COVID-19 Evidence Accelerator Collaborative

Diagnostics Evidence Accelerator #38

Thursday*, October 21, 2021, 12-1 PM ET*

Call Summary

Introduction to Diagnostics Evidence Accelerator Meeting #38

This week's Diagnostics Evidence Accelerator meeting consisted of 2 presentation:

1. Viral Diagnostics and Sequencing for SARS-CoV-2 (Dr. Stacey Gabriel, Broad Institute)
2. Discussion of Minimum Data Sets

As always, thank you to all of the analytic partners, strategic advisors, and scientific advisors that are participating in Project One of Diagnostics Evidence Accelerator.

Viral Diagnostics and Sequencing for SARS-CoV-2 (Dr. Stacey Gabriel, Broad Institute)

Broad Institute is a non-profit biomedical institute that was formed in collaboration between MIT, Harvard, and Harvard Hospitals.

Broad Institute developed a dashboard that is updated daily with the number of cumulative tests completed, cumulative positive tests, daily volume of tests and daily positive rate. In total, Broad Institute has delivered 24 million diagnostics tests to over 1,200 institutions (e.g., colleges and universities, state and public sites, hospitals, nursing homes, and employers). Their current capacity of tests is approximately 80,000 test/day which is down from their peak of 150,000 tests/day. The results are delivered within 24 hours with an average of approximately 14 hours. Tests cost $15-25 per test. Given the surge in case, they hired/re-hired 450+ people to help with the volume of tests coming in to the lab. Broad Institute has completed 300,000 pooled tests and 45,000 viral sequences.

They began their testing program preparations March 10, 2020 and began the program on March 23, 2020. Between that time, they defined their Laboratory Developed Tests (LDT) and obtained the necessary regulatory clearance. They designed the capabilities around supply chain issues by using a kit that many organizations were not using. Additionally, they repurposed the existing infrastructure and built a new, lightweight software to track test information.

Clinical testing took place in 2 phases. Phase 1, called Small Covid, began in April 2020 and lasted until July 2020. During phase 1, Broad Institute reached the scale of 5,000 test/day. Also during phase 1, they observed that symptomatic people and asymptomatic people carry the same viral load in the community through testing Massachusetts Nursing Homes residents and staff. However, there were

many lessons learned during this phase. They found that samples and orders came in different ways leading them to adjust their approach.

In July 2020, they launched phase 2 also known as “the pod”. In this phase they deconstructed the testing paradigm where they moved to using bulk reagents with modular automation where no individual had to touch the tube once it was scanned. They also standardized the collection so that only sample that use their tools can be tested. Additionally, they began using tubes that used dry anterior nasal swabs. They simplified the software that they used so that any hospital would be able to use it. Finally, they applied their operational and process design to the test.

The presentation discussed the process of running the sample once it reaches the lab. The process is

1. The sample is accession. This is where the tube is scanned to ensure that the name on the tube matches the orders and the information on the tube is readable. This is the last time that a human will touch the tube.
2. The tube is loaded into a rack that is ready for automation.
3. The rack is put in a de-capping machine where the cap from the tube is removed.
4. The tubes are filled with a lysis buffer by a robot.
5. The tubes with the lysis buffer are loaded onto a Hamilton robot where the robot extracts the sample and transfers it to a PCR plate. The robot has learned to move around the swab therefore, it does not come out of the tube.
6. The RNA is extracted and set up for PCR. Then, it is loaded on to a Thermo Quants Studios for detection.

One important lesson that was learned was the importance of interfaces. Broad Institute implemented major integration through large channels. Figure 1 shows the different channels that they integrated into their system.

