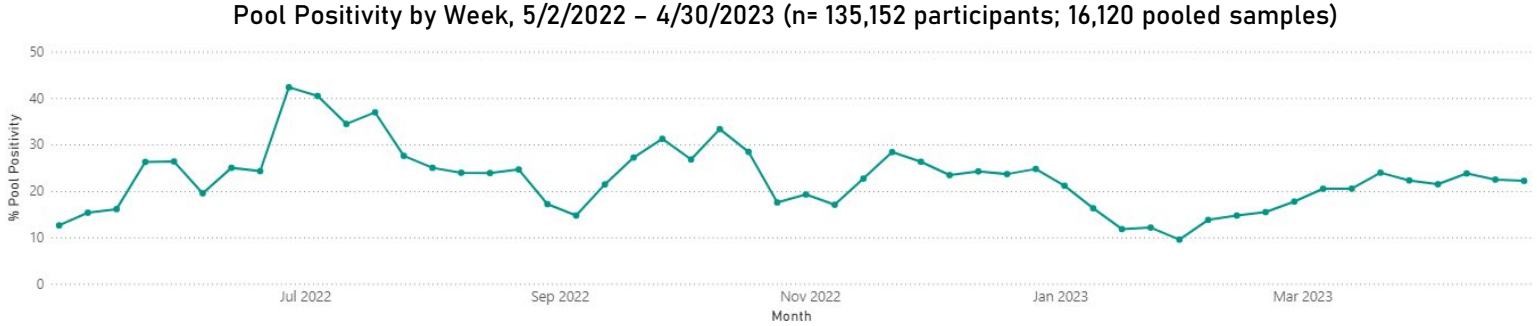
A C.D.C. airport surveillance program found the earliest known U.S. cases of Omicron subvariants.

Locations of airports currently in the program: San Francisco, New York, Newark, Atlanta, Washington DC, Seattle and Los Angeles

Traveler-based Genomic Surveillance (TGS)



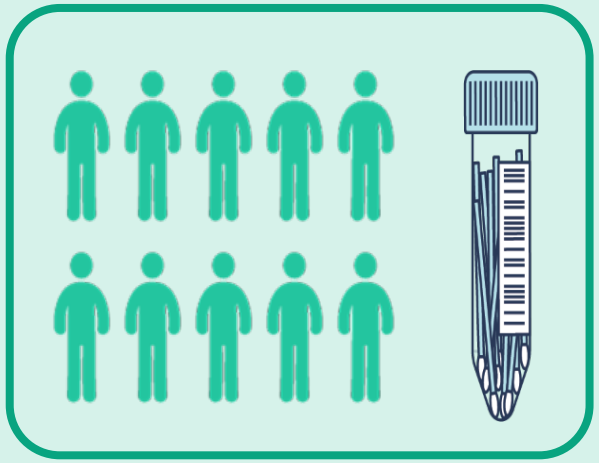
Data for the week of 4/24/23 – 4/30/23 are incomplete.



- Led by CDC's DGMQ Travelers' Health Branch **initiated in November 2021**.
- **Seven airports:** Atlanta, Los Angeles, Newark, New York – JFK, San Francisco, Seattle, and Washington–Dulles. Travelers voluntarily self-collect swabs; swabs pooled and sent to lab for PCR and sequencing.
- **TGS is now the second largest contributor to U.S sequencing in GISAID**
- **~195,000 participants since inception**
  - ~7500 participants per week
- **~3020 pooled sequences**
  - ~40 sequences per week
  - ~1700 individual sequences since 2023

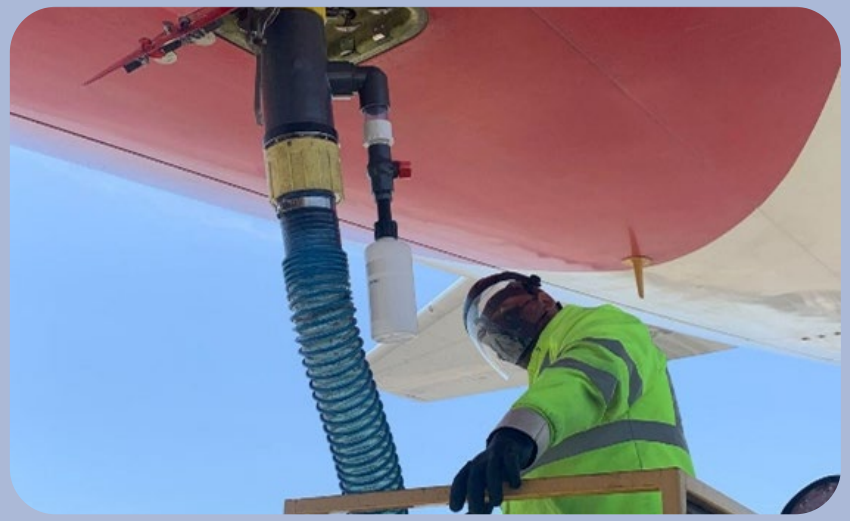
Traveler Genomic Surveillance leverages more than one modality

Airport Pooled Testing



Nasal samples: collected from international travelers are pooled by flight, tested, and sequenced.

Aircraft Wastewater Testing



Wastewater samples: collected from the aircraft lavatory tanks, tested and sequenced.

