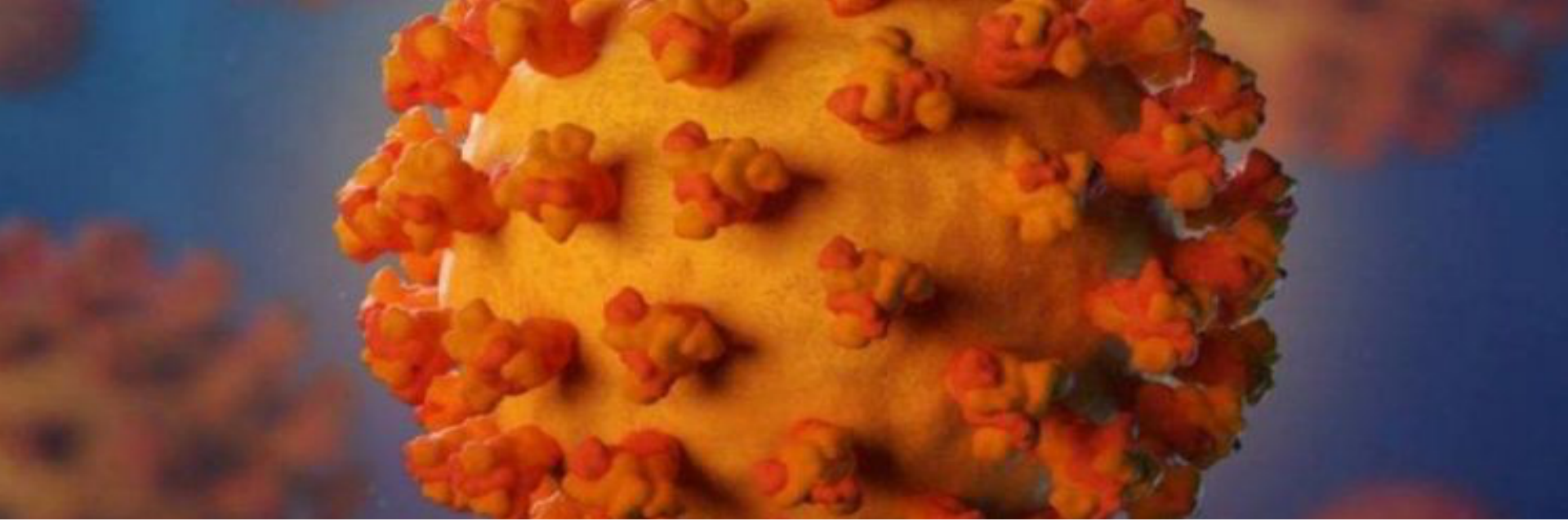
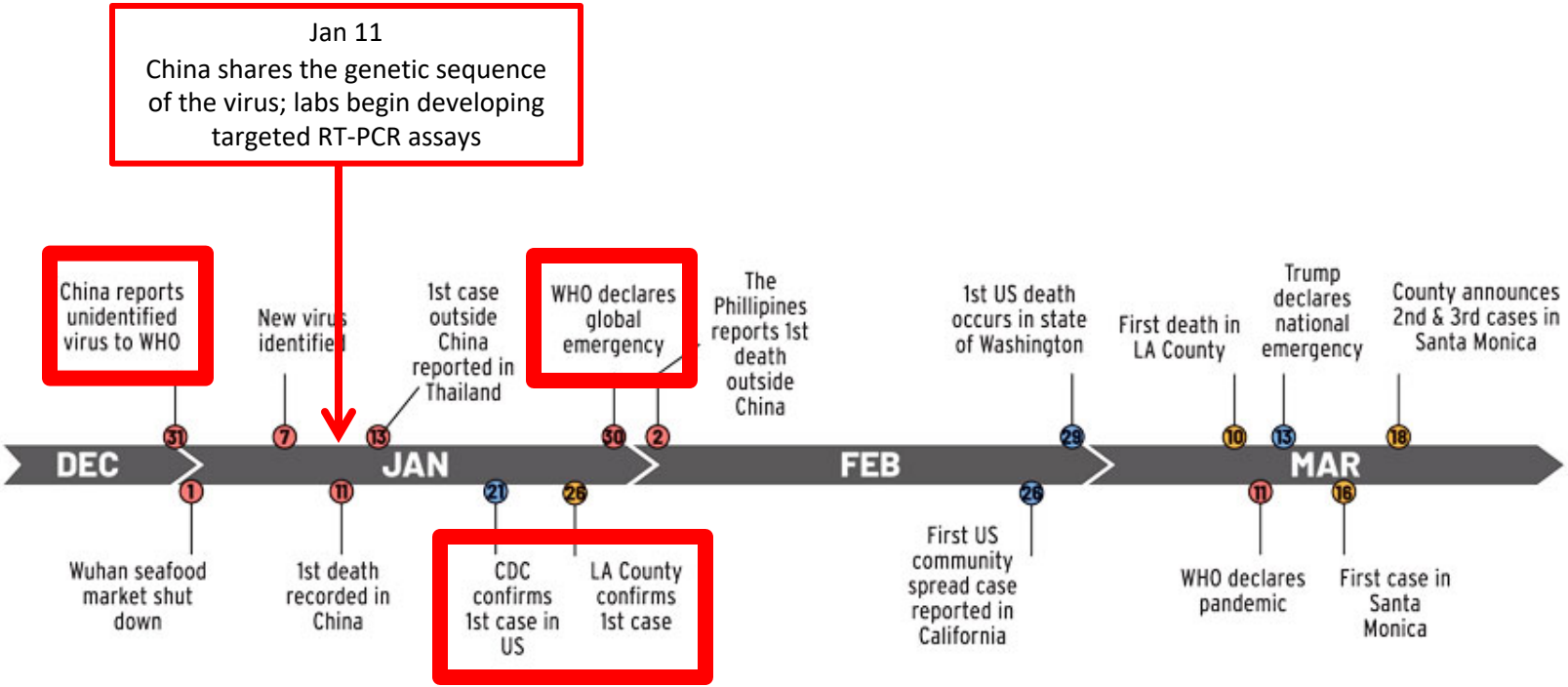