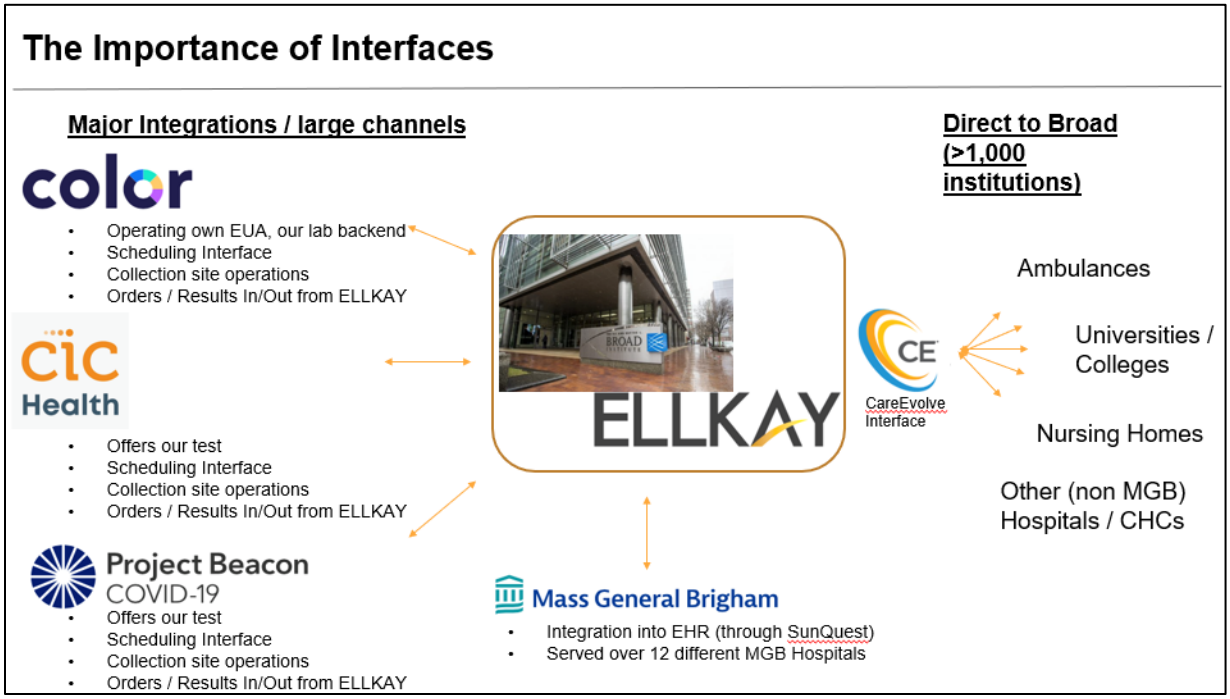

Figure 1: The channels that were integrated into Broad Institute system.

There were many hurdles throughout the implementation of COVID-19 testing. The hurdles were

- Supply Chain Issues
- Software for Ordering and Resulting
- Staffing / Customer Support
- Sensitivity and Specificity of the test
- Learning the regulatory landscape in real time

Broad Institute also conducted pooled tests. They had the notion that there may be a need to test hundreds of thousands of school kids every day. Therefore they designed a program where there was on-site pooling, so that it limits the number of tubes that come to the lab. The approach that they took was to pool 10 swabs per tube. The cost of the test is $2.50 per test. They have processed over 300,000 of these for the K 12 schools. If the pool comes back positive, then a reflex tester is needed to identify the individual who is positive, however, schools are finding it useful to identify if there's an infection to be to be concerned about.

Broad Institute is also conducting viral sequencing. This work was funded by the CDC. By working in collaboration with Broad Investigators (Bronwyn MacInnis, Danny Park), they stood up a large-scale amplicon-based viral sequencing effort that has a capacity for 2,000 samples / week. They have delivered 45,000 samples so far. They are moving samples from diagnostics into sequencing daily.

As next steps, the Broad Institute will continue scaling up their testing strategy conducting viral sequencing. They want to ensure that the “playbooks are remembered” since this may not be the last time we will need a testing strategy.

Question and Answer:

- How calibrated is your PCR detection system with similar tests using equivalent technology?
    - This is not a quantitative assay so they do not run a standard, however, they do run a human control, so that they have a CT value for the amount of human RNA was that that was there. Additionally, they run a negative and positive control on every plate.
- What plans are there for continued viral surveillance? What is the right sampling strategy?
    - Sequencing is important, so therefore they will continue with sequencing. They sample 5% of the positive cases, however their sampling strategy is a work in progress.

Discussion of Minimum Data Sets

One of the challenges of diagnostic testing that the COVID-19 Evidence Community has been thinking about is data flow. The HHS guidance stated that there are data elements that must be collected and reported. Figure 2 shows the required data elements that must be reported. However, there are still challenges in getting the data to flow.