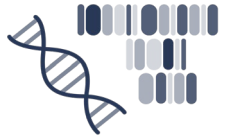
Traveler-based Genomic Surveillance Program
Collection, processing and sequencing of aircraft wastewater samples

Airport
(Aircraft wastewater sample collection)

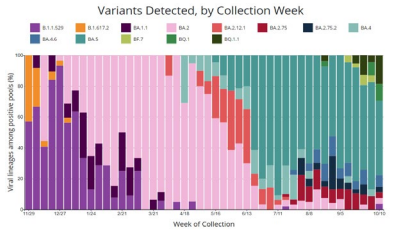
Laboratory
(Testing and sequencing SARS-CoV-2)

International flights arrive at airports.

Samples are collected from the aircraft waste tank using device and protocol.



Samples sent to lab for PCR. Positives sequenced; select samples saved for further analysis.



Testing and sequencing results shared to support public health decision making and inform response.

Early Detection Timeline: Day 1 → Day 2 → Day 8

Aircraft lavatory wastewater SARS-CoV-2 sequencing pilot project at JFK airport August- September 2022

Aircraft Wastewater Surveillance for Early Detection of SARS-CoV-2 Variants — John F. Kennedy International airport. MMWR, February 24, 2023; 72(8).

Aircraft Wastewater testing and sequencing: High-level Technical Summary

Sample intake and PCR testing

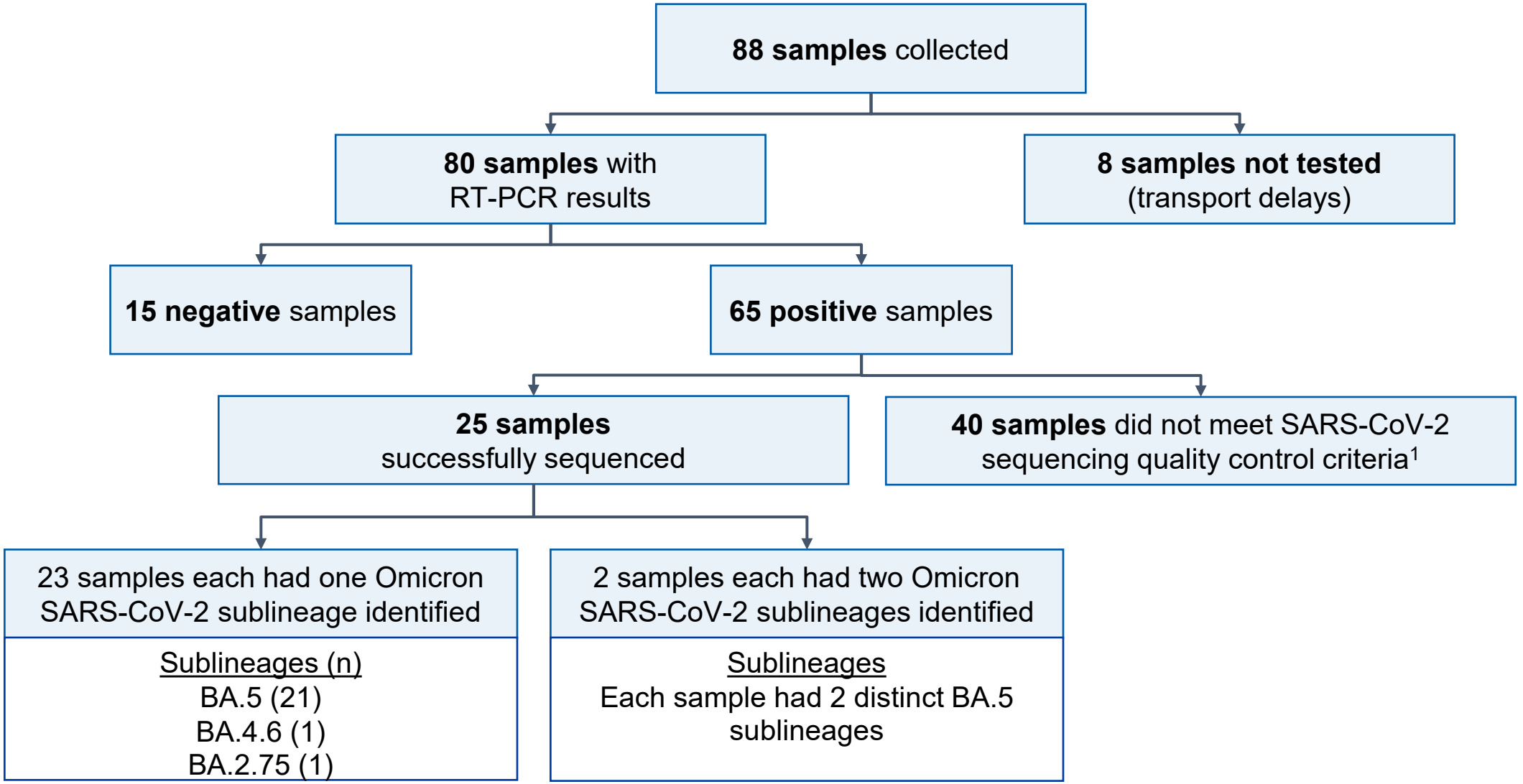
- Samples are held at 4-8 C, and processed within **24 hours** from lab receipt.
- SARS-CoV-2 **captured and concentrated** using magnetic nanobeads. Process is automated to improve throughput.
- **RNA extraction** performed using a wastewater specific kit.
- Virus quantified using **RT-qPCR** performed in triplicate.
- Additional **RNA extract** sent for sequencing of positive samples.

