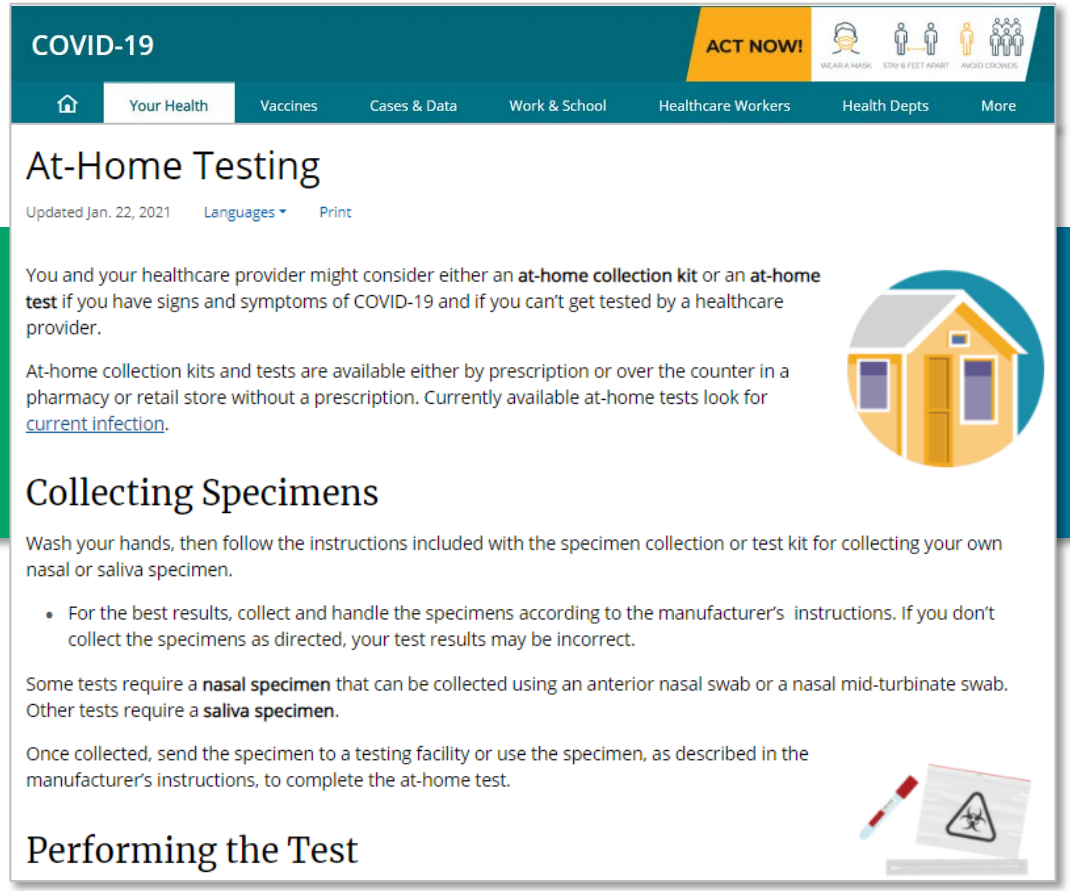
Clinical Laboratory COVID-19 Response Call

Monday, January 25th, 2021 at 3:00 PM ET

- **Welcome**
  - Jasmine Chaitram, CDC Division of Laboratory Systems (DLS)
- **What Are the Clinical Laboratory Result Abnormalities in Patients Hospitalized with COVID-19?**
  - Nadia Ayala-Lopez, Johns Hopkins Medical Institute
- **COVID-19 Variants and Surveillance**
  - Chris Elkins, CDC COVID-19 Laboratory and Testing Task Force
- **CMS Billing Update**
  - Sarah Harding, Centers for Medicare and Medicaid Services (CMS)
- **FDA Update**
  - Tim Stenzel, U.S. Food and Drug Administration (FDA)