Notes from the field on establishing and operating a high-demand clinical laboratory for SARS-CoV-2 testing; Initial observations on CAP PT

Bobbi S. Pritt, MD, MSc

Chair of Clinical Microbiology, Mayo Clinic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First death in LA County
Trump declares national emergency
County announces 2nd & 3rd cases in Santa Monica
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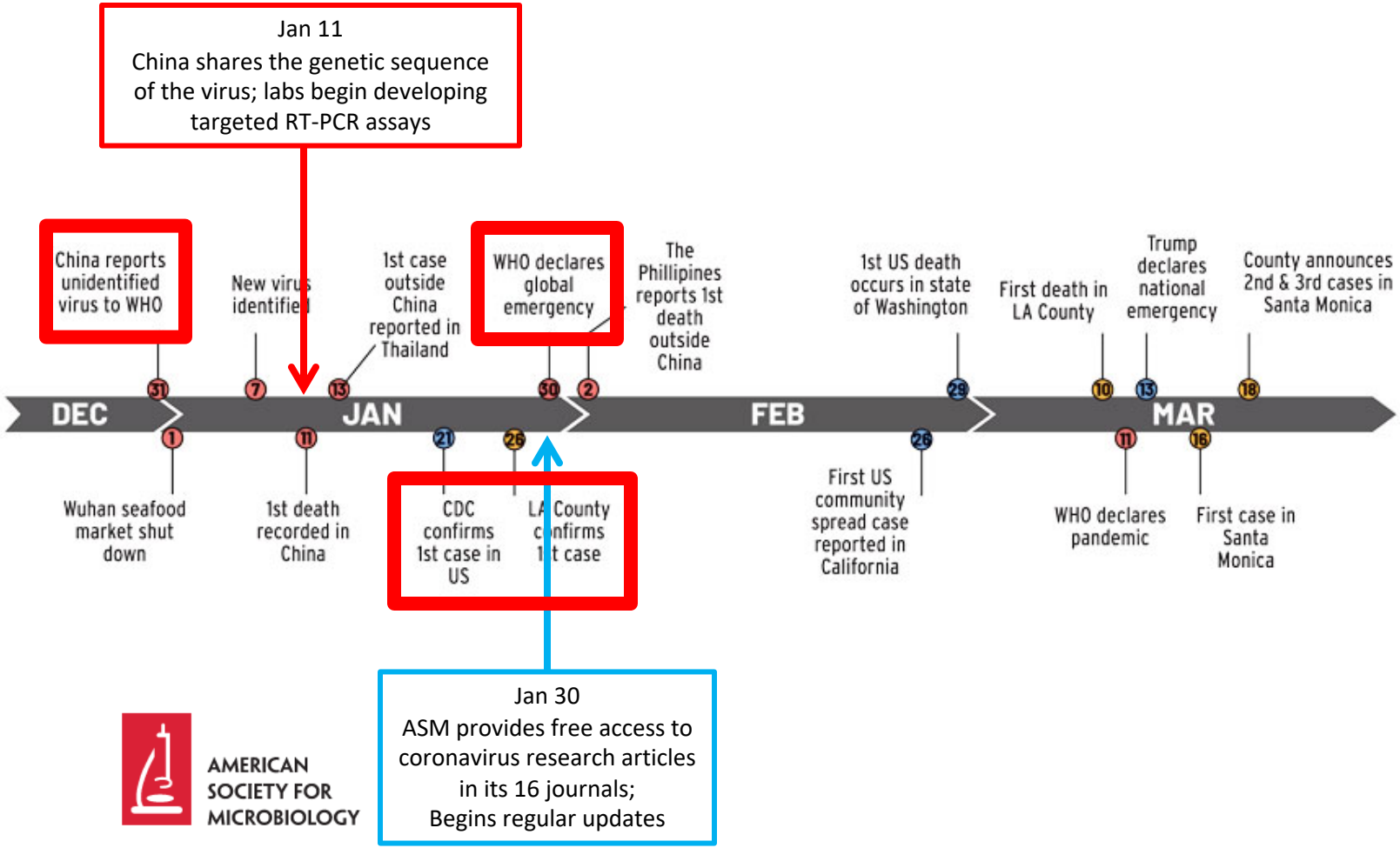
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AMERICAN SOCIETY FOR MICROBIOLOGY
Jan 30
ASM provides free access to coronavirus research articles in its 16 journals;
Begins regular updates