Whole Genome Sequencing

- **ARTICv4.1 protocol** to amplify reverse-transcribed RNA.
- Sequenced on **NovaSeq 6000** (2 x 50 bp).
- Reads aligned to the SARS-CoV-2 reference (MN908947.3).
- **Variants called and consensus genome generated**, <10X depth variant replaced with ambiguous nucleotides.
- Identify **SARS-CoV-2 lineages** using pangolin.
- Reported lineage cutoff: 70% coverage.

Courtesy of Gingko Bioworks

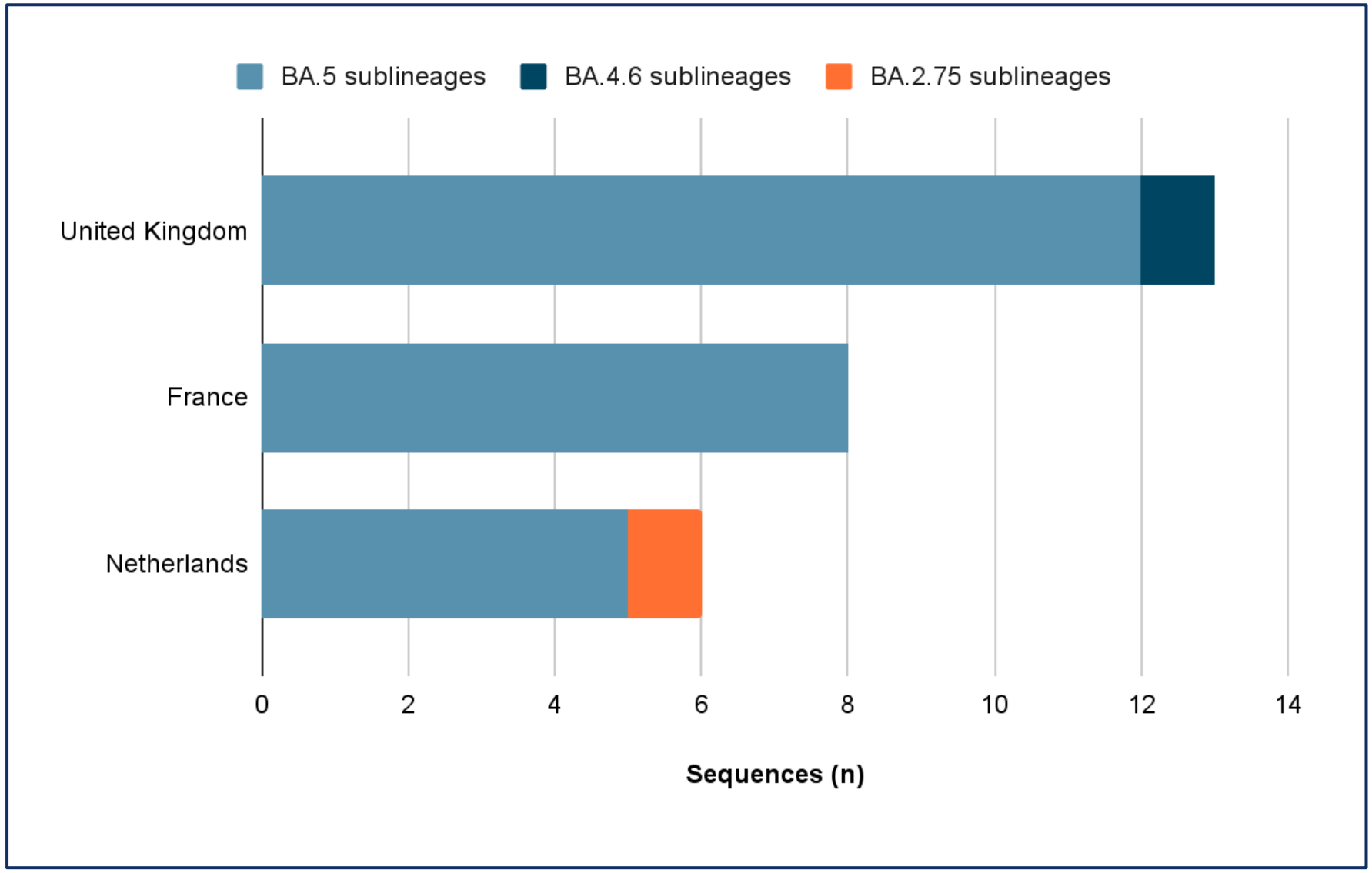
Flow chart of collection, SARS-CoV-2 testing, and genomic sequencing of aircraft wastewater samples during August–September 2022



1 Quality control criteria include: >70% breadth of coverage and >10X depth of coverage

Aircraft Wastewater Surveillance for Early Detection of SARS-CoV-2 Variants — John F. Kennedy International airport. MMWR, February 24, 2023; 72(8).