COVID-19 At-Home Testing Webpage

https://www.cdc.gov/coronavirus/2019-ncov/testing/at-home-testing.html



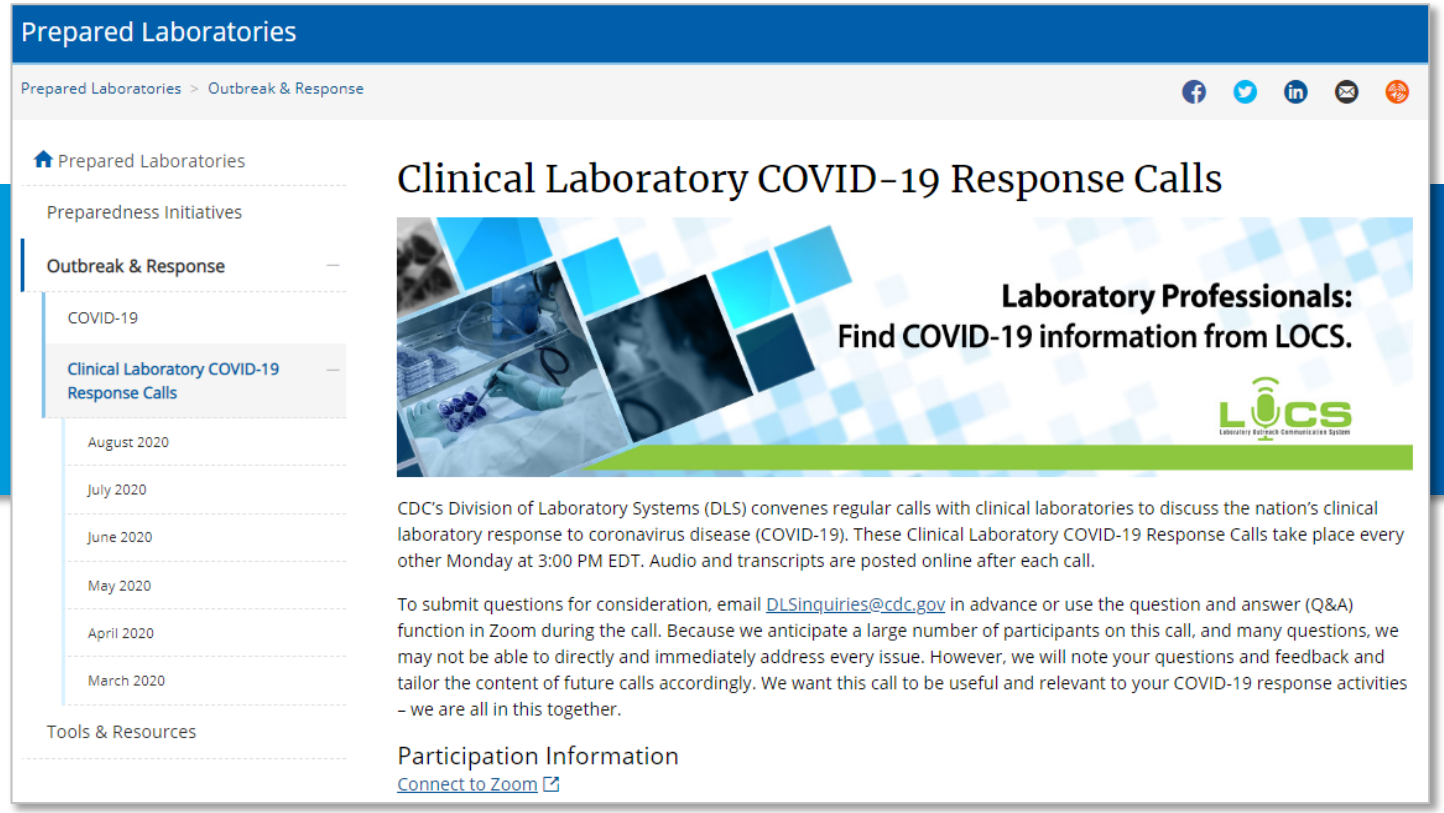
COVID-19 Resources for Laboratories

- **LOINC In-Vitro Diagnostic (LIVD) Test Code Mapping for SARS-CoV-2 Tests**
  https://www.cdc.gov/csels/dls/sars-cov-2-livd-codes.html
- **IVD Industry Connectivity Consortium**
  https://ivdconnectivity.org/livd/
- **Antigen Testing Guidance**
  https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html
- **Frequently Asked Questions about COVID-19 for Laboratories**
  https://www.cdc.gov/coronavirus/2019-ncov/lab/faqs.html
- **Interim Guidance for Collecting, Handling, and Testing Clinical Specimens**
  https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html
- **Diagnostic Tools and Virus**
  https://www.cdc.gov/coronavirus/2019-ncov/lab/tool-virus-requests.html
- **Emergency Preparedness for Laboratory Personnel**
  https://emergency.cdc.gov/labissues/index.asp
- **CDC Laboratory Outreach Communication System (LOCS)**
  https://www.cdc.gov/csels/dls/locs/

CDC Preparedness Portal

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

Find CLCR call information, transcripts, and audio recordings on the CDC Preparedness Portal



Schedule for Clinical Laboratory COVID-19 Response Calls

The next call will be on **Monday, February 8th**

from **3:00 PM to 4:00 PM ET**

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

What are the clinical laboratory result abnormalities in patients hospitalized with COVID-19?

Nadia Ayala-Lopez, PhD, MLS (ASCP)

Clinical Chemistry Fellow
Department of Pathology

Clinical laboratory hallmarks of severe COVID-19

Markers of

- Inflammation
- Coagulation
- Tissue injury

Inflammation

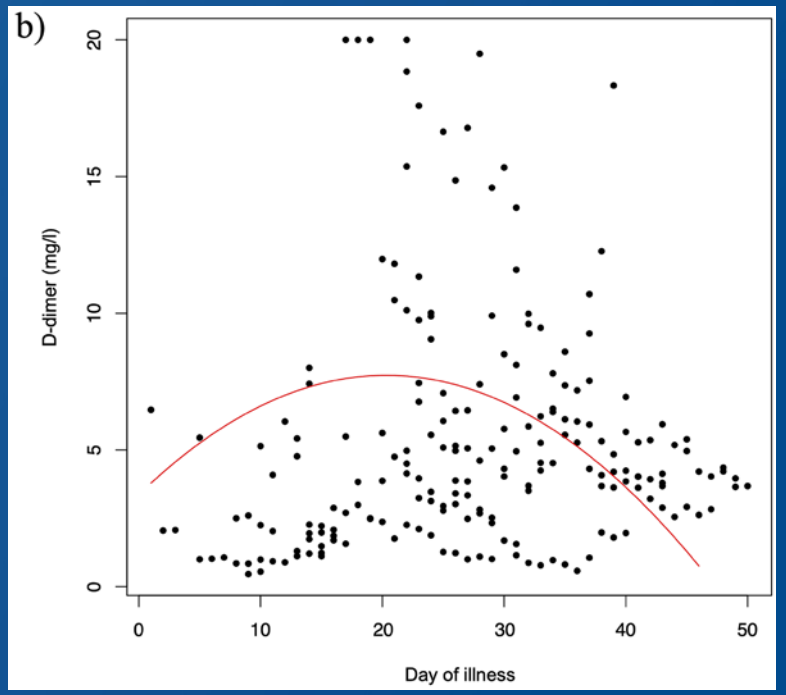
- ↑ **C-reactive protein (CRP)**[1]
- ↑ **IL-6,** TNFα, IL-1, IL-10, IL-2[2]
- ↑ ferritin[4]
- ↑ neutrophils and WBCs[1]
- ↑ procalcitonin[1]
- **Lymphopenia**
  - Specific reductions in CD3+, CD4+ and CD8+ subpopulations of T-cells[2]

Proposed biomarkers for severity of COVID-19

- ↑ IL-6 and CRP have a high predictive value for severe COVID-19[5]
- A high neutrophil-to-lymphocyte ratio (NLR; RI ≤3) and low lymphocyte-to-CRP ratio[4,6]
- A meta-analysis of 22 studies on hospitalized COVID-19 patients found that lymphopenia and neutrophilia at admission were associated with poorer outcomes[7]
- Elevated red cell distribution width (RDW) at admission associated with mortality risk[8]

