Software as a Medical Device (SaMD) Lifecycle Challenges

AI in the Time of COVID

BD

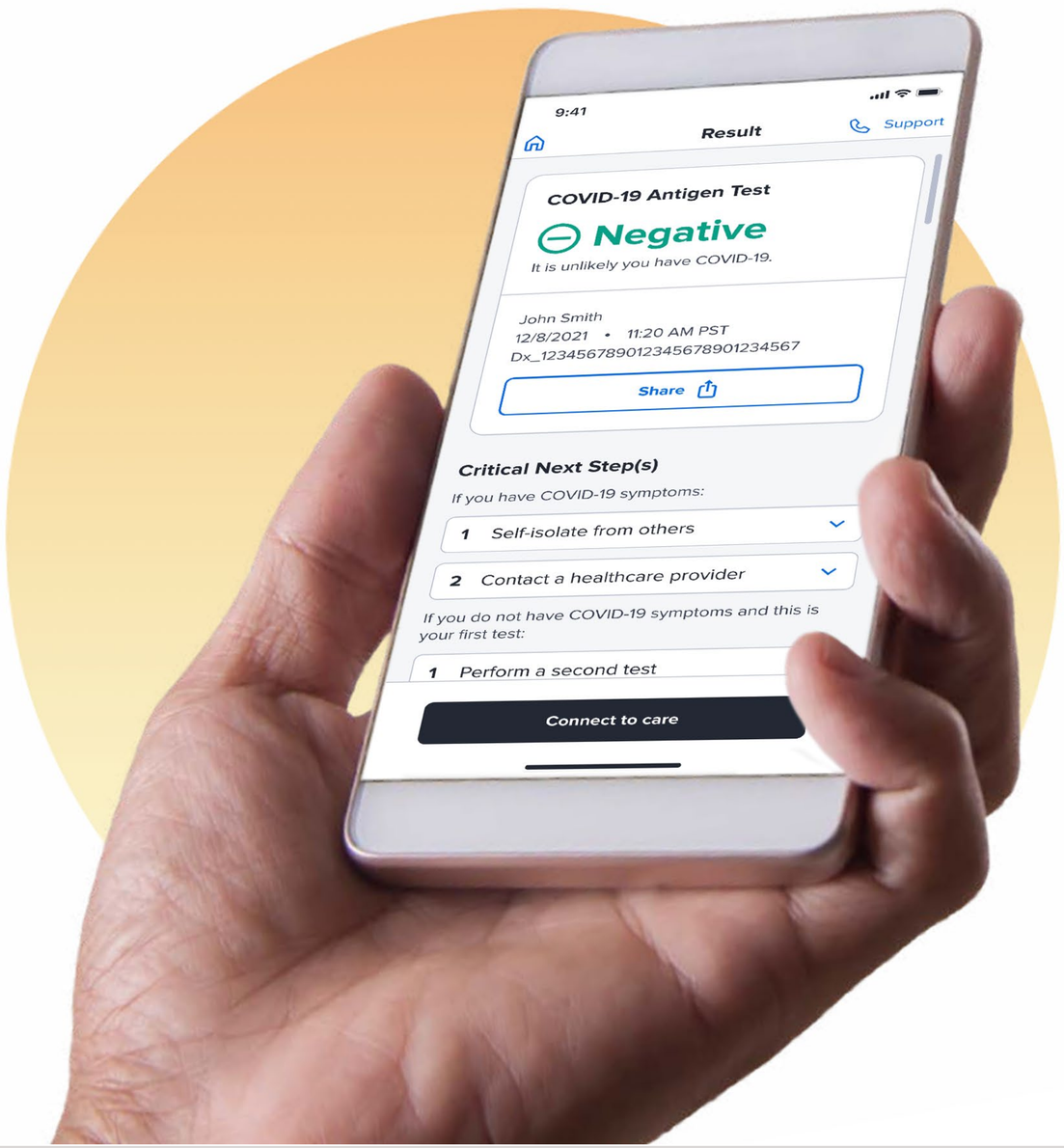
Device description

The BD Veritor™ At-Home COVID-19 Test:

