U.S. FOOD & DRUG ADMINISTRATION

Use of EUA Authorities for Medical Devices

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EUAs for Medical Devices

- COVID-19 is the 7th consecutive public health emergency or material threat where use of EUAs for medical devices was authorized through declaration by HHS Secretary
- Tests granted EUAs in each of the 7 PHEs and EUA applies to all tests because false results can adversely impact the nation's response – the same "playbook" for PHEs was implemented at the start of COVID-19
- We continually adapted our policies, as appropriate, based on changing circumstances of the pandemic and evolving science
- During pandemic, EUAs granted for tests, personal protective equipment, ventilators and respiratory assist devices, circulatory support devices, products for dialysis, remote or wearable monitoring devices, and more

Workload in CDRH During COVID-19

Number of EUA Submissions

3,621	2,557	936
Original EUAs received	Pre-EUAs received	EUA supplements received

38% Overall increase in premarket submissions in 2020

EUA Devices Authorized

IVD				Non-IVD		
292	35	88	3	221	119	52
Molecular	Antigen	Antibody	Other	PPE	Ventilator	Other

1749 COVID-19 medical devices so far (excluding supplements)

Devices for COVID-19 with 510(k) Clearance

53	385	84	417
Tests / Supplies	PPE	Ventilators	Other

Represents 20% of CDRH FDA is not resourced in advance to handle additional workload

Workload for All COVID Activities

The equivalent of >360 people working full-time for a year

Data as of September 24, 2021

Communication and Engagement

330+ — **Frequently Asked Questions**

- Shortages of Medical Gloves
- Home-use Blood Glucose Meters Utilized Within Hospitals
- 3D Printing
- Diagnostic Testing
- Face Masks
- Ventilators
- EUAs for Devices
- PPE
- Non-NIOSH Approved Respirators

29 — **Letters to Healthcare Providers and Safety Communications**

- Diagnostic Tests
- Antibody Tests
- PPE
- Protective Barrier Enclosures
- Ventilators

13 — **EUA Templates**

- Diagnostic Tests
- Antibody Tests
- Ventilators
- Surgical Masks

90+ — **Webinars and Virtual Town Halls**

- PPE
- 3D printed swabs
- Test development and validation
- Interruption in Manufacturing during PHE

400,000+ — **Inquires Addressed**

Through 17 mailboxes and 2 phone lines

28 — **Guidance Documents**

- Clinical trials
- PMA and HDE supplements
- PPE
- Tests
- Ventilators
- ECMO
- Imaging
- Coagulation system
- Infusion pumps
- Sterilizers
- + 17 revisions
- Formal meetings and user fees
- Mammography Quality Standards Act
- Shortages

2,557 — **PEUAs Received**

Includes frequent interactions with FDA staff and rolling review of information received