Coagulopathy

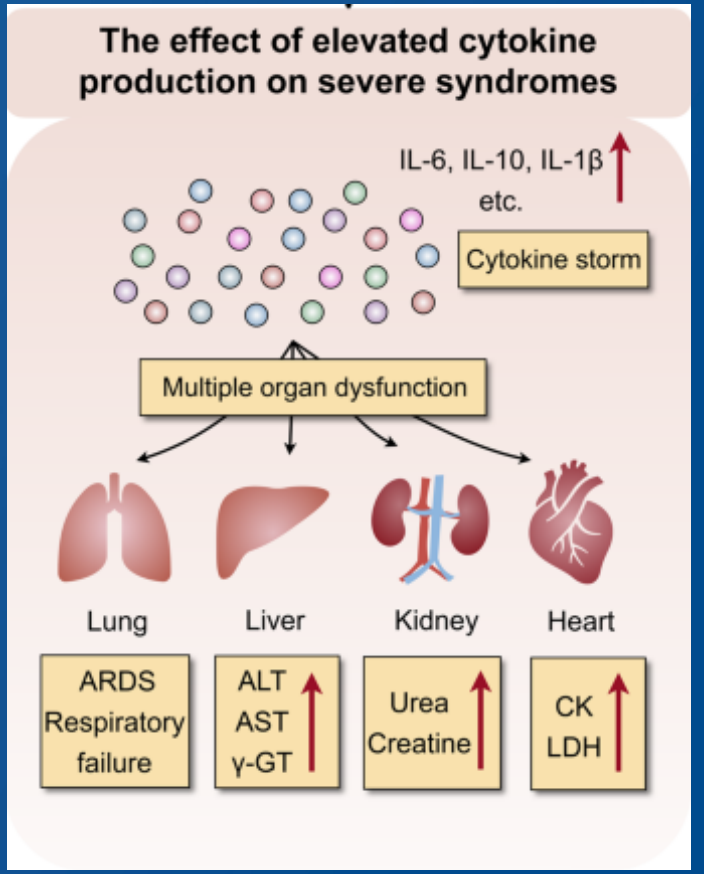
- Abnormalities in coagulation leading to venous and thromboembolic complications are found in 10-25% of COVID-19 patients requiring hospital care.[10]
- ↑ D-dimer in patients with COVID-19-coagulopathy
  - Higher risk of mortality (18-times) was observed with patients with D-dimer concentrations above 1 mg/L[3]
- Prolongation of the prothrombin time (PT) and ↓ platelets, which may be mild. [3]
- Fibrinogen concentrations may be either increased or decreased, depending on their stage in the progression of the disease.[3]



D-dimer values in ICU patients with COVID-19. Friedrich et al. 2020[9]

Tissue injury

- Lung, liver, renal and cardiac injury
  - Liver injury[11]:
    - ↑ liver injury-associated enzymes: alanine aminotransferase (ALT) and aspartate aminotransferase (AST)[11]
    - ↓ albumin with diminished liver function.[1]
  - Acute kidney injury[2]
    - ↑ serum creatinine and serum urea nitrogen are associated with high risk of mortality in COVID19.
  - Cardiac injury[2]
    - ↑ in troponin present in 7-17% of hospitalized COVID-19 patients[10]
    - ↑ lactate dehydrogenase (LDH)



Yang et al. 2020[11]

Conclusion

- Clinical laboratory findings in COVID19 include parameters of
  - Inflammation: IL-6, procalcitonin, CRP, lymphopenia and neutrophilia.
  - Coagulopathy: D-dimer, PT, platelets, fibrinogen
  - Tissue injury: LDH, AST, ALT, creatinine, troponin

- More studies are needed on the associations of laboratory markers and predictive calculations to outcomes as therapies for COVID-19 evolve, as well as understanding the impact of comorbidities on these laboratory markers.

- The ability for laboratories to provide valuable, timely, and accurate testing in the setting of COVID-19 is essential in the management of the pandemic.

@drayalalopez

References

1. Lippi, G., & Plebani, M. (2020). The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks, Clinical Chemistry and Laboratory Medicine (CCLM), 58(7), 1063-1069.
2. Weidmann, Maxwell D, et al. “Laboratory Biomarkers in the Management of Patients With COVID-19.” American Journal of Clinical Pathology, 2020, doi:10.1093/ajcp/aqaa205.
3. Marcel Levi, Jecko Thachil, Toshiaki Iba, Jerrold H Levy. Coagulation abnormalities and thrombosis in patients with COVID-19, The Lancet Haematology, Volume 7, Issue 6, 2020, Pages e438-e440
4. Griffin DO, Jensen A, Khan M, Chin J, Chin K, Saad J, Parnell R, Awwad C, Patel D. Cytokine storm of a different flavour: The different cytokine signature of SARS-CoV-2, the cause of COVID-19, from the original SARS outbreak. J Glob Antimicrob Resist. 2020 Nov 23;24:90-92. doi: 10.1016/j.jgar.2020.11.005. Epub ahead of print.
5. Herold T, Jurinovic V, Arnreich C, Lipworth BJ, Hellmuth JC, von Bergwelt-Baildon M, Klein M, Weinberger T. Elevated levels of IL-6 and CRP predict the need for mechanical ventilation in COVID-19. J Allergy Clin Immunol. 2020 Jul;146(1):128-136.e4. doi: 10.1016/j.jaci.2020.05.008. Epub 2020 May 18.
6. Lagunas-Rangel, F.A. (2020), Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. J Med Virol. doi:10.1002/jmv.25819
7. Henry B, Cheruiyot I, Vikse J, Mutua V, Kipkorir V, Benoit J, Plebani M, Bragazzi N, Lippi G. Lymphopenia and neutrophilia at admission predicts severity and mortality in patients with COVID-19: a meta-analysis. Acta Biomed. 2020 Sep 7;91(3):e2020008.
8. Foy BH, Carlson JCT, Reinertsen E, Padros I Valls R, Pallares Lopez R, Palanques-Tost E, Mow C, Westover MB, Aguirre AD, Higgins JM. Association of Red Blood Cell Distribution Width With Mortality Risk in Hospitalized Adults With SARS-CoV-2 Infection. JAMA Netw Open. 2020 Sep 1;3(9):e2022058.
9. Friedrich MS, Studt JD, Braun J, Spahn DR, Kaserer A. Coronavirus-induced coagulopathy during the course of disease. PLoS One. 2020 Dec
10. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. JAMA. 2020;324(8):782–793.
11. Yang, L., Liu, S., Liu, J. et al. COVID-19: immunopathogenesis and Immunotherapeutics. Sig Transduct Target Ther 5, 128 (2020).