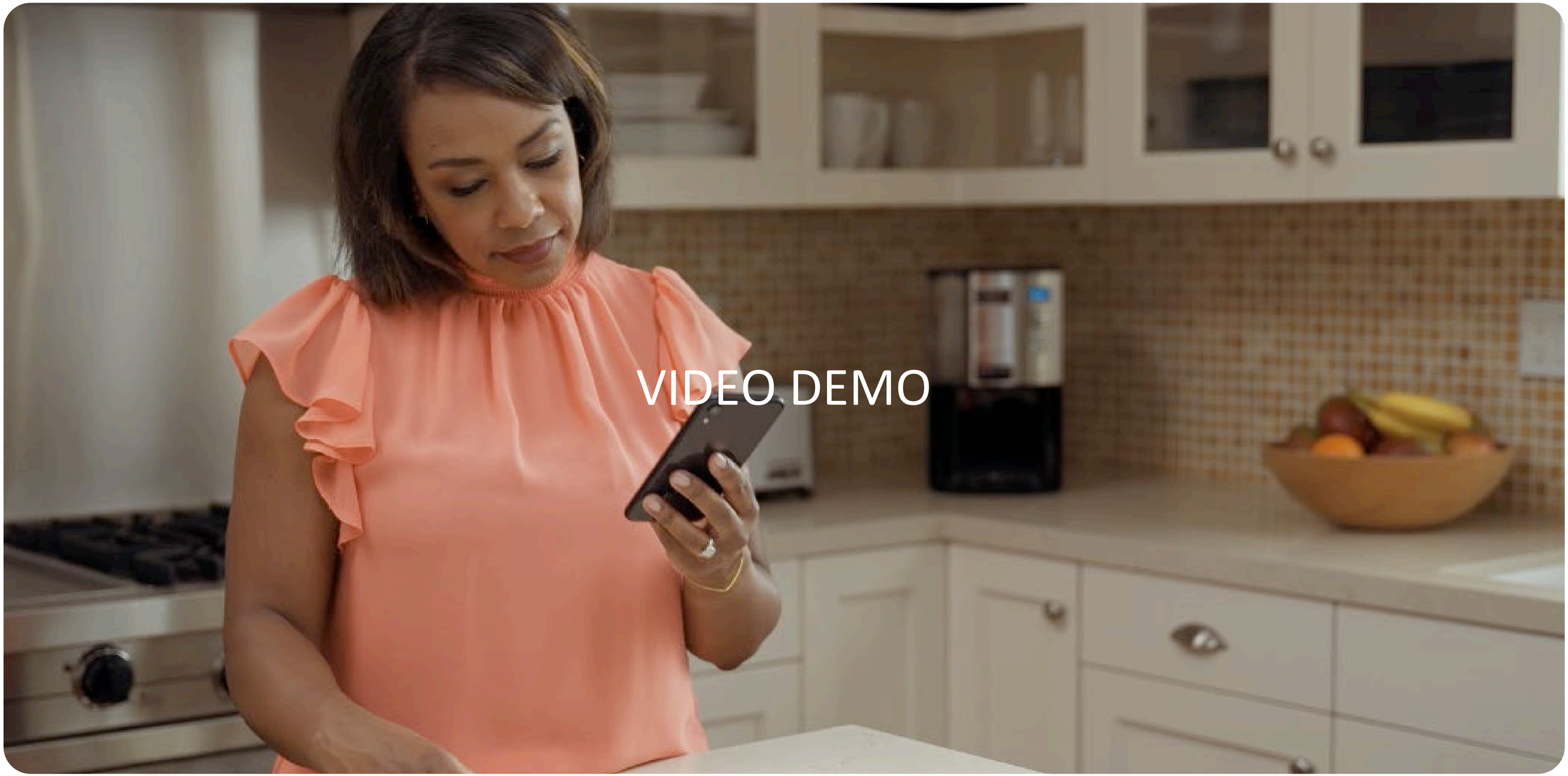
Provides Digitally Displayed Results in 15 Minutes