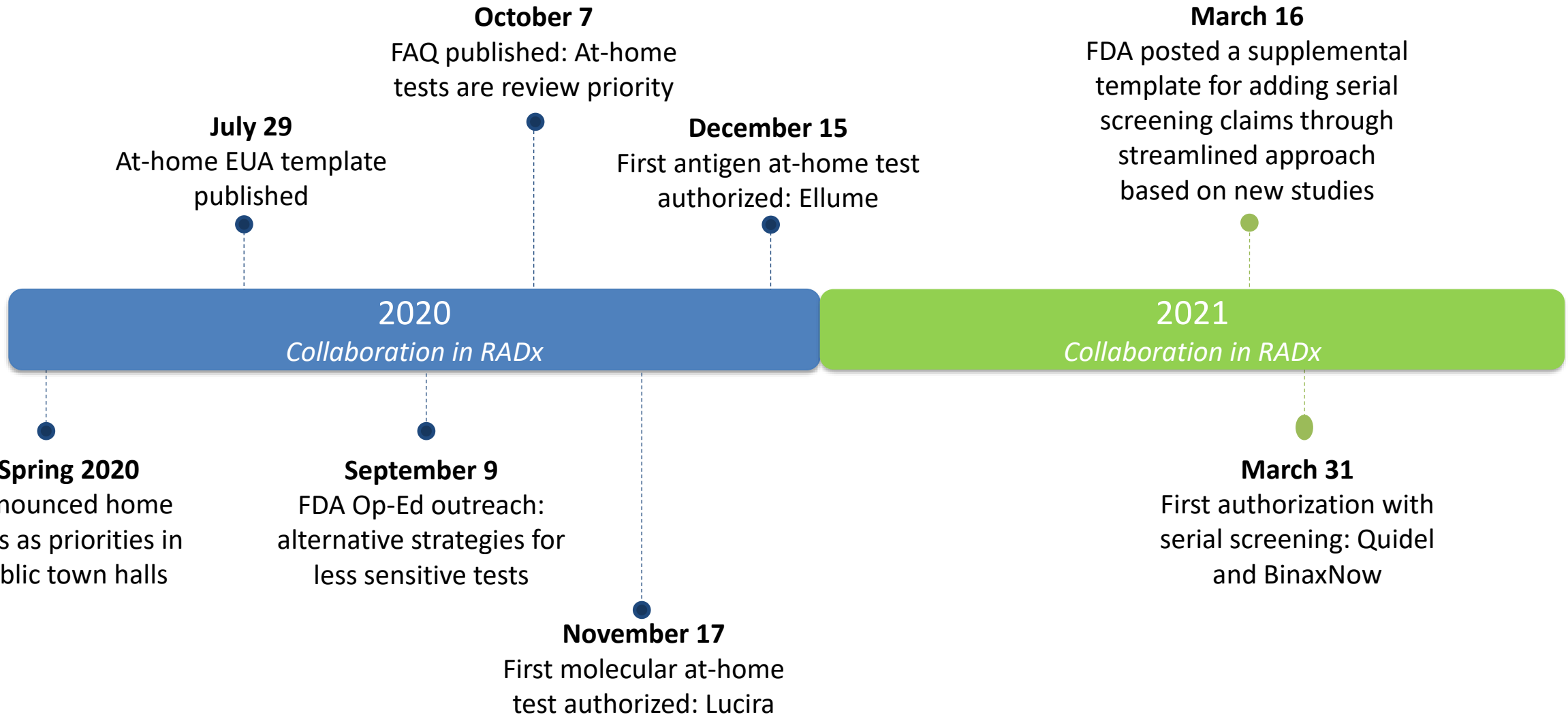
Participation in RADx

Information Sharing Among Global Regulators

EUA vs. Full Market Authorization for Tests

Analytical Sensitivity	• Use synthetic contrived specimens when viral isolate or natural specimens unavailable to determine assay Limit of Detection (LoD)
Clinical Evaluation	• Evaluate 30 positive and 30 negative contrived (live, inactivated, or synthetic virus/viral material) specimens when natural specimens unavailable in lieu of ~400 patient prospective study
Other Studies	• Rely on *in silico* (computer simulation) analyses where possible • Waive inclusivity, precision, reproducibility, stability
GMPs	• Typically waived • Select elements may be required for certain tests

Home Test Timeline



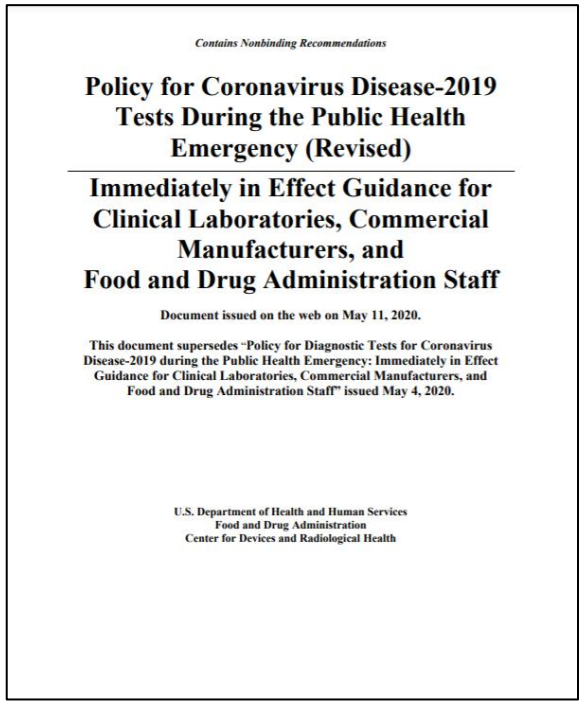
Flexibility & Innovation in EUAs

- Developed umbrella EUAs to streamline device authorizations
- Immediately in Effect Guidance Documents developed to streamline novel process implementation, including:
  - Policy to allow notification to FDA prior to EUA review for some laboratory tests[1]
  - Policy to help expand availability and capability of remote monitoring devices[2]
  - Enforcement policy to not require 510(k)s for some transport media devices to address availability concerns[3]
  - Enforcement policy for modifications to ventilators, accessories, and other respiratory devices to address availability concerns[4]