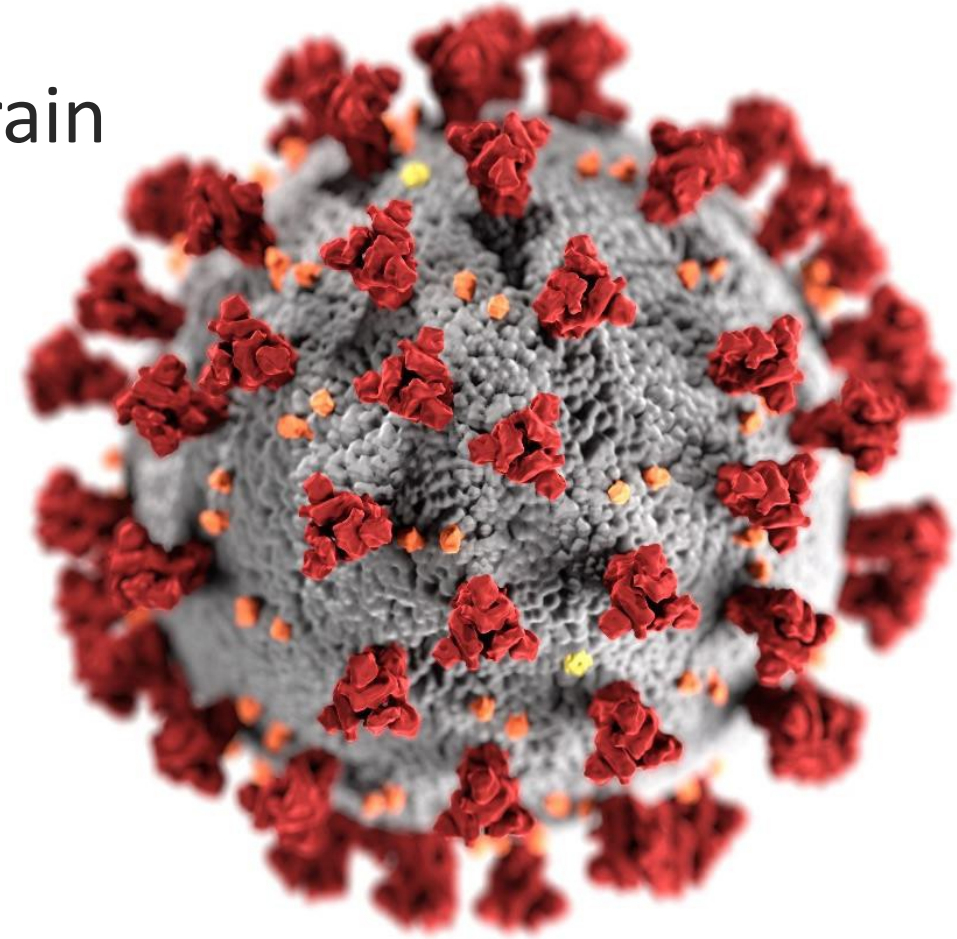
COVID-19 Variants and Surveillance

Chris Elkins
CDC COVID-19 Laboratory and Testing Task Force

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

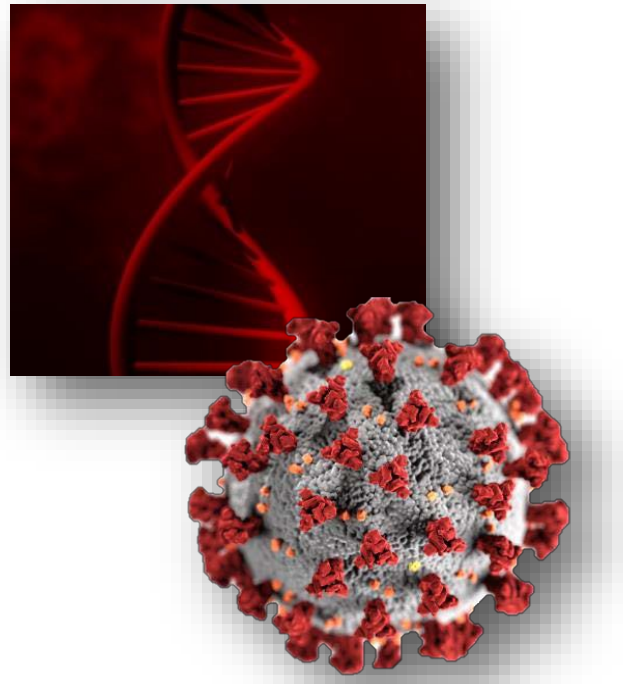
SARS-CoV-2 Variants and Surveillance Update

- Overview of National SARS-CoV-2 Strain Surveillance (NS3)
- Update on SARS-CoV-2 variants
- Summary