The BD Veritor™ At-Home COVID-19 Test is the better way to self-administer a COVID-19 test, featuring:

- **Clarity without the guesswork**— reliable test results in 15 minutes
- Digital results displayed **in words**— **not lines**—on your smartphone
- **Pain-free** nasal swab and **easy** testing process
- **Professional-grade technology** that doctors trust

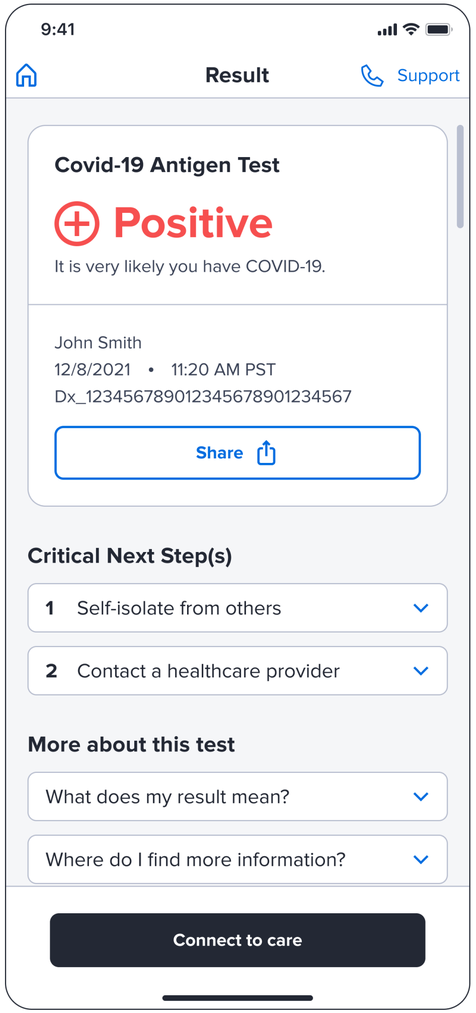


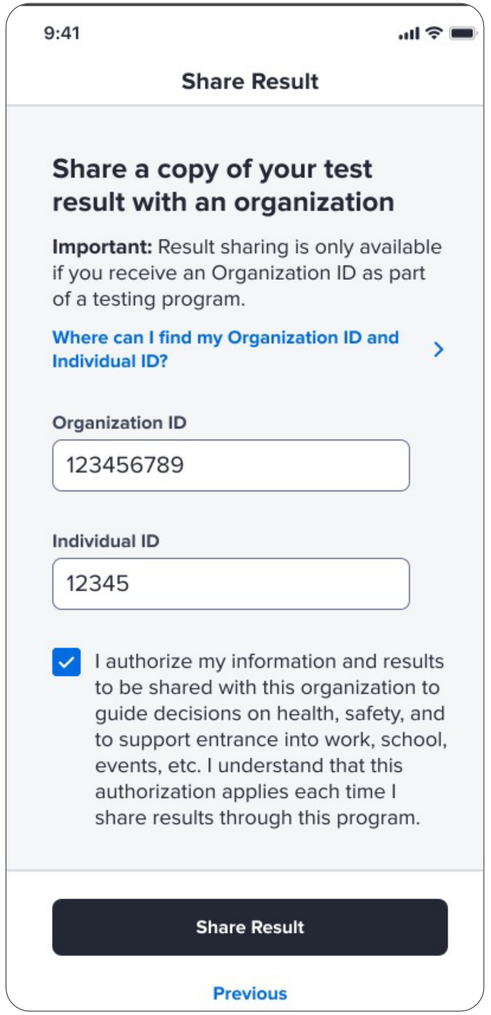
"This product has not been FDA cleared or approved; but has been authorized by FDA under EUA. This product has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of IVDs for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner."


VIDEO DEMO

The tech – a peek behind the curtain

- Why introduce a mobile device to the testing process?
  - Objective vs subjective
  - Image quality checks & real-time feedback
  - Results are natively digital and can be shared with ecosystem partner
  - Automatic result reporting to state and federal authorities
  - Ability to evolve and expand the user experience through app
- Why computer vision vs machine learning?