- Developed a reference panel for molecular diagnostic tests
- Partnership with NIH/NCI to conduct independent evaluation of serology test performance
- Partnership with NIH RADx to drive testing innovation by supporting manufacturers to mature, scale, and commercialize tests, particularly point-of-care and at-home
- Function as scientific clearinghouse for test supply alternatives; communicated through posting of FAQs on website

1. Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff
2. Enforcement Policy for Non-Invasive Remote Monitoring Devices Used to Support Patient Monitoring During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (Revised)
3. Enforcement Policy for Viral Transport Media During the Coronavirus Disease 2019 (COVID19) Public Health Emergency
4. Enforcement Policy for Ventilators and Accessories and Other Respiratory Devices During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency

Notification Policy for COVID-19 Tests



Contains Nonbinding Recommendations

Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised)

Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff

Document issued on the web on May 11, 2020.

This document supersedes "Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency: Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff" issued May 4, 2020.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

- Initially (Feb. 29) just for molecular dx laboratory developed tests, expanded to commercial manufacturer molecular dx (March 16) and serology tests (May 4)
- Never available for tests conducted outside a clinical lab (e.g., at Point-of-Care or Home)
- Unintended consequence: some poorly performing tests used clinically

Developer validates test → Developer notifies FDA → Developer offers test for clinical use → Developer submits EUA within 3* weeks → FDA review of test already in clinical use