AMERICAN SOCIETY FOR MICROBIOLOGY

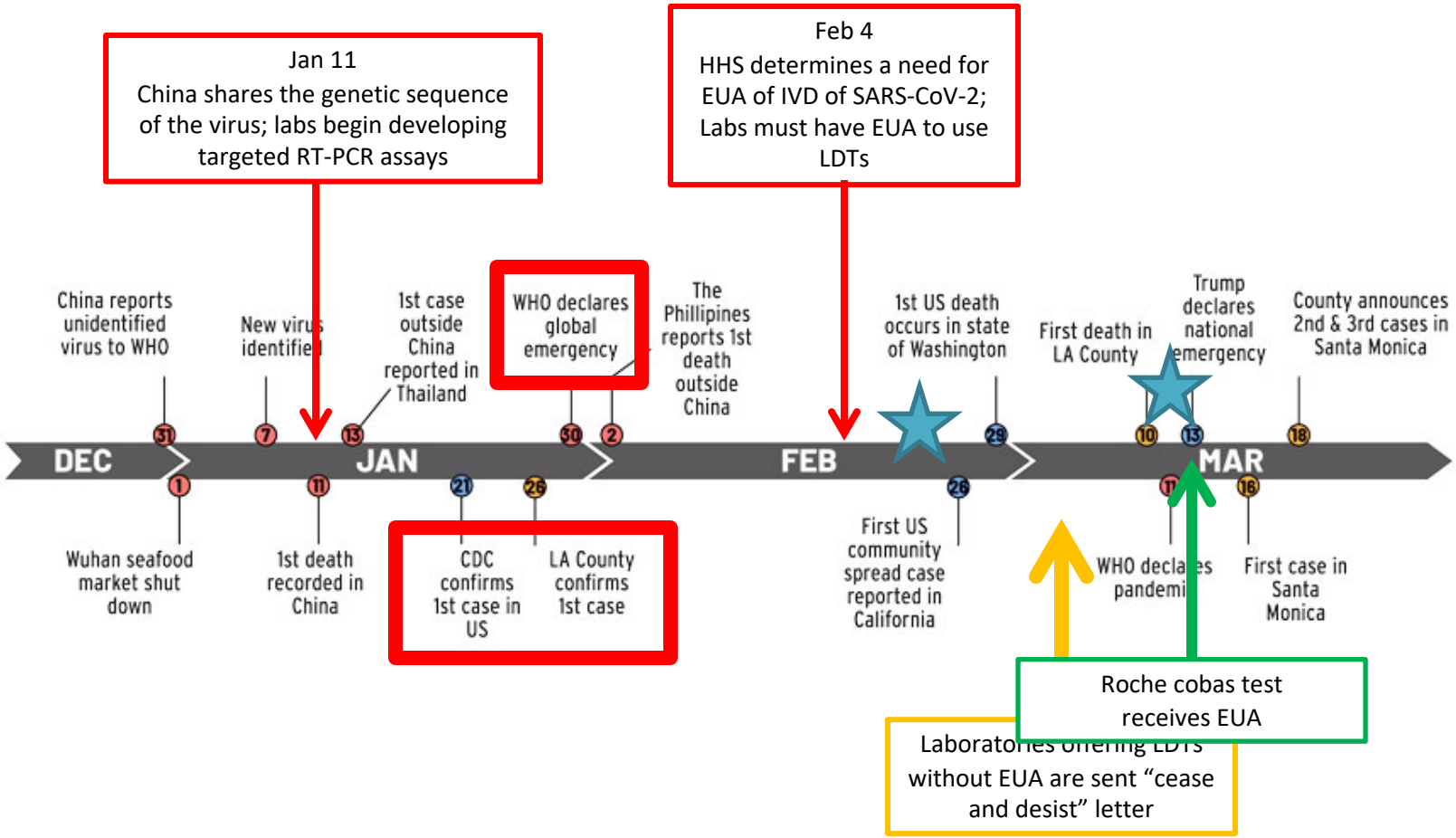
- March 4: ASM Applauds Action on Coronavirus Emergency Supplemental Appropriation
- March 3: ASM Urges Senate Support for Coordinated Efforts to Combat COVID-19
- Feb. 28: Amid COVID-19, ASM Voices Concerns about Clinical Access to Tests
- Feb. 28: What to Know About the New Coronavirus: An Interview with Dr. Stanley Perlman