The development process

Technical & regulatory process

Development challenges

- Team members on West Coast, East Coast & Europe
- Internal version of the app developed to generate benchtop data
- Growing pains for our team:
  - Large data packet
  - Internet connectivity issues
  - Lack of familiarity with the app

Regulatory challenges

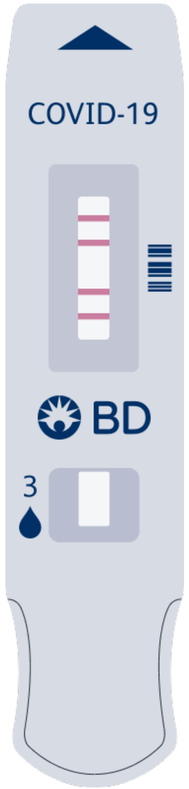
- No at-home template when we started
  - Non-lab template became available in July 2020
- Evolving requirements:
  - Internal human control (”sample adequacy line”)
    - Agency was concerned about mitigating false negatives (i.e. from incorrect sampling / self-sampling)
    - These same controls were later seen to be risk mitigation factors against lay users manipulating tests to get positive results
    - Official position was that if an internal control was not available, an alternative risk mitigation like video proctoring was required

Non-lab template (published July 2020)

Because of the greater potential for error in specimen collection at home, FDA recommends that the assay, which per the intended use allows specimens to be collected outside of a healthcare facility, have an internal control to indicate that adequate human sample was collected and placed into the test for analysis. If your assay does not have such a control you should address this risk using another mitigation, such as video observation of user by a trained professional or a design feature of the collection device.

Our solution

- Employs a “sample adequacy control” line that only appears when a human sample is present.



BD Veritor™ At-Home COVID-19 Test has more lines than a typical visually read COVID test due to presence of additional internal controls.

Regulatory challenges

- Evolving requirements:
  - FDA included reporting in the original non-lab template, but has relaxed their stance on reporting requirements over time

Non-lab template (published July 2020)

