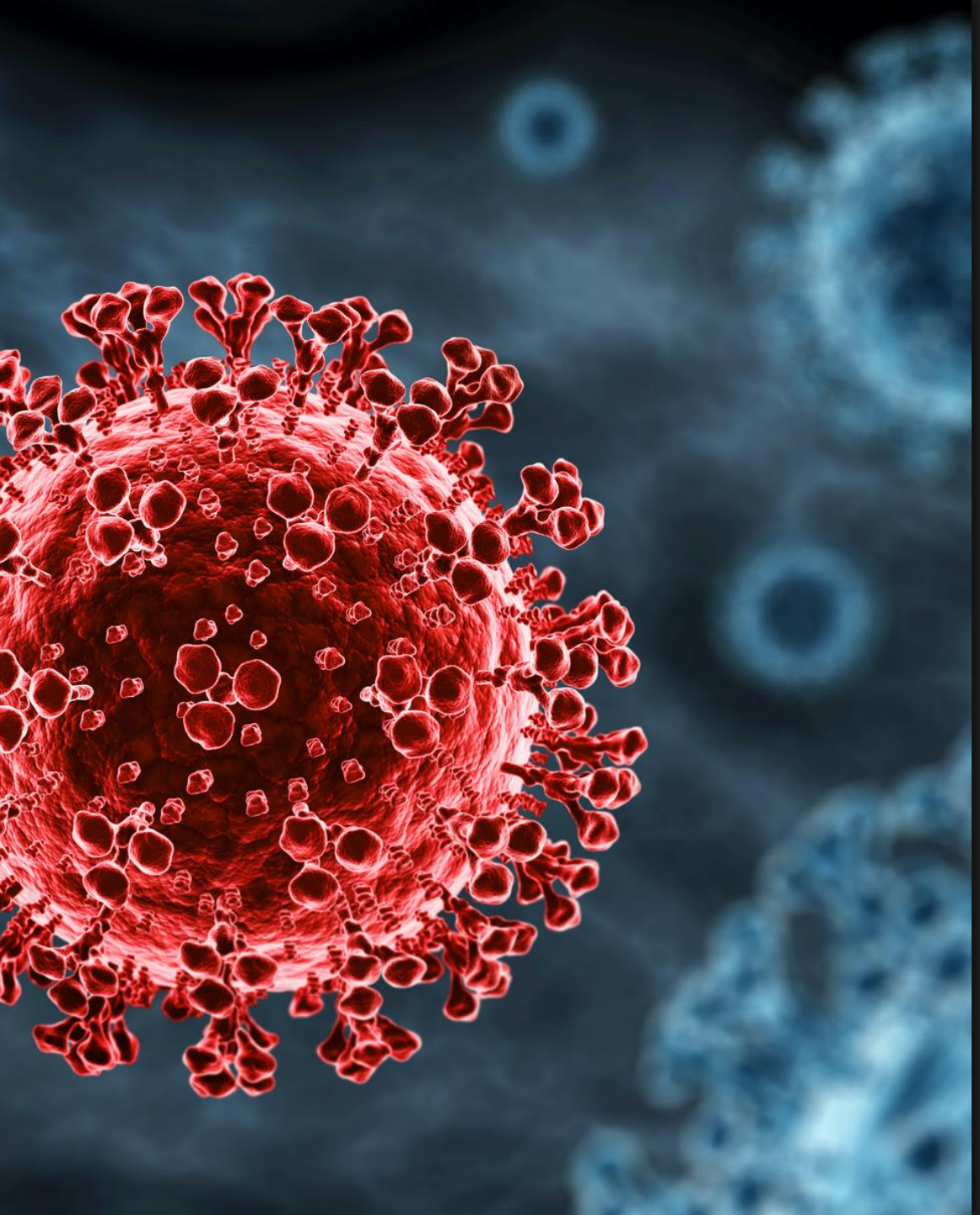


The 3 Rs to Authorization for the COVID-19 At-Home Test: Roche, RADx, Rapid

What we learned from the success and how can we build for the future.