clinmicronet *(919)*

The ClinMicroNet is composed of an international group of clinical microbiology laboratory directors who openly and daily communicate with one another through this medium. The criteria for membership in ClinMicroNet are a Contributing Member of ASM and are Doctoral-level clinical microbiology laboratory director or Laboratory manager with national standing and peer recognition. To request a subscription please contact Mike Miller at jmm8@comcast.net.

Coronavirus (COVID-19) Outbreak

- Jan. 30: Anthony Fauci Addresses Coronavirus at ASM Biothreats Conference
- Jan. 30: Novel Coronavirus (COVID-19) Receptors Show Similarities to SARS-CoV, According to New Analysis
- Jan. 30: ASM Provides Free Access to Coronavirus Research Articles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Roche cobas test receives EUA
Laboratories offering LDTs without EUA are sent "cease and desist" letter

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- Feb. 26: ASM Issues Response to House Hearing on FY2021 HHS Budget and Coronavirus
- Feb. 5: ASM Responds to House Hearing on Wuhan Coronavirus
- Feb. 3: Novel Coronavirus Lab Protocols and Responses: Next Steps
- Jan. 31: 2019 Novel Coronavirus (2019-nCoV) Update: Uncoating the Virus
- Jan. 31: Sharing Research Data and Findings Relevant to the Novel Coronavirus (COVID-19) Outbreak
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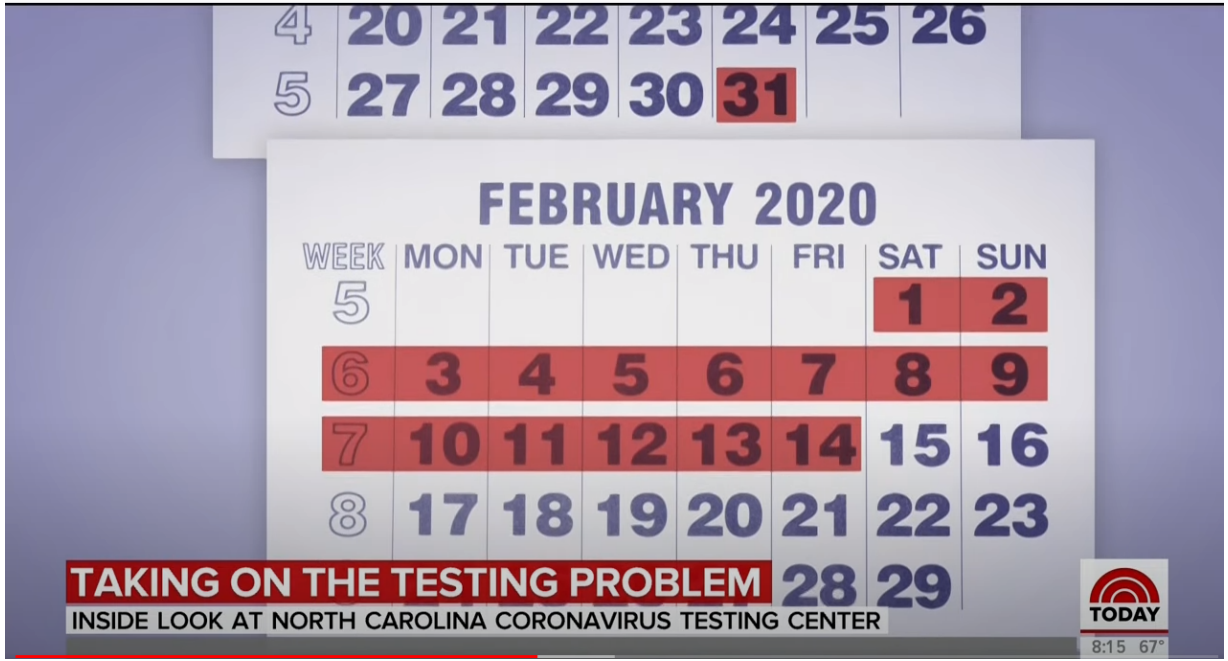
We respectfully ask that you consider adjustments to the regulations to allow clinical laboratories to have access to the test assay from CDC **in addition to** the public health laboratories. Clinical laboratories follow a rigorous process for validation and implementation of laboratory-developed tests. If this pathway was considered during an outbreak, it would allow for a more rapid response to implementation of diagnostic testing. Many clinical laboratories have already validated high-complexity LDTs for SARS-CoV-2 and could begin testing tomorrow, but cannot do so due to the FDA EUA process. Testing is overseen by board-certified doctoral-level directors of clinical laboratories that are routinely inspected and certified to perform CLIA high-complexity testing. While we appreciate that the intent of the EUA is to safeguard the public and ensure tests are safe and effective early in outbreaks, the EUA process is proving a hindrance to rapid identification of potential COVID-19 infections. If we have tests that are safe and effective that cannot be used, this can put people at risk.

UNC Health's Melissa Miller & CEO Wesley Burks discuss COVID-19 testing on NBC TODAY Show