5) **Test Result Reporting:**

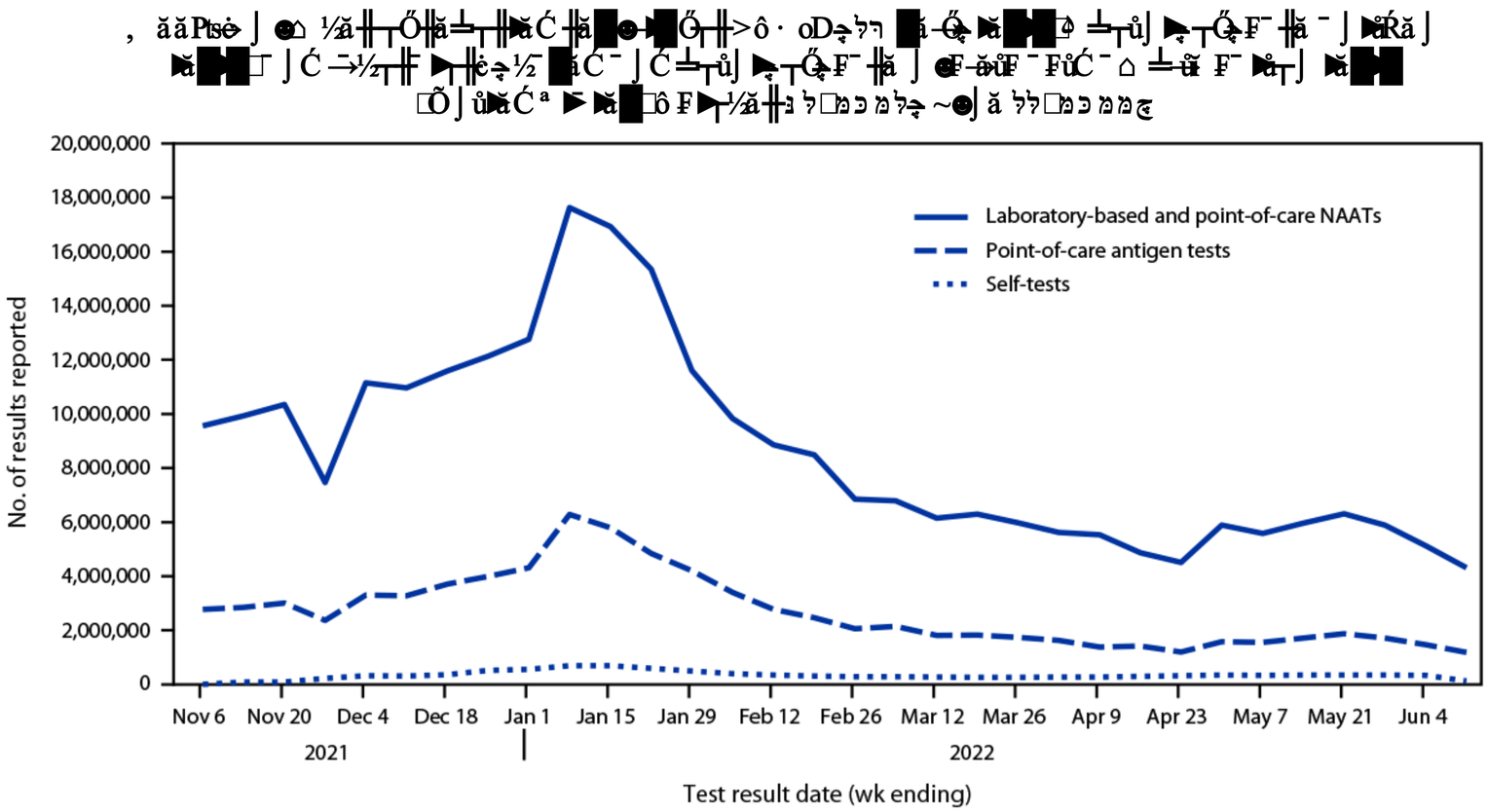
All test results will be reported to healthcare providers and relevant public health authorities in accordance with local, state, and federal requirements, using appropriate LOINC and SNOMED codes, as defined by the Laboratory In Vitro Diagnostics (LIVD) Test Code Mapping for SARS-CoV-2 Tests provided by CDC.

You should describe how you will ensure all users of the test can report all test results to public health and/or other authorities to whom reporting is required, in accordance with local, state, and federal requirements. The approach adopted should facilitate reporting by all users and be easy to use and understand. There are several options to allow for reporting of test results including, but not limited to: *automatic reporting through mobile app, instructions directing users to a website where reporting is easily facilitated, etc.* FDA is open to alternative approaches to reporting that ensure appropriate reporting.

You should also describe how test reporting will capture the appropriate LOINC and SNOMED codes, in addition to location data, and other patient information that may be relevant or required.

Regulatory challenges

- Reporting requirements:
  - Well established that user reported results for self-tests remain low
  - While reporting requirements remain a condition of authorization, NIBIB/RADx-MARS program's third-party solutions take pressure off test developers to fulfill result reporting requirements themselves



Ritchey MD, Rosenblum HG, Del Guercio K, et al. COVID-19 Self-Test Data: Challenges and Opportunities — United States, October 31, 2021–June 11, 2022. MMWR Morb Mortal Wkly Rep 2022;71:1005–1010. DOI: http://dx.doi.org/10.15585/mmwr.mm7132a1.

Predetermined change control plan

Or the “Software Update Plan”

Software development lifecycle

- App updates are an expected part of the mobile development lifecycle.
- Broadly categorized into app (UX) changes, algorithm changes, server changes.
- No “deciding when to submit a new 510(k)” equivalent guidance/flowcharts provided for EUA climate, so we created our own.