Kelli Turner, Regulatory Program Manager, Roche Diagnostics
Gail Radcliffe, Ph.D., President, Radcliffe Consulting, Inc.

April 28, 2022
Public Use

Reacting to the COVID Pandemic

Need OTC SARs-CoV-2 tests on the market immediately

Typical IVD Development

- User Needs
- Analytical study designs
- Clinical Study design
- Pre-submission
- Conduct analytical studies
- Conduct clinical study
  - Set up 3 sites
  - Statistical analysis
  - Draft clinical study report
- Draft Submission

- **Total Time = 1.5-2 years?**

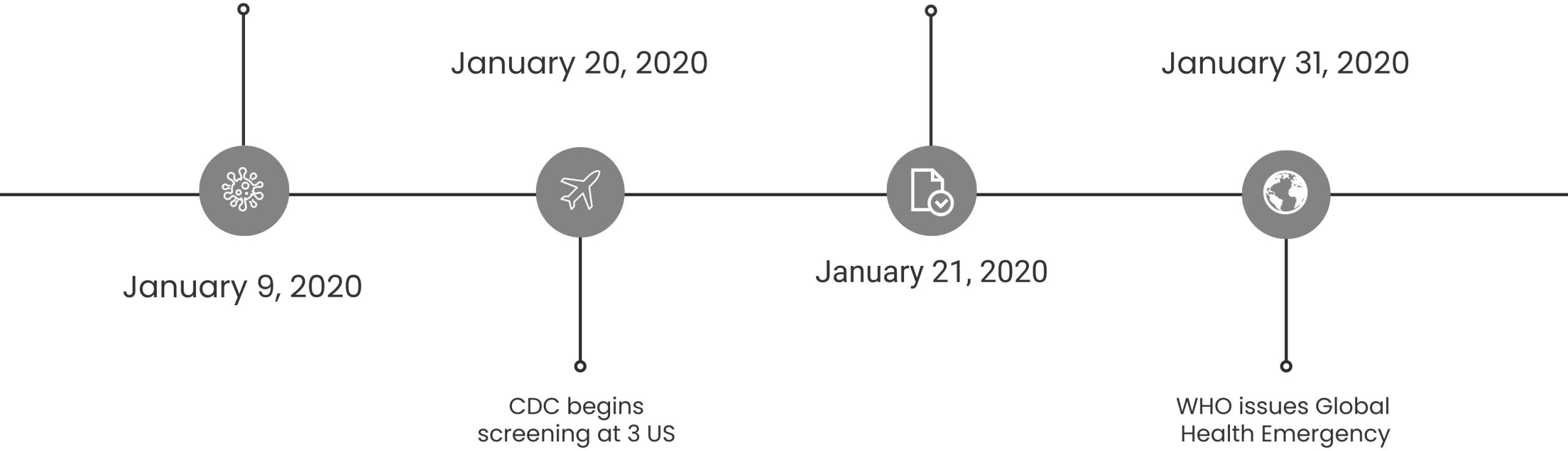
RADx ITAP Program

- Complete application
  - Product must have data to show capable of rapid development
  - Submission passes RADx intro vetting process
- Analytical studies performed by external test lab using universal protocols
- CRO assigned for clinical
  - Universal protocol sent to IRB, site initiated
  - Statistics and clinical study report provided by CRO
  - Modular submission to FDA throughout process