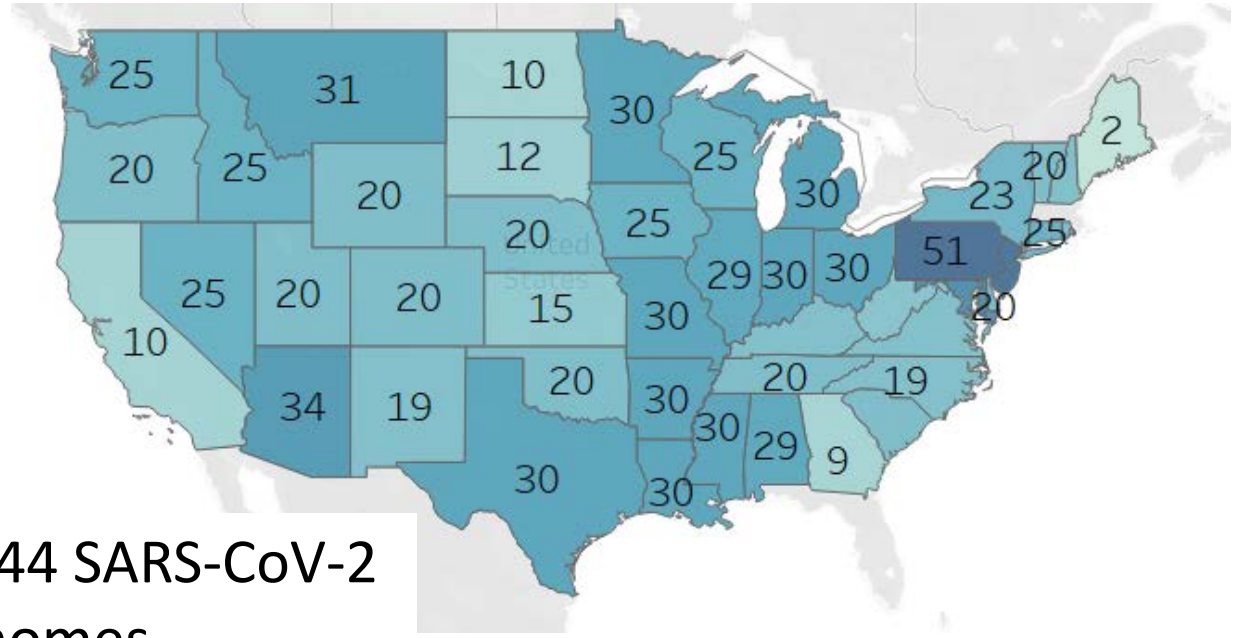


Enhancing Surveillance for SARS-CoV-2
NS3

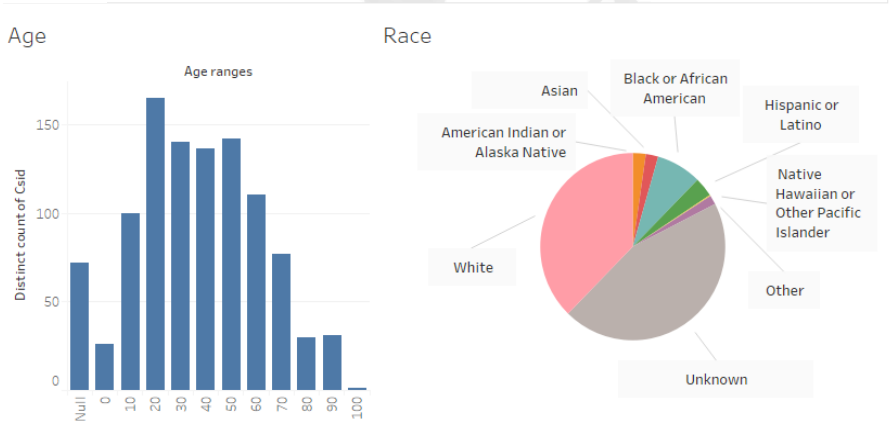
- **National SARS-CoV-2 Surveillance System (NS3)**
  - **Goals**
    - Establish a representative system for baseline virus surveillance
    - Build a collection of representative SARS-CoV-2 specimens and sequences
    - Isolation and characterization of viruses
  - **Strategy**
    - Public Health labs initially providing ~600 specimens to CDC every 2 Weeks
      – Expanded to 1,500 specimens to CDC every 2 weeks
    - Specimens from a variety of geographic locations over time
    - Demographic and clinical metadata contributed
    - Provide viruses, reagents, and constructs for USG, academic, and private developers



National SARS-CoV-2 Surveillance System (NS3)



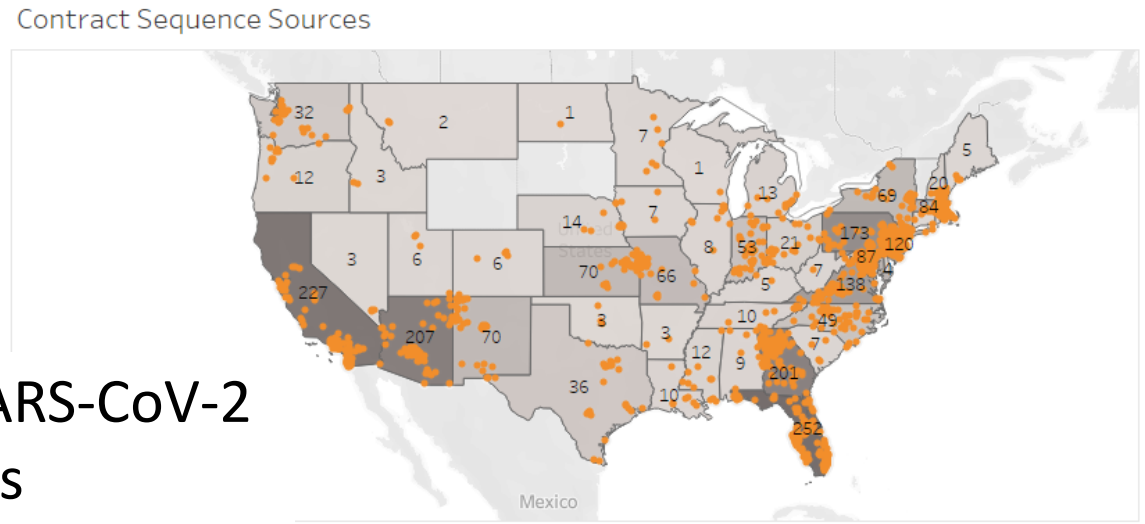
1,144 SARS-CoV-2 genomes



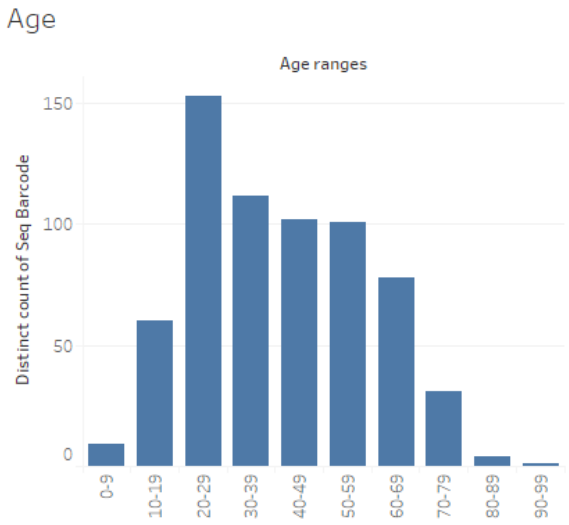
- November 2020 – present
  - Establish a representative system for baseline virus surveillance
  - Most states and territories participating
  - 1,144 specimens sequenced
  - Expanded to 1,500 specimens to CDC every 2 weeks