Melissa Miller, PhD
UNC; Laboratory Director

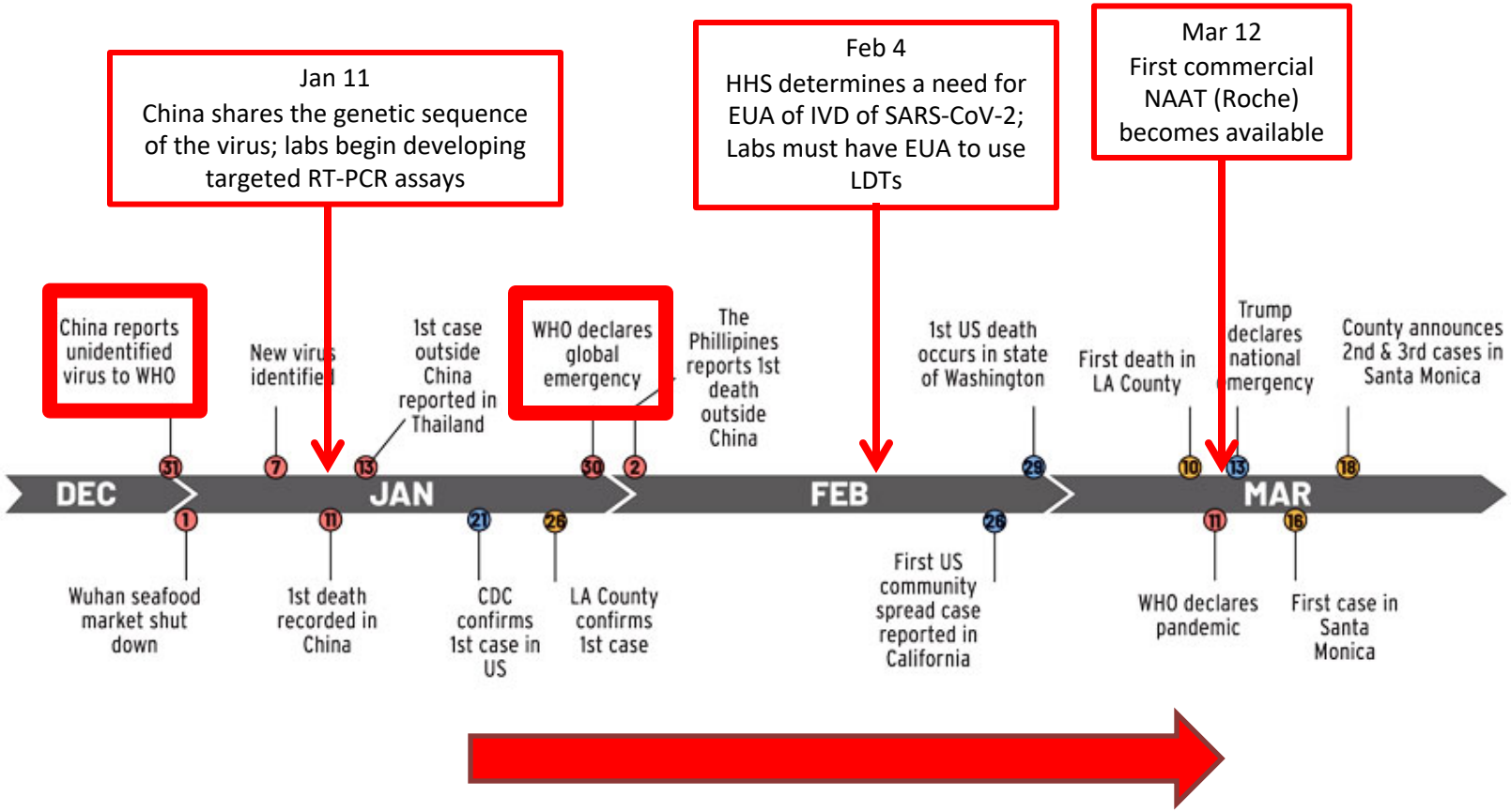
AMERICAN SOCIETY FOR MICROBIOLOGY

Expediting COVID-19 Testing and Expanding Access to Clinical Labs

March 9, 2020 SHARE THIS

By Robin Patel and Stefano Bertuzzi

The FDA responded to our letter the next day and took steps to expand testing for the new coronavirus and to allow clinical microbiology laboratories to use their own tests prior to FDA clearance. We were also happy that the FDA specifically asked to speak with ASM leaders on Monday morning prior to a public webinar on the changes. The call was an opportunity to engage with FDA leadership and share additional questions and concerns gathered from ASM clinical members. This was an important win for ASM and for the rest of the clinical microbiology community who called for expanded testing access.