- **Total Time = 2 months!!**

A Look Back

Uncharted and unknown



A Look Back

Uncharted and unknown

US declares Public Health Emergency

February 3, 2020

February 10, 2020

China's COVID-19 death toll exceed those of SARS Crisis

CDC Says COVID-19 is Heading toward Pandemic Status

February 25, 2020

March 11, 2020

WHO declares COVID-19 a Pandemic

US Government's Response for SARS-CoV-2 Testing

Rapidly Responding

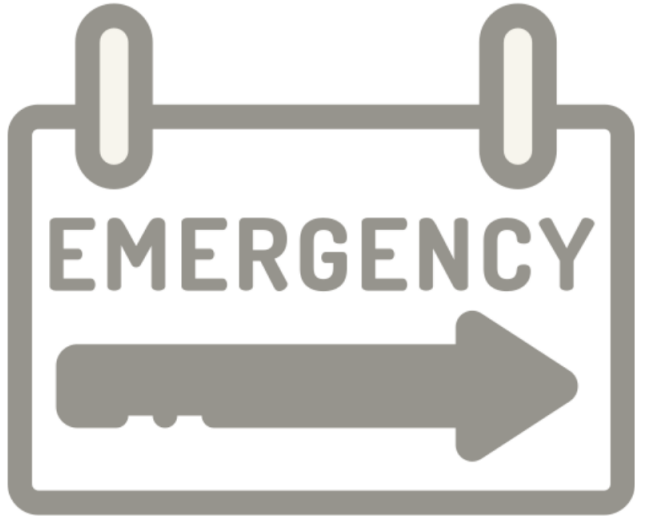
- Federal agency collaborations (BARDA, CDC, DOD, FDA, NIH)

- Urgent need for framework around diagnostic testing
  - Within 2 months of the declaration of a global pandemic, FDA delivered templates to guide developers and manufacturers:
    - Need for rapid development
    - Minimal validation to demonstrate product was safe enough to help fill the need for diagnostics

- CDC developed a PCR based assay for SARs-CoV-2

- NIH launched RADx Tech for Rapid acceleration of diagnostics

- FDA authorizes:
  - Feb 4, 2020- FDA authorized CDC test
  - March 12, 2020 - 1st EUA for lab based molecular test (Roche rtPCR)
  - March 27, 2020 – 1st isothermal test- Abbott ID Now
  - May 11, 2020 – 1st Antigen test (Quidel)
  - December 15, 2020 – 1st OTC antigen test (Ellume)



Surge in COVID cases: No Tests on the Shelves

Fall 2021

White House, NIH, FDA, RADx: Initiate Independent Test Assessment Program (ITAP) Program October 25, 2021

- $70 million
- Identify companies with rapid lateral flow antigen tests on market outside US
- Minimum Manufacturing requirements must be fulfilled
- Goal to get tests on market by the end of the year

ITAP Program

- Developed universal protocols for analytical and clinical testing
- Provided external testing for analytical & clinical studies
- Subject area experts in regulatory, quality, clinical, manufacturing, commercialization

Project Teams

- Agreed to work with ITAP team- provide quick turnaround
- Manufacturing emphasis
- Labeling reviewed iteratively

A device ready for US clinical trials…

RADx, Roche and SD Biosensor

Looking for the fastest path

- Roche regular engagements with the USG- informed of a NIH new program focused on expediting availability of Rapid Antigen OTC tests to the U.S. market
- Knowing our development efforts were already underway, Roche engaged NIH to learn more about the program and potential collaboration
- We gained alignment with the Roche senior leadership (locally and globally) and prioritized the collaboration
- We officially signed up with NIH to participate in the ITAP program according to the below timeline:
  - Introductory call with NIH on October 13, 2021
  - Official kick off call with RADx: October 21, 2021
  - Official acceptance: October 28, 2021 Roche/SD Biosensor received

Working Independently and Together

Finding rapid solutions to complex processes

- November 2021 RADx and Roche worked to finalize
  - Aligned and agreed upon protocols

- RADx and FDA
  - Aligned on protocols
  - Created a modular EUA review for ITAP
    - Enabled iterative review by module
      - Background, test contents, manufacturing, preliminary labeling
      - LoD study
      - Analytical and Flex Studies
      - Clinical and labeling
    - FDA returned feedback within ~ 2 days for each module

Benefits of ITAP

Independent and familiar smooths the process

Universal Analytical Protocols

The FDA knew what to expect from universal analytical protocols

- Review was quick because protocols were vetted
- Independently performed, so FDA did not have questions about implementation