Mobile launch strategy

iOS first…

- Chose a single, mid-range iPhone as the “representative device” for clinical and analytical studies
- iPhone XR

…then Android

- Developed a validation protocol used to onboard new phones and validate OS updates, algorithm updates, etc
- Validated phones added to a dynamic list of compatible devices available on our website

Get the Scanwell® App

Check That Your Device Is Compatible and Get the Scanwell® Health App

Apple

Apple device must be running iOS 10, 11, 12, 13, 14, or 15

iPhone SE 3rd Gen (2022)
iPhone 13 Pro Max
iPhone 13 Pro
iPhone 13 mini
iPhone 13
iPhone 12 Pro Max
iPhone 12 Pro
iPhone 12 mini
iPhone 12
iPhone SE 2020
iPhone 11 Pro Max
iPhone 11 Pro
iPhone 11

Samsung

Android device must be running OS 9, 10, 11 or 12

Samsung Galaxy Z Flip3
Samsung Galaxy Z Flip
Samsung Galaxy Z Fold3
Samsung Galaxy Z Fold2
Samsung Galaxy Fold
Samsung Galaxy Note20 Ultra
Samsung Galaxy Note20
Samsung Galaxy Note10+
Samsung Galaxy Note10
Samsung Galaxy Note9
Samsung Galaxy Note8
Samsung Galaxy S22

Google and LG

Google
Android device must be running OS 9, 10, 11 or 12

Google Pixel 6 Pro
Google Pixel 6
Google Pixel 5a
Google Pixel 5
Google Pixel 4a
Google Pixel 4 XL
Google Pixel 4
Google Pixel 3a XL
Google Pixel 3a
Google Pixel 3 XL
Google Pixel 3
Google Pixel 2 XL
Google Pixel 2

Motorola

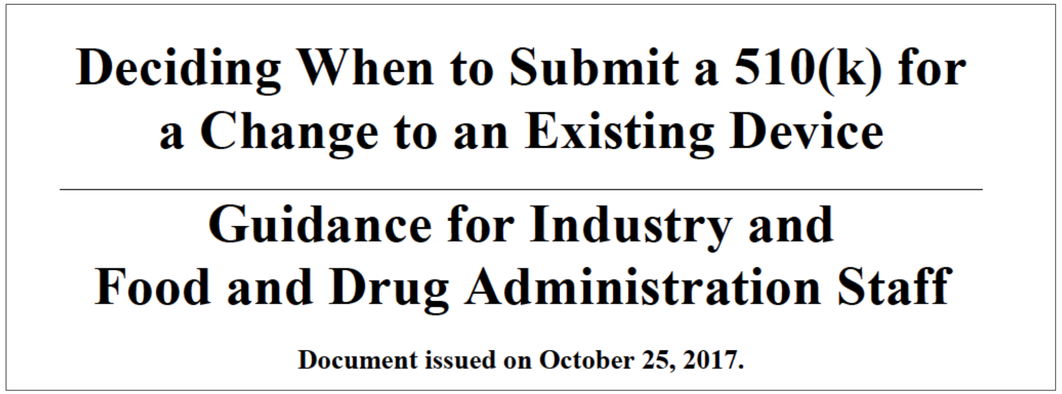
Android device must be running OS 9, 10, 11 or 12