*2 weeks for serology tests

Consequences of Notification Policy

Problems with Tests

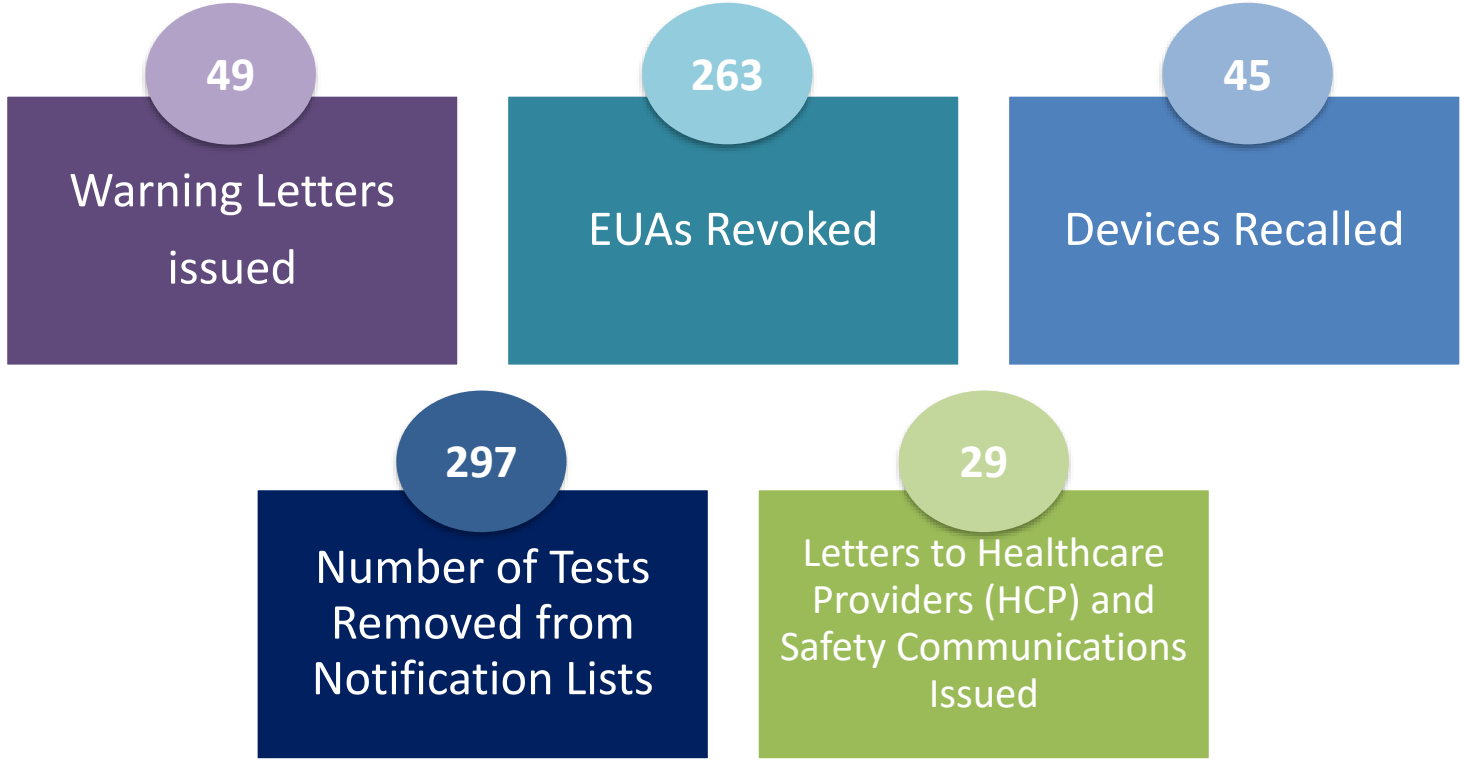
Molecular Diagnostic Tests

- Analysis of first 125 EUA requests from labs found 82 (66%) with design and/or validation issues
  - Some tests not validated at all
  - Some tests had poor performance
  - Some tests not validated appropriately, and revalidation unmasked poor performance
  - Some tests redesigned to address problems found in review and some removed from the market

Serology

- After notification policy released in March 2020:
  - Government officials promoted the use of serology tests to reopen the economy
  - Market flooded with poorly performing tests
  - Tests misused to diagnose or exclude active infection
  - Required policy change in May 2020 to correct these problems