Sequencing Results by Flight origin



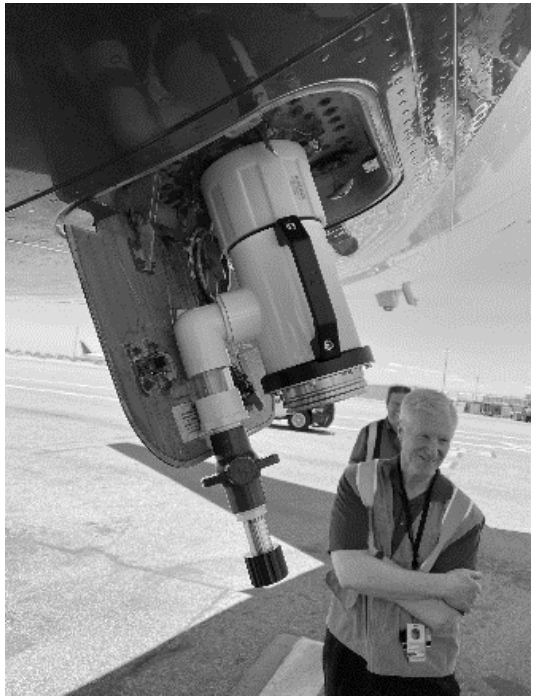
Percent of lineages in GISAID belonging to the BA.5.X subgroup between 8/1 and 8/28/2022

Country	Percent
France	92%
Netherlands	90%
United Kingdom	85%

Source: GISAID

Aircraft Wastewater Surveillance for Early Detection of SARS-CoV-2 Variants — John F. Kennedy International airport. MMWR, February 24, 2023; 72(8).

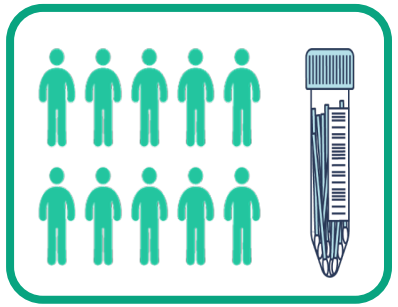
Aircraft lavatory wastewater SARS-CoV-2 sequencing pilot project at JFK airport August- September 2022

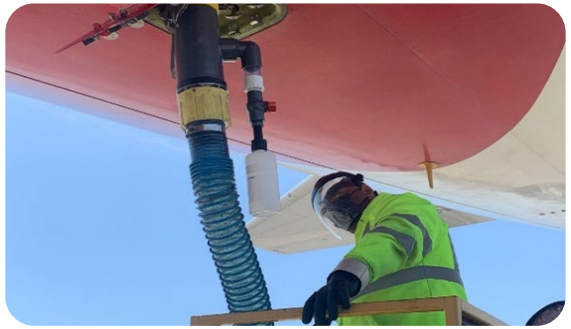


- Wastewater samples were successfully collected from 88 flights without disruption to ground handlers' regular duties.
- SARS-CoV-2 was detected in 65 of 80 (81%) aircraft wastewater samples tested.
- SARS-CoV-2 genomes identified were consistent with Western European sequences uploaded to the Global Initiative on Sharing Avian Influenza Data (GISAID) at the time (approximately 90% BA.5).

Aircraft Wastewater Surveillance for Early Detection of SARS-CoV-2 Variants — John F. Kennedy International airport. MMWR, February 24, 2023; 72(8).

Aircraft wastewater and traveler-based nasal swab surveillance are complementary





Traveler-based genomic surveillance provides more precise data

- Not all travelers participate, must target multiple flights
  - Expanding to global transportation hubs can improve scope
- Sampling individual travelers can be resource intensive
  - Pooled sampling is a unique and valuable approach that allows detection of multiple variants while conserving resources.

Aircraft wastewater does not require traveler engagement

- Not all travelers use the lavatory on flights
  - Chance of defecation ~36%[1] on long haul flights (> 6 hours)
- Not all travelers originate in flight country of origin
  - Wastewater may not reflect the true country of variants detected
- Potential for residual virus in lavatory tanks may make origin attribution challenging
  - We are investigating the impact of viral RNA carryover.

D. Jones et al., “Suitability of aircraft wastewater for pathogen detection and public health surveillance”, Science of the Total Environment, DOI https://doi.org/10.1016/j.scitotenv.2022.159162

TGS can be a cost effective way to perform surveillance at international hubs and borders

- **Airports/borders are key nodes in travel flow** and can play an important role in surveillance to detect and prevent cross-border transmission of pathogens beyond SARS-CoV-2.

- **Aircraft wastewater testing is a cost-effective** way to obtain biological samples from larger groups in an anonymous way, while preserving some key information, e.g., country of origin.

- **TGS programs can** be implemented using existing local testing and sequencing infrastructure to **detect multiple pathogens reducing cost.**

- **Aircraft wastewater surveillance in the transportation sector will require coordination** for standardized methods and analysis, **data sharing**, and engagement of partners beyond public health e.g. airline industry

Where the program is heading

- PHE expiration will not impact the TGS Program, in FY 23 the program will:
  - Sustain current footprint for COVID-19 variant surveillance and integrate multi-pathogen targets
  - Expand TGS Aircraft Wastewater sampling integrating multi-pathogen targets.
  - Expand to 2-3 new airports

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- Kevin O'Laughlin
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- Ashley Brown
- Clive Brown
- Sarah Meehan
- Matthew Palo
- Quarantine and Border Health Services Branch