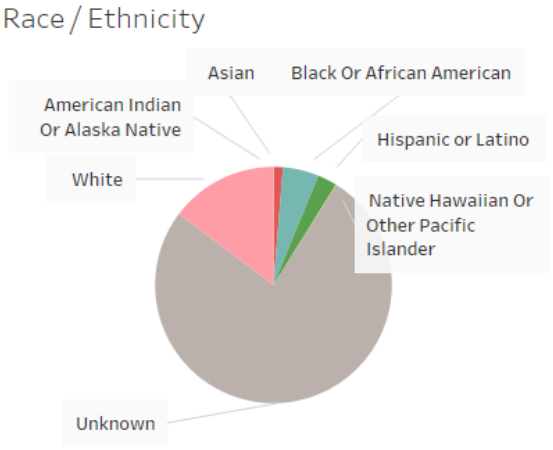
- NS3 Diversity
  - Baseline surveillance
  - Representative specimens
  - Demographics

Enhancing Surveillance for SARS-CoV-2
Expanded Commercial Laboratory Support



3,081 SARS-CoV-2 genomes





New and Expanded Sequencing Contracts through CDC

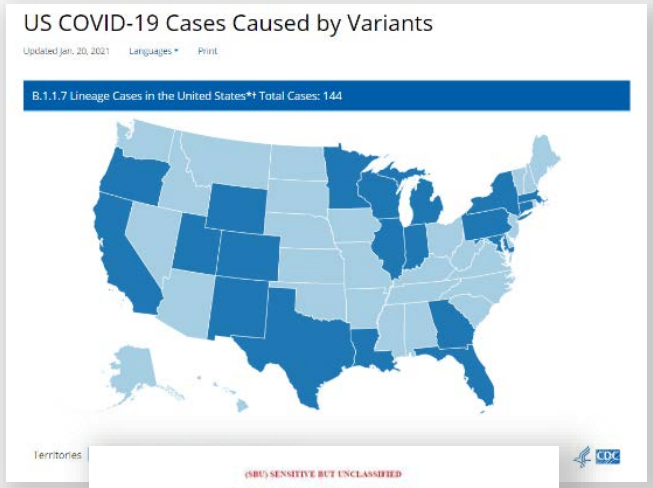
	Current/ week	Planned/ week
Illumina	1,500	3,000
LabCorp	1,000	2,000
Quest	0	1,000
Total	**2,500**	**6,000**

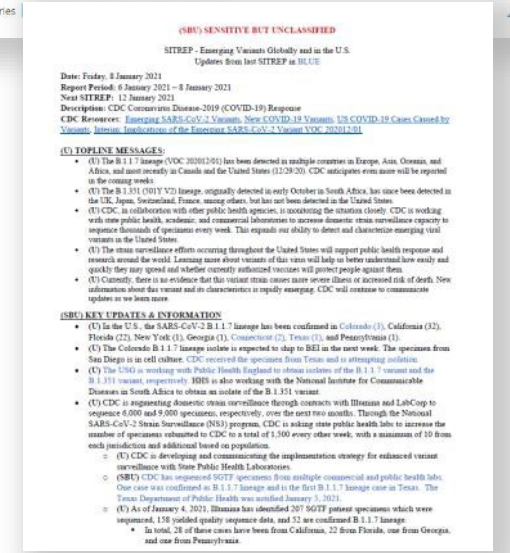
SARS-CoV-2 Emerging Variants

- **B.1.1.7 lineage (20I/501Y.V1, VOC 202012/01)**
  - Emerged in U.K. September 2020
  - In more than 55 countries, including U.S. and Canada
  - N501Y, P681H, ORF8 stop codon (Q27stop)
  - 69/70 deletion (produces S-gene target failure with ThermoFisher TaqPath)
  - Associated with increased transmissibility
- **B.1.351 lineage (20H/501Y.V2)**
  - First detected in South Africa October 2020, now in >15 countries
  - Multiple substitutions in the spike protein: K417T, E484K, N501Y
  - Some evidence indicated E484K may affect neutralization by antibodies
- **P.1 lineage (a.k.a. 20J/501Y.V3)**
  - Branch off the B.1.1.28 lineage
  - First reported by the NIID in Japan in four travelers from Brazil
  - Contains 17 unique amino acid changes and 3 deletions
  - K417T, E484K, N501Y, D614G, H655Y
  - May additionally be circulating in Brazil without K417T and N501Y

Enhancing Surveillance for Variant SARS-CoV-2
NS3 and Expanded Commercial Laboratory Support

- **NS3: Additional specimens sent to CDC to address SARS-CoV-2 variants of interest**
  - Targeted surveillance
  - Specimens shipped to CDC **weekly** from Public Health Labs
  - More narrow selection criteria
  - Dynamic, short-term requests
  - Guidance continually updated
    - B.1.1.7 lineage
    - B.1.351 lineage
    - Future variant viruses
- **Commercial Laboratories: Initial focus prioritize S-gene target failures (SGTF) to improve detection of B.1.1.7 (UK Variant)**