CDC assay
LDTs

Other challenges early on

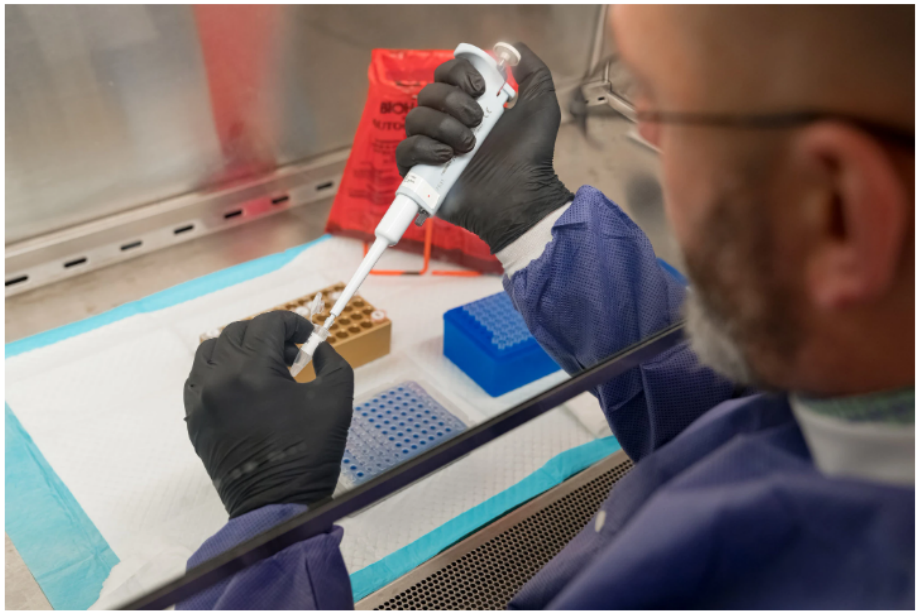
- Limited access to virus samples
  - Only through CDC and public health labs
- CDC is not designed to be a manufacturer
  - Initial kits were only sent to public health labs with limited capacity
  - Testing was restricted (strict criteria)