Resources

CDC Program Webpages

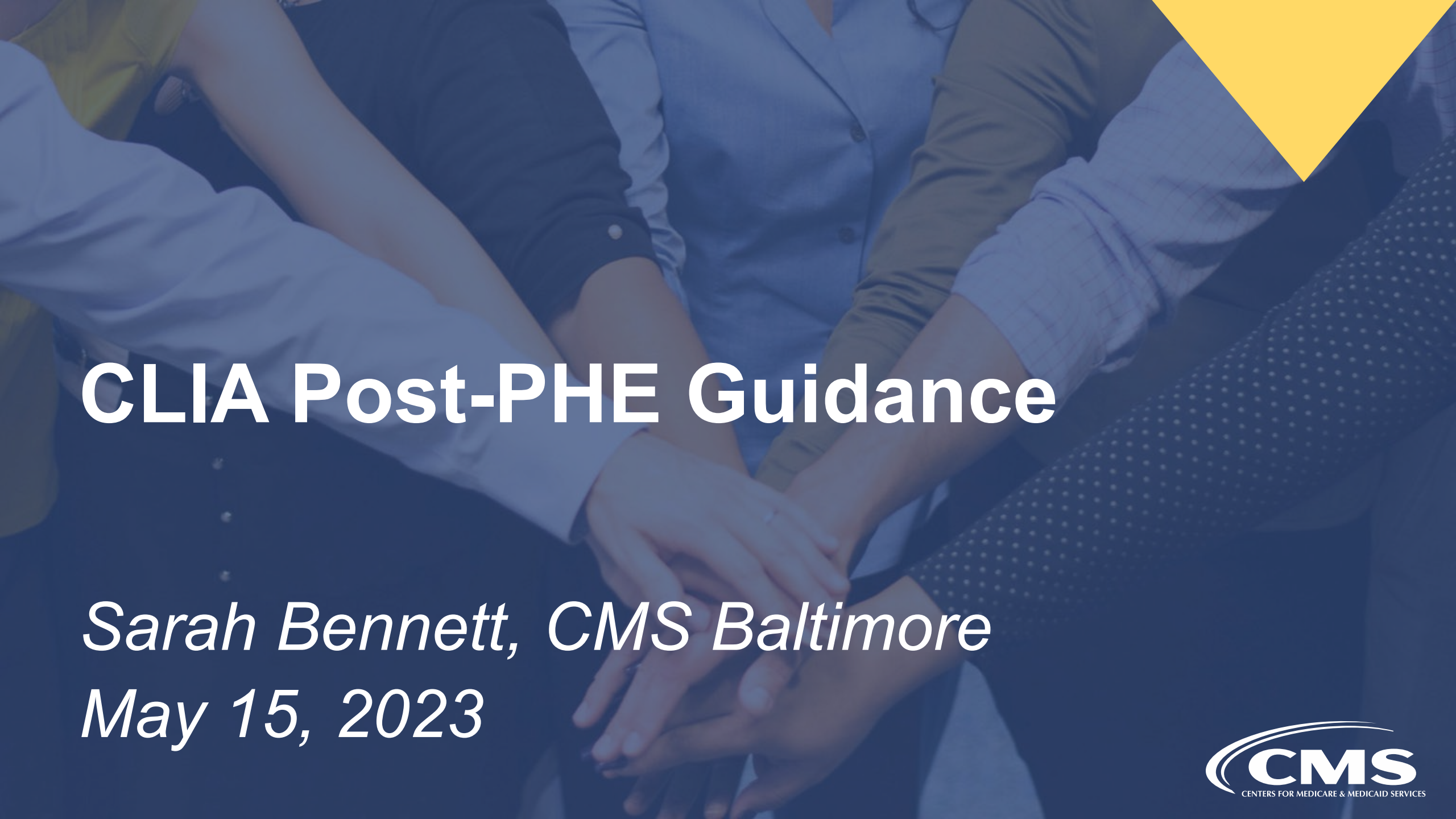
- CDC Travelers' Health TGS Program Page
  - https://wwwnc.cdc.gov/travel/page/travel-genomic-surveillance
- CDC launches Traveler-Based SARS-CoV-2 Genomic Surveillance Program
  - https://www.cdc.gov/amd/whats-new/airport-genomic-surveillance.html
- CDC COVID Data Tracker, TGS Program Page
  - https://covid.cdc.gov/covid-data-tracker/#traveler-genomic-surveillance

Publications

- Early Detection of Severe Acute Respiratory Syndrome Coronavirus 2 Variants Using Traveler-based Genomic Surveillance at 4 US Airports, September 2021-January 2022. Clinical Infectious Diseases. 2022 Jun 10. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac461/6605116?login=true
- *Aircraft Wastewater Surveillance for Early Detection of SARS-CoV-2 Variants — John F. Kennedy International airport.* MMWR, February 24, 2023; 72(8).
- *Effect of Predeparture Testing on Postarrival SARS-CoV-2–Positive Test Results Among International Travelers — CDC Traveler-Based Genomic Surveillance Program, Four U.S. Airports, March–September 2022.* MMWR, February 24, 2023; 72(8).

Select Media

- Airplane lavatories deliver new hope for the CDC's variant hunt – POLITICO
- Searching for new variants among travelers | AP News
- Why the CDC is inviting travelers from China to swab their noses at LAX - Los Angeles Times
- C.D.C. Airport Surveillance Found the First Known U.S. Case of BA.2 - The New York Times
- XpresSpa and Ginkgo Bioworks Are Hunting For New Covid Variants at Airports - Bloomberg
- At Airports, U.S. Health Officials Track COVID-19 Variants | Time



CLIA Post-PHE Guidance

Sarah Bennett, CMS Baltimore

May 15, 2023

CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

Disclaimer

This presentation was prepared for informational purposes and is not intended to grant rights or impose obligations. Every reasonable effort has been made to assure the accuracy of the information within these pages.