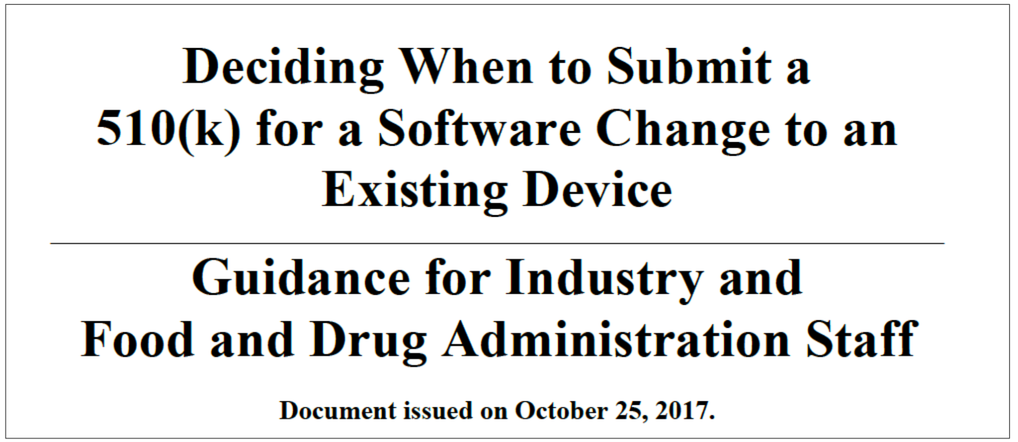
Motorola G Stylus 5G (2021)
Motorola G Stylus (2021)
Motorola G Stylus (2020)
Motorola Z3
Motorola Z4
Motorola E6
Motorola Edge (2020)
Motorola Edge (2021)
Motorola One 5G Ace
Motorola Moto G Play (2021)
Motorola Moto G Power (2021)

https://www.bdveritorathome.com/en-us/devices

Our PCCP approach

- Largely modeled after “deciding when to submit a new 510(k)” guidance, but with examples that were more specific to our product
- Indicated what types of validation would be performed with each type of change, and that most changes could be made without engaging with the FDA in efforts to be agile / least burdensome





From FDA Guidance:
Deciding When to Submit a 510(k) for a Software Change to an Existing Device (Published 25 Oct 2017)

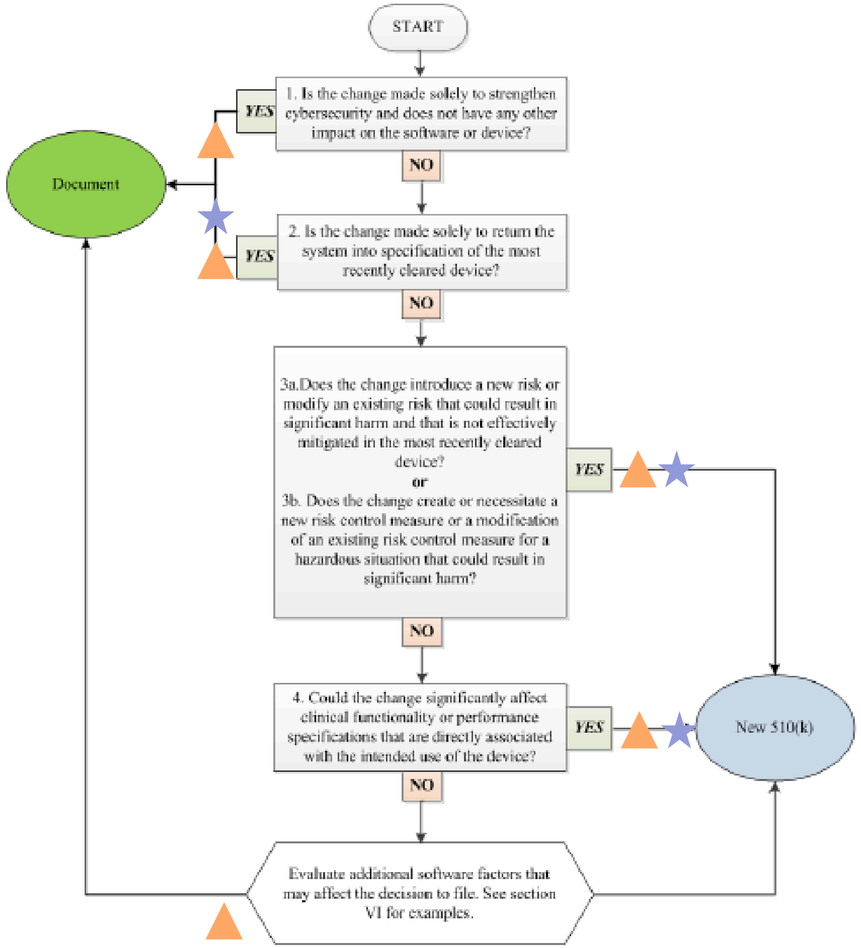


Figure 1. When to Submit a New 510(k) For a Software Change to an Existing Device.