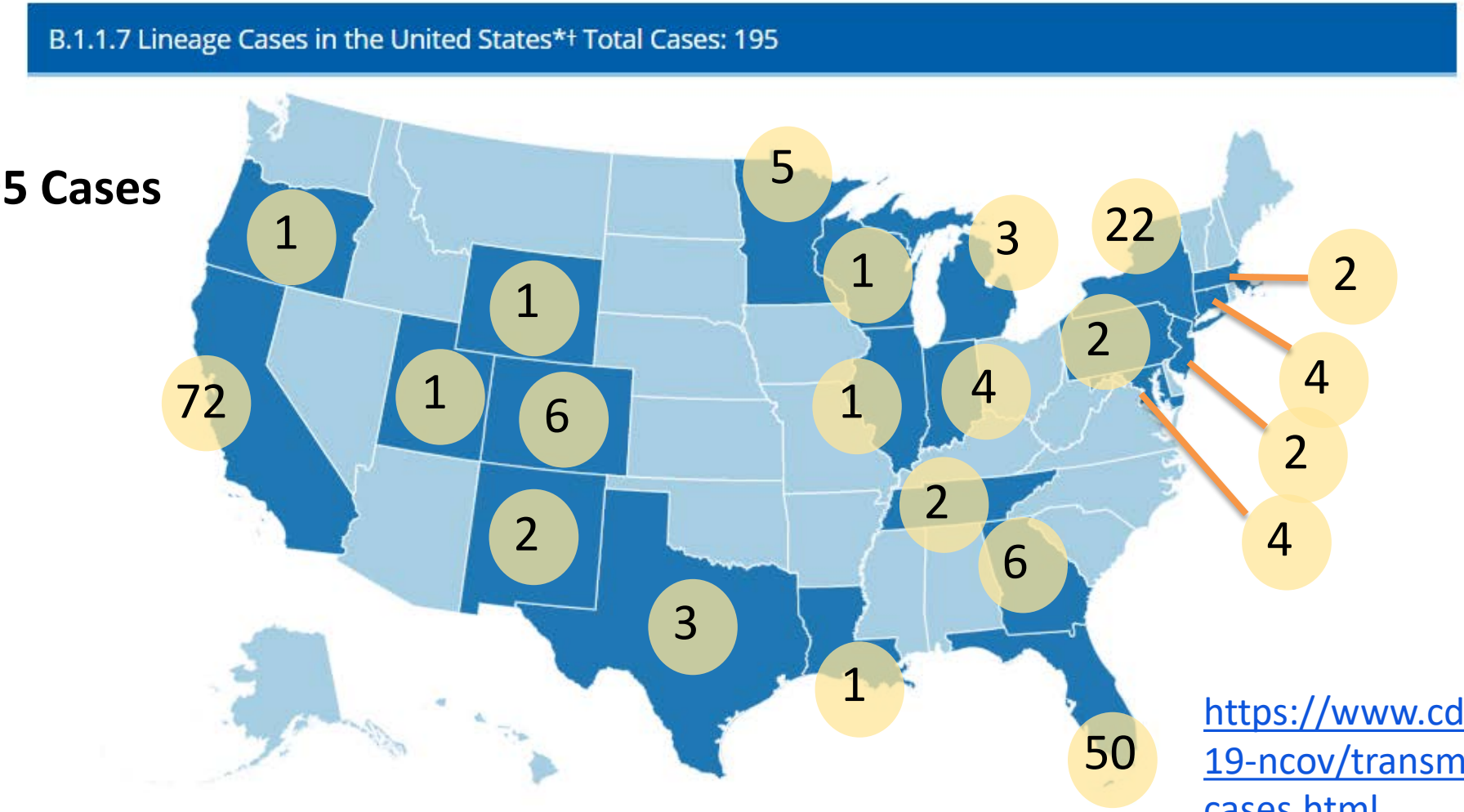




U.S B.1.1.7 Variant SARS-CoV-2 Cases

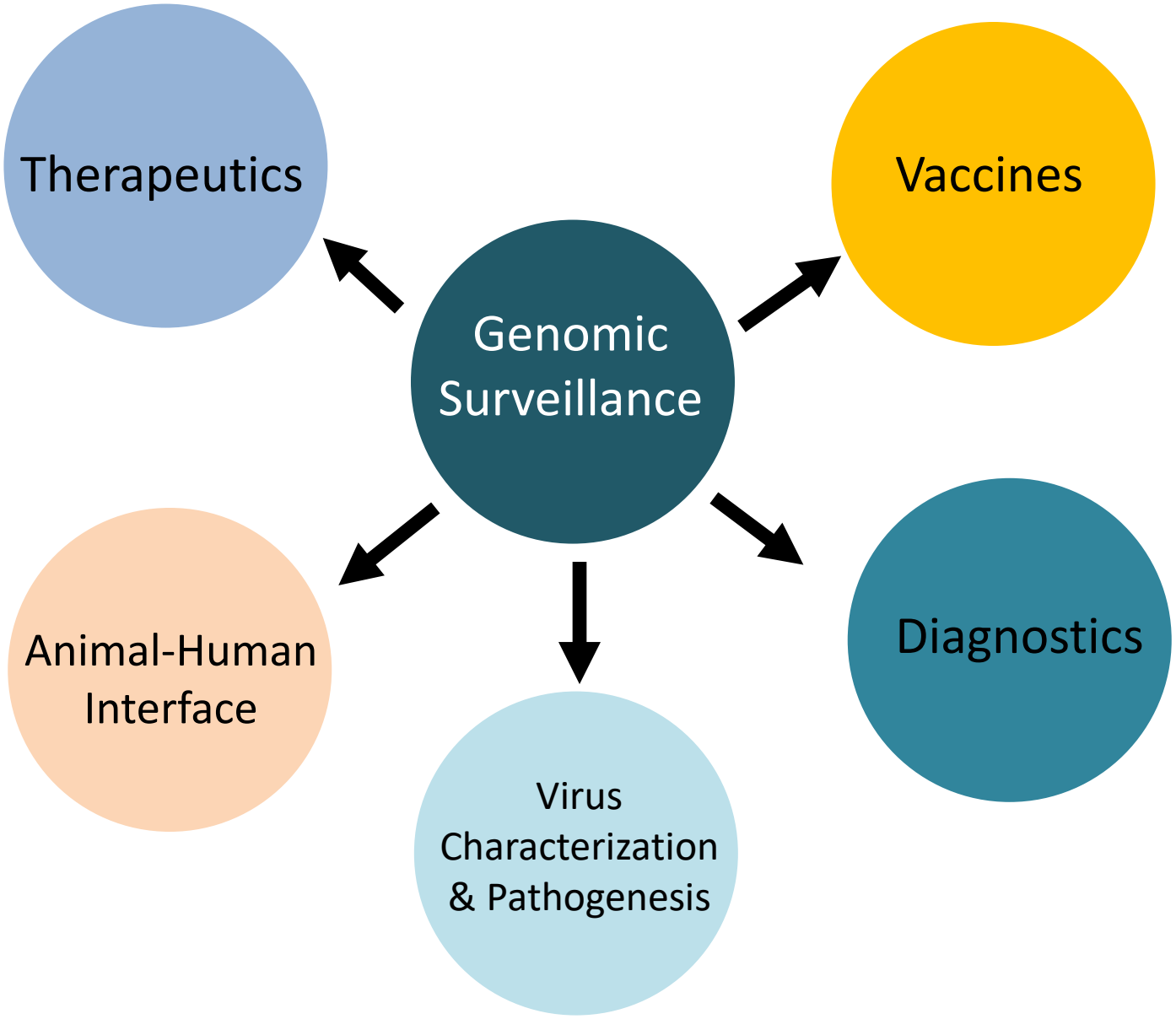
January 24, 2021

195 Cases



https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html

Genomics for Public Health Decisions



CMS Billing Update

Sarah Harding
Centers for Medicare & Medicaid Services (CMS)

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Centers for Medicare and Medicaid Services (CMS)

- **CLIA Laboratory Guidance During COVID-19 Memo and FAQs**

  https://www.cms.gov/medicareprovider-enrollment-and-certificationsurveycertificationgeninfopolicy-and-memos-states-and/clinical-laboratory-improvement-amendments-clia-laboratory-guidance-during-covid-19-public-health

- **FAQs Only**

  https://www.cms.gov/medicare/quality-safety-oversight-general-information/coronavirus

FDA Update

Tim Stenzel
U.S. Food and Drug Administration (FDA)