This publication is a general summary that explains certain aspects of the Clinical Laboratory Improvement Amendments (CLIA) Program, but is not a legal document. The official CLIA Program provisions are contained in the relevant laws, regulations, and rulings. Links to the source documents have been provided within the document for your reference.

The Centers for Medicare & Medicaid Services (CMS) employees, agents, and staff make no representation, warranty, or guarantee that this compilation of CLIA information is error-free and will bear no responsibility or liability for the results or consequences of the use of this guide.

Emergency Declarations

- Declared by the Secretary of HHS ("Secretary")
- Two types of declarations related to COVID-19:
  - ❖Section 319 of the Public Health Service (PHS) Act
  - ❖Section 564 of the Federal Food, Drug, and Cosmetic (FD&C) Act

Section 319 of the PHS Act

- Under section 319 of the PHS Act, the Secretary can declare a PHE if he/she determines, after consulting with such public health officials as may be necessary, that 1) a disease or disorder presents a PHE or 2) a PHE, including significant outbreaks of infectious diseases or bioterrorist attacks, otherwise exists.
- Lasts until Secretary declares PHE no longer exists or expiration of declaration.
- **Ends May 11, 2023**

Section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

- The Secretary makes determination that circumstances justify the Emergency Use Authorization (EUA)
- Continues until the Secretary terminates it
- The FDA can allow the use of unapproved medical products, or unapproved uses of approved medical products, to diagnose, treat, or prevent serious or life-threatening diseases when certain criteria are met
- **<u>Does not end</u> May 11, 2023**

So what does this mean?

- An EUA may remain in effect beyond the duration of the section 319 PHE declaration if the 564 declaration is still in effect
  - ❖EUA may remain authorized
  - ❖New EUAs may continue to be issued
  - ❖EUA authorization continues until the test is approved and categorized by the FDA or the 564 emergency declaration ends
- Laboratories may continue to use EUA test kits past 5/11/2023 as long as the FDA allows the tests to be marketed as an EUA or the FDA categorizes them

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CLIA

QSO-23-15-CLIA, Clinical Laboratory Improvement Amendments of 1988 (CLIA) Post-Public Health Emergency (PHE) Guidance

SARS-CoV-2 Test Result Reporting Requirements

- CMS only has authority to require reporting during the PHE
- The CLIA requirement that all certificate types report SARS-CoV-2 test results will end when the PHE is terminated on May 11, 2023.

Exercise of Enforcement Discretion and Other Flexibilities

- This memorandum supersedes previous guidance
- Useful during the initial response to COVID-19 but may no longer needed
- Allowances for not meeting certain CLIA regulatory requirements have ended with the termination of the PHE

Note: Laboratories with a CoA are advised to contact their Accreditation Organization (AO) for specific guidance, as the AO may have more stringent requirements. In addition, laboratories located in states with State licensure requirements must contact their State Agency as state requirements may be more stringent than CLIA.

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CLIA

Digital Clinical Laboratory Data, Digital Results and Digital Images

- **This enforcement discretion <u>will</u> continue post-PHE**
- Pathologists and laboratory personnel will be allowed to review digital data, digital results and digital images remotely at a remote location under a primary location's CLIA certificate

Digital Clinical Laboratory Data, Digital Results and Digital Images, Criteria

- The primary, home site, laboratory has a current, unrevoked or unsuspended certificate
- The primary laboratory complies with other applicable Federal laws, including HIPAA
- The laboratory director of the primary site CLIA number is responsible for all testing, including testing and reporting performed remotely
- Survey findings will be cited under the primary laboratory's CLIA certificate

Digital Clinical Laboratory Data, Digital Results and Digital Images, Criteria cont.

- The primary laboratory's test reports must indicate the remote site location where the testing is performed; may use a coding; must be available upon request
- The primary laboratory must be certified in the specialties and/or subspecialties of the work performed at the remote site
- The primary laboratory must provide CMS a list of all staff working remotely, upon request

Digital Clinical Laboratory Data, Digital Results and Digital Images, Criteria cont.

- The primary location is responsible for retaining all documentation, including testing performed by staff working remotely
- The individual(s) performing remote review must be on the primary laboratory's Form CMS-209

Physical Slides

- **This enforcement discretion <u>will not</u> continue post-PHE**
- Pathologists, cytotechnologists, and medical laboratory scientists reading physical slides cannot do so remotely under a primary location CLIA certificate
- Sites reading physical slides must have its own CLIA certificate and meet applicable CLIA requirements

Physical Slides, cont.