Postmarket Actions for All COVID-19 Devices

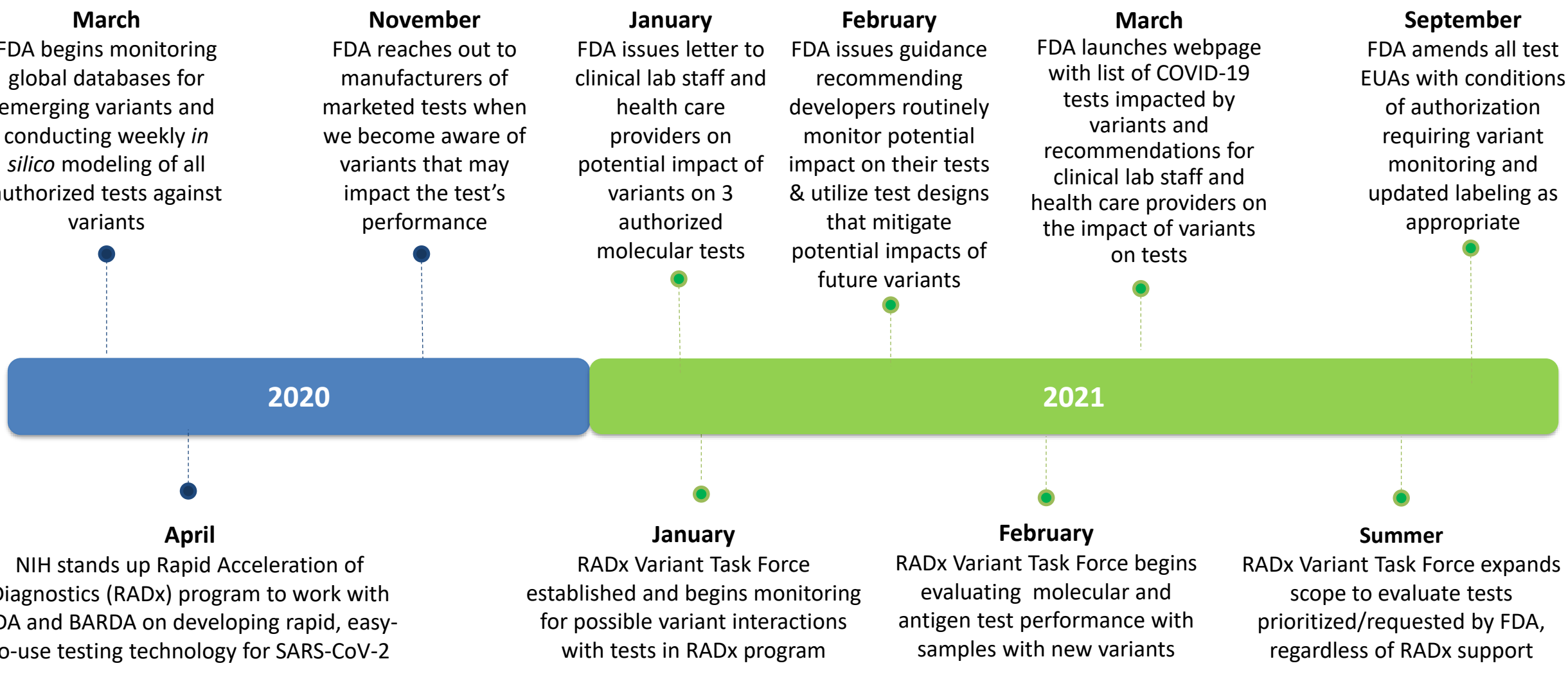


Conditions of Authorization:

- Test developers must evaluate their test postmarket with a reference panel, provided by FDA
- Test developers must monitor the impact of variants on their tests postmarket
- All devices are required to comply with postmarket reporting requirements
- Post-authorization studies for certain devices, as appropriate

Data as of September 17, 2021

Monitoring for Impact of Variants on Test Performance



March
FDA begins monitoring global databases for emerging variants and conducting weekly *in silico* modeling of all authorized tests against variants

November
FDA reaches out to manufacturers of marketed tests when we become aware of variants that may impact the test's performance

January
FDA issues letter to clinical lab staff and health care providers on potential impact of variants on 3 authorized molecular tests

February
FDA issues guidance recommending developers routinely monitor potential impact on their tests & utilize test designs that mitigate potential impacts of future variants

March
FDA launches webpage with list of COVID-19 tests impacted by variants and recommendations for clinical lab staff and health care providers on the impact of variants on tests

September
FDA amends all test EUAs with conditions of authorization requiring variant monitoring and updated labeling as appropriate

April
NIH stands up Rapid Acceleration of Diagnostics (RADx) program to work with FDA and BARDA on developing rapid, easy-to-use testing technology for SARS-CoV-2

January
RADx Variant Task Force established and begins monitoring for possible variant interactions with tests in RADx program

February
RADx Variant Task Force begins evaluating molecular and antigen test performance with samples with new variants

Summer
RADx Variant Task Force expands scope to evaluate tests prioritized/requested by FDA, regardless of RADx support

South Korea's COVID-19 Response

Advanced preparations translated into successful response

- Pre-positioned tests: Invested in select commercial test manufacturers to develop and launch tests quickly in an emergency
- Stockpiled testing supplies
- De-risked the testing enterprise by guaranteeing minimum purchasing and reimbursement of tests, once authorized

EUA process & validation requirements similar in US and South Korea, but some key differences

- South Korea opened EUA process up for one month and only for commercial manufacturers whereas US opened EUA process to all comers without time limitation
- South Korea molecular diagnostic test validation criteria essentially the same as US, except South Korea did not allow use of contrived specimens because of early access to Chinese patient specimens
- South Korea established a central capacity to evaluate the clinical performance of all tests seeking EUA

Established a centrally-coordinated national testing program

- Launched nationwide once the first tests were authorized in early February 2020
- Established test result reporting from labs to public health authorities, contact tracing and quarantine program, combined with strategy for population to adopt social behaviors such as mask wearing and social distancing.

Key Lessons Learned

Premarket Review	Tests need to be reviewed prior to clinical use but consider prior certification of the developer as an alternative
Validation Framework	Work with developer community on a framework for how to validate diagnostic tests during an outbreak
Pre-position Commercial Developers	Establish contracts to pre-position a handful of commercial developers to be ready to respond in an outbreak
De-risk the Enterprise	De-risk test development, as was done for COVID-19 vaccines, through guarantees of minimum purchases, reimbursement, and production support
Centralized Performance Validation	Establish a centralized clinical validation program to support test development and validation
Sample Sharing	Establish more effective mechanisms for sample sharing in outbreaks to facilitate test development and validation
Invest in Novel Technologies	Continue to invest in novel test development, particularly point-of-care (POC) and at-home technologies
Regulatory Flexibility	Regulatory flexibility has been critical during the pandemic and should be a capability during peacetime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