The New York Times

March 2, 2020

As Coronavirus Numbers Rise, C.D.C. Testing Comes Under Fire

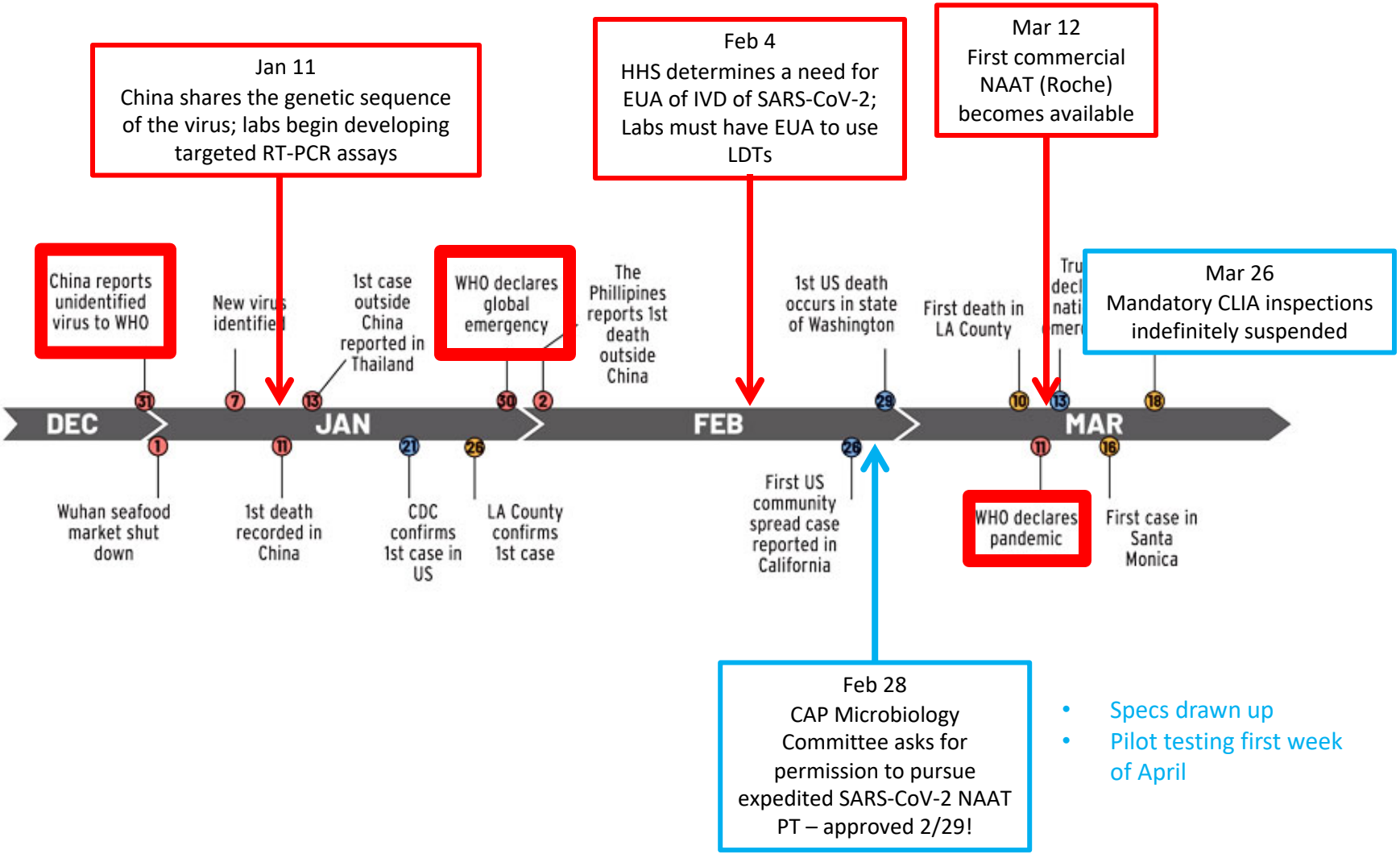
Federal health officials botched an initial diagnostic test and restricted widespread screening. Missteps may have raised the risks to Americans, critics say.