- A microscope and other laboratory equipment is necessary to perform the testing
- Physically transferring slides from one site to another constitutes a referral to another laboratory
- Includes pathologists and other staff working for a primary site laboratory

Expedited Review of CLIA Applications

- **This flexibility <u>will not</u> continue post-PHE**
- Laboratories may only begin testing after they pay applicable laboratory fee(s) and receive a CLIA number or a CLIA certificate

Molecular and Antigen Point of Care Test Asymptomatic Testing

- **This enforcement discretion <u>will not</u> continue post-PHE**
- FDA has authorized numerous antigen, molecular, OTC tests that allow testing in asymptomatic individuals
- IFU: “individuals suspected of COVID-19 by their healthcare provider” – not a modification; decision of suspected COVID-19 made by healthcare provider
- **Not the laboratory’s** responsibility to ensure that subsequent testing, e.g. serial testing, stated in the IFU, is performed (healthcare provider responsibility)

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CLIA

Multiple Site Exceptions

Laboratories Located at Contiguous Buildings on the Same Campus and Temporary Testing Sites

- **This was identified as a flexibility during the PHE but is allowed in the regulations**
- This requirement allowed in CLIA regulations at 42 C.F.R. §§ 493.35(b)(3), 493.43(b)(3), 493.55(b)(3))

Alternate Specimen Collection Devices

- **This flexibility <u>will not</u> continue post-PHE**
- If IFU do not include using alternative specimen collection devices/media instruction → laboratory must establish performance specs before reporting patient test results
- CLIA is not prescriptive how laboratories establish performance specs; laboratory director is response that the establishment studies meet regulatory requirements

Use of Expired Reagents

- **This enforcement discretion will not continue post-PHE**
- Laboratories cannot use expired reagents (§ 493.1252(d))
- Use of expired reagents = modification → laboratory must establish performance specifications
- Test would default to high complexity

Abbott iSTAT

- Abbott iSTAT, G3+
  - ❖**This enforcement discretion <u>will not</u> continue post-PHE**
  - ❖The G3+ (BLUE) cartridge analytes are included as analytes in the CG4+ (BLUE) cartridge, which is categorized by the FDA as moderate complexity
- Abbott iSTAT, Troponin
  - ❖**This enforcement discretion <u>will</u> continue post-PHE**
  - ❖Laboratories with a CoR (CoC) or CoC can use the cTnI test cartridge as a moderate complexity test until such time that the FDA clears troponin and posts the categorization on their website
  - ❖Laboratories with a CoA must contact its AO for guidance

Surveillance, University, Genetic Variant Testing

- **This enforcement discretion <u>will not</u> continue post-PHE**
- All laboratories performing surveillance and genetic variant testing that report patient-specific results, including positive, negative, and inconclusive, are required to have a CLIA certification

Summary Table of Post-PHE Enforcement Discretions and Flexibilities

Enforcement Discretion (E), Flexibility (F)	(E) or (F)	Post-PHE Guidance
Remote Staff Performing Review of Digital Clinical Laboratory Data, Digital Results and Digital Images	E	This enforcement discretion will continue post-PHE. Pathologists and laboratory personnel will be allowed to review digital data, digital results and digital images remotely at a remote location under a primary location's CLIA certificate.
Remote Staff Performing Examination of Physical Slides, including Pathology	E	This enforcement discretion will not continue post-PHE. Pathologists, cytotechnologists, and medical laboratory scientists reading physical slides cannot do so remotely under a primary location CLIA certificate.
Expedited Review of CLIA Applications	F	This flexibility will not continue post-PHE. A laboratory must receive a CLIA number and pay the applicable laboratory fee(s) before testing begins.
Molecular and Antigen Point of Care Test Asymptomatic Testing	E	This enforcement discretion will not continue post-PHE.
Hospital Laboratories Located at Contiguous Buildings on the Same Campus	N/A	This was identified as a flexibility during the PHE but is allowed in the regulations.
Temporary Testing Sites	N/A	This was identified as a flexibility during the PHE but is allowed in the regulations.
Alternate Specimen Collection Devices	F	This flexibility will not continue post-PHE.
Use of Expired Reagents	E	This enforcement discretion will not continue post-PHE.
Abbott iSTAT, G3+	E	This enforcement discretion will not continue post-PHE for G3+.
Abbott iSTAT, Troponin	E	This enforcement discretion will continue post-PHE, but will not be tied to the PHE.
Surveillance, University, Genetic Variant Testing	E	This enforcement discretion will not continue post-PHE.

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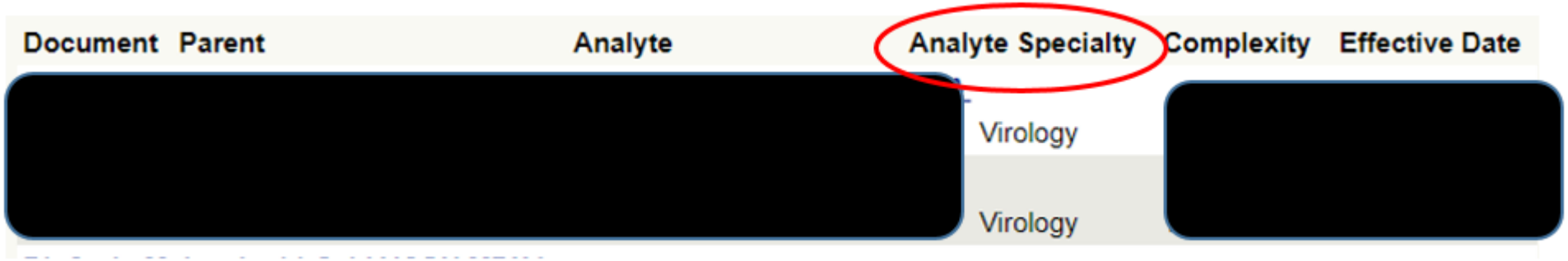
CLIA

Will CMS continue to use the remote survey process after the PHE is over?

No. All CLIA surveys, including those performed by accreditation organizations, will be performed onsite

Has SARS-CoV-2 been assigned a specialty by the FDA?