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

U.S. Food and Drug Administration (FDA)

- **COVID-19 Emergency Use Authorization (EUA) Information for Medical Devices**
  https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations
- **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/coronavirus-disease-2019-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/

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Food and Drug Administration (FDA)

- **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

U.S. FOOD & DRUG ADMINISTRATION

CDC Social Media

https://www.facebook.com/CDC

https://twitter.com/cdcgov

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

Thank You For Your Time!

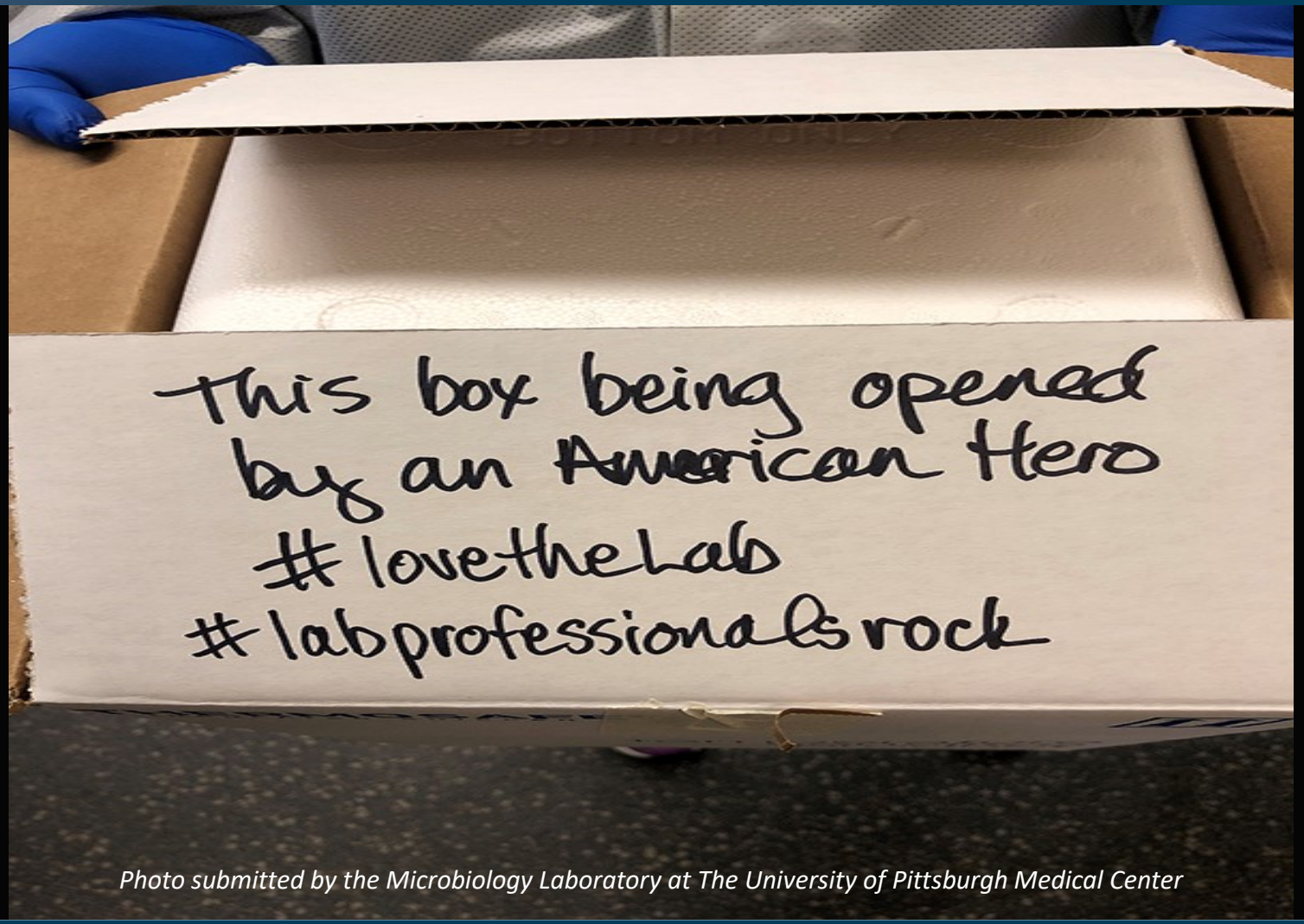


Photo submitted by the Microbiology Laboratory at The University of Pittsburgh Medical Center