A researcher at the Virology Laboratory at the New York State Department of Health prepared samples of coronavirus for testing. The state is using its own F.D.A.-approved test for diagnosing coronavirus.
New York State Department of Health

Other challenges

- A need for PT material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China shares the genetic sequence of the virus; labs begin developing targeted RT-PCR assays
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Mar 12
First commercial NAAT (Roche) becomes available
Mar 26
Mandatory CLIA inspections indefinitely suspended
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CAP Microbiology Committee asks for permission to pursue expedited SARS-CoV-2 NAAT
PT – approved 2/29!
Specs drawn up
Pilot testing first week of April

CAP proficiency testing - NAATs

- Initially: recombinant product containing the N, E, RdRp, and ORF1a targets; housed within a non-infectious, non-replicating mammalian virus
- First mailing in May
- Now contains the entire viral genome
- Targeted amounts: 5,000 c/mL and 10,000 c/mL

Continued challenges

- Limited testing reagents
- Many labs have verified 4+ NAATs for SARS-CoV-2 and still can’t meet clinical demand
- At Mayo Clinic: 8 NAATS including the LDT; running at ~50% capacity
- Currently performing 10,000 tests/day; goal is 30,000 tests/day by the end of August
- Questions regarding: alternate sources (e.g., saliva), testing of pooled specimens, at-home collection options, rapid POC testing, use of Ct values to predict infectivity, prognosis, monitor response to treatment, etc.

History of deadly plagues, epidemics and global pandemics

Major outbreaks

● 1 million or more deaths*
● Less than 1 million

Before 1300

Plague of Athens
430 BC
Estimated deaths:
100,000

Antonine plague
165 - 180
3.5 - 7 million

Japanese smallpox
735 - 737
1 million

Plague of Justinian
541 - 542
25 - 100 million

After 1300

Black death
(Bubonic plague)
1347 - 51
25 - 50 million

Great plague
of London
1665 - 66
100,000

Spanish flu
1918 - 19
50 million

HIV
1981-
32 million+

COVID-19
2020-
75,000+
as of Apr 7

Measles

Zika

Avian flu

Smallpox
(in Mexico)
1520
8 million

Cocoliztli
(possibly typhoid, Mexico)
1545 - 48
15 million

Cocoliztli
1578
2 million

Great
plague of
Marseille
1720 - 23
40,000

Russian plague
1770 - 72
100,000

Russian flu
1889-90
1 million

Asian flu
1957-58
1.1 million

Hong Kong flu
1968 - 70
1 million

Swine flu
2009 - 10
151,700-575,00

SARS
2002 - 03
770

**Toll estimates vary according to different sources*

Source: livescience.com/cdc.gov/ljidonline.com/britannica.com/ph.ucla.edu/history.com/ncbi.nlm.nih

Summary of primary challenges

- Current U.S. system does not allow for rapid initiation of testing at clinical laboratories
  - The CDC gets first access to positive material
  - CDC test has limited distribution
  - EUA process – especially initially – hampered LDT use
  - EUA process FAVORS manufacturers, and allows for rapid deployment of commercial tests (BUT limited availability)

A word about serology

- FDA initially did not require EUA for serologic tests
- This led to a large quantity of poor-quality tests flooding the market
- FDA now requires EUA for serologic assays

Successes

- International collaborations quickly formed
- United States professional organization (ASM, CAP) advocated on behalf of the laboratories
- Proficiency products were quickly developed.