The FDA has categorized several tests under the subspecialty of virology. The specialty/subspecialty information can be found on the FDA CLIA Complexity Database in the “Analyte Specialty” column.



Will PT be required for SARS-CoV-2 testing after the PHE has ended?

PT is required for the subspecialty of virology in laboratories that perform viral antigens or test for viral structures. This would include both antigen and molecular testing for tests that the FDA has determined fall under the subspecialty of virology. Laboratories will need to enroll in PT, if PT is available.

If a laboratory has previously verified an EUA test, will it need to re-verify the test once the FDA clears/approves that test?

As long as the EUA and cleared/approved products have the same from an intended use, design, chemistry, sample processing, consumables and procedures standpoint, and as long as the manufacturer's instruction regarding performance verification remain the same, the laboratory does not need to re-verify the test once the manufacturer receives FDA clearance/approval of that test.

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What does a laboratory need to do if an authorized EUA sample type is not listed in FDA-cleared/approved test?

Testing on a sample type not listed in the FDA-cleared/approved test system would be a modification, and the laboratory would be required to establish performance specifications for this sample type.


“A hero is an ordinary individual who finds the strength to persevere and endure in spite of overwhelming obstacles.”
-Christopher Reeve

FDA Update

Timothy Stenzel, MD, PhD
U.S. Food and Drug Administration

Next Scheduled Call

Monday, June 26
3 PM - 4 PM EDT

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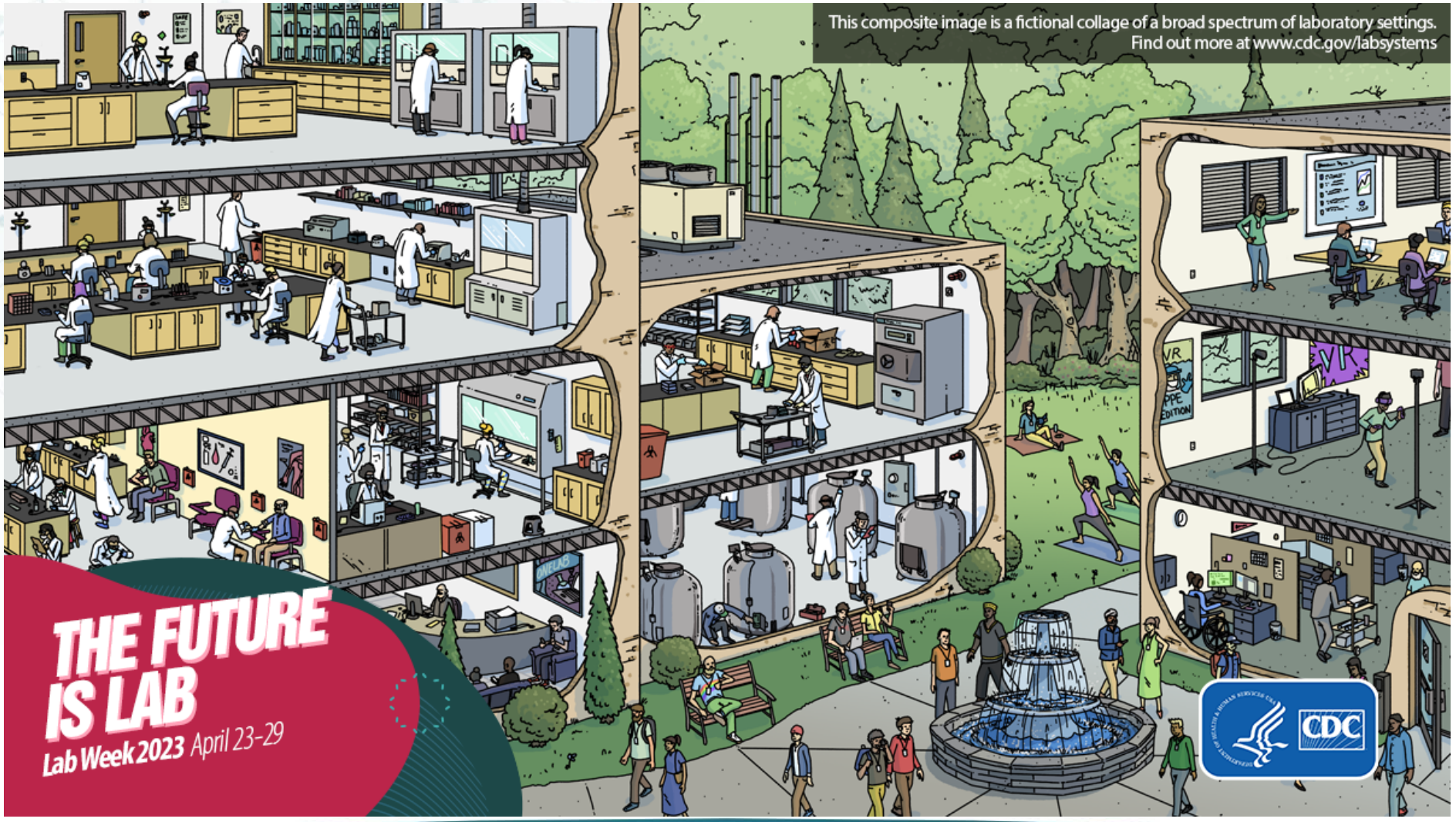
Thank You For Your Time!



For more information, contact CDC
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