Our additions

▲ Execute App V&V

★ Execute Algorithm V&V

Continuing challenges

12 months after EUA

Will this approach hold for 510(k)?

- PCCP guidance for AI/ML based SaMD expected to be published later this year

From FDA Discussion Paper:
Proposed Regulatory Framework for Modifications to Artificial Intelligence / Machine Learning (AI/ML) – Based Software as a Medical Device (SaMD) (Published 2 April 2019)

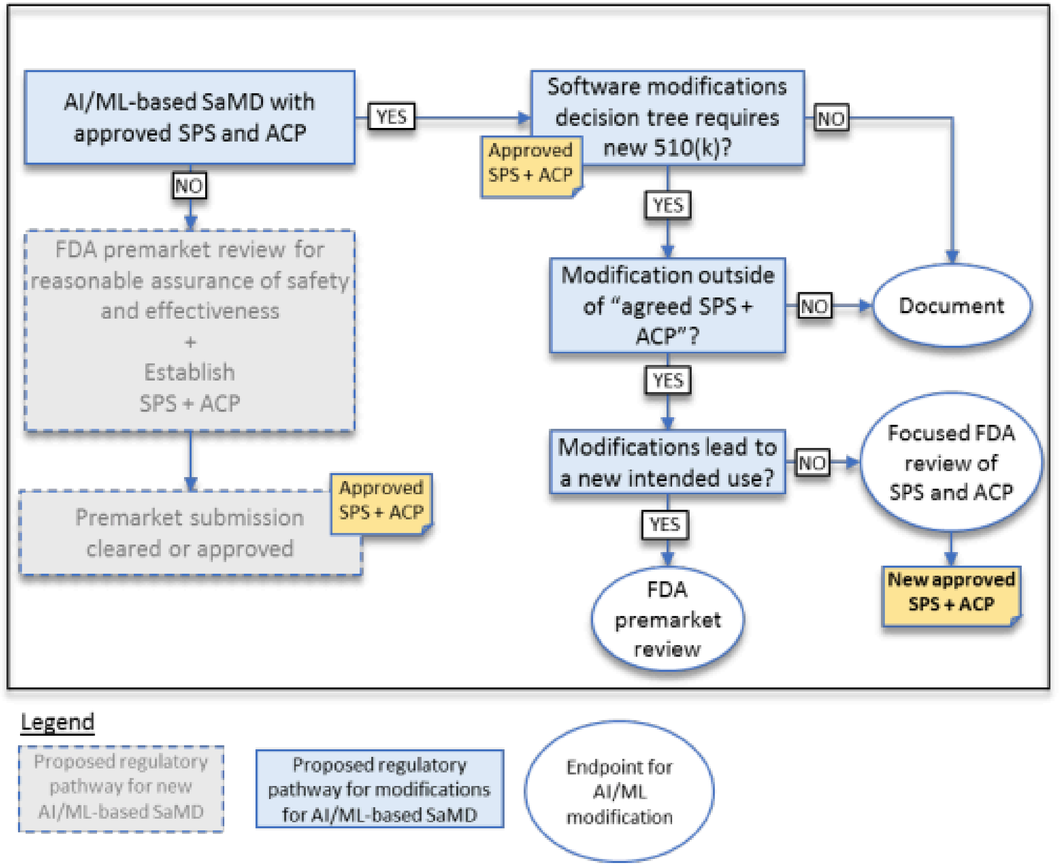


Figure 5: Approach to modifications to previously approved SaMD with SPS and ACP. This flowchart should only be considered in conjunction with the accompanying text in this white paper.

Continuing challenges

Transition to multi-analyte tests

At-home testing for COVID-19 has been widely adopted and encouraged by the federal government. Flu presents with very similar symptoms.

However, still no OTC multi-analyte tests on market (POC only).

A race to 510(k)s

FDA updates COVID-19 test policy on 27 Sep 2022 – majority of test developers will now need to pursue traditional pathway.