Universal Clinical Protocol

- FDA reviewed the protocol before initiation
- ITAP met with FDA weekly to discuss any issues that arose
- ITAP had access to FDA almost 24/7

Waived Requirements

FDA waived requirement for usability study

Additional Assistance

Assistance with shipping, customs (call from FDA to release product)

Special Analysis Made Possible

Equal evaluation applied

Samples

RADx obtained large volumes of excess samples from clinical labs performing CDC surveillance testing

Emory Analytical Core

- ~250K clinical samples with unique S and N genes mutations
  - Including Omicron with various mutations
- Variant wet testing
  - Known variants were pooled and all LFAs were wet tested
  - Data from wet testing was included in labeling
- Epitope Mapping

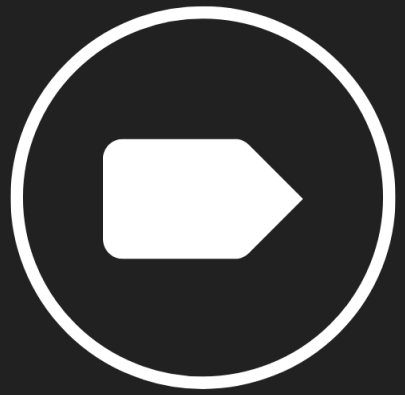
Bioinformatics Platform

Bioinformatics platform with ~9.0M GISAID sequences

- Real-time view of mutation prevalence trends
- Robust *in silico* analysis

Speed Bumps
Proceed with care

Review of Study Reports



Labeling

Clinical Data Review

Review of Study Reports

- Review of study reports required extra caution as test reports designed for universal protocols
- Some items were specific to the SD Biosensor/Roche kit

Labeling

- FDA changed intended use
  - serial testing and pediatric text needed extra review
- Number of tests in a box
- FDA added warnings and precautions

Clinical Data Review

- FDA asked for letter from clinical site while PI at Christmas party!

The Rapid Process Leads to a Christmas Miracle

Rapid work leads to authorization

ITAP- Independent Test Assessment Program

- Analytical studies performed at external site
- Clinical study CRO assigned to study
  - Clinical study performed in 3 weeks (5 sites, 128 subjects, 43 positives)

Important Dates

- December 9, 2021- Modular submission initiated with sections: 1-4 submitted to FDA
  - New modular template required a little finesse
- December 14, 2021- sections 6 (LoD) and 10 (IFU and labeling)
  - Let the labeling revisions begin
- December 17, 2021- section 8 (flex studies)
- December 20, 2021- section 5 (Product manufacturing)
- December 21, 2021- section 7 (analytical studies)
- December 23, 2021- section 9 (clinical studies)
- December 24, 2021- authorization granted at 7:03 pm CET (1:03 pm EST)

Merry Christmas !!!

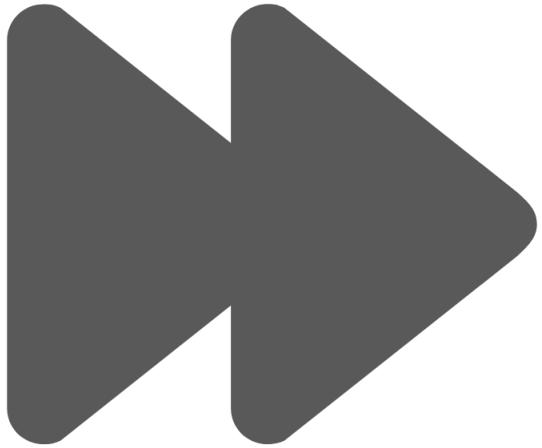
Authorization achieved

The Future and Beyond

Building on success

Can we carry lessons learned forward?

- ITAP useful in responding to a pandemic quickly
- Evaluation of new high medical value products by a team of subject experts is useful
- Vetted protocols allow FDA to concentrate on data, not on process
- Clinical and analytical testing agencies selected by government eliminate bias



Doing Now What Patients Need Next

QUESTIONS

Doing now what patients need next