Data Element	Reporting Requirement to Federal Agencies		Data Element	Reporting Requirement to Federal Agencies	
	Lab Reporting	Non-Lab Reporting		Lab Reporting	Non-Lab Reporting
Test ordered	Yes	Yes	Performing facility name and/or CLIA #	Yes (if known)	
Test result	Yes	Yes	Performing facility zip code	Yes	
Test result date	Yes	Yes	Specimen source	Yes	Yes
Test report date	Yes	Yes	Patient name	No	No
Test ordered date	Yes		Unique patient identifier	No	No
Specimen collected date	Yes	Yes	Patient street address	No	No
Device Identifier	Yes		Patient phone number	No	No
Accession # / Specimen ID	Yes		Ordering provider address	No	No
Patient age	Yes	Yes	Ordering provider phone number	No	No
Patient date of birth	No	No	Ask at Order Entry (AOE): First test	Optional	Yes
Patient race	Yes	Yes	AOE: Employed in healthcare	Requested	Yes
Patient ethnicity	Yes	Yes	AOE: Symptomatic per CDC	Requested	Yes
Patient sex	Yes	Yes	AOE: Hospitalized (at time of testing, for COVID)	Requested	
Patient residence zip code	Yes	Yes	AOE: ICU (at time of testing, for COVID)	Requested	
Patient residence county	Yes	Yes	AOE: Resident in congregate care/living setting	Requested	Yes
Ordering provider name and NPI	Yes (as applicable)	Yes	AOE: Pregnant	Requested	Yes
Ordering provider zip code	Yes	Yes	Patient email address	No	Yes

Figure 2: Required data elements for reporting.

CDRH/FDA established 4 priority regulatory uses cases (Figure 3) to understand what elements flow and do not flow.

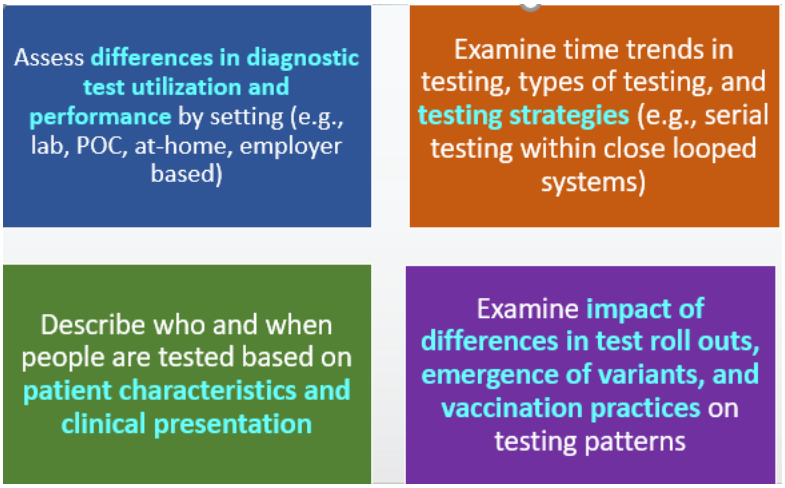

Figure 3: Priority regulatory use cases.

The Evidence Accelerator community was asked what data elements are needed to address the use case. The following discussion was ensued

- Patient identifiers are important to be able to understand what individual trends are and who's getting weekly testing versus just getting one test.
    - However, patient identifiers are not a required data element that need to be reported to federal agencies
- We need to know who the patient is and what tests is received. These two go hand in hand, would help us to get a better picture of what's happening and from FDA regulatory perspective.
- Knowing who received the test (patient identifier), what (device identifiers), when (specimen collection date and test result date), and test result.

- Real world performance of tests is critical to understand to keep an eye on too. Additionally, we need to know one who is getting tackled what tests are being used, who is getting tested and what are the results that are coming back to better understand I get a full picture of what exactly is happening throughout the system.
- We have a lot of different date of test being reported there and one thing that we saw from the Diagnostics parallel analysis work group is that sometimes test date is being associated with the result. Therefore, we cannot consistently get the result date as we'd like.
- Labs do not always receive time and data sample collection takes place. Therefore, the date that is most likely to be reported is the test result date.
- Sample collection date is also important. Depending on where you are in the public health world, there will be different data elements that would be needed to understand a public health crisis.
- The device identifier is actually more helpful than the test ordered because that gives us a level of granularity on the test. Then capture test report date and test results date.
- The data elements circled in blue in Figure 4 were selected as important in defining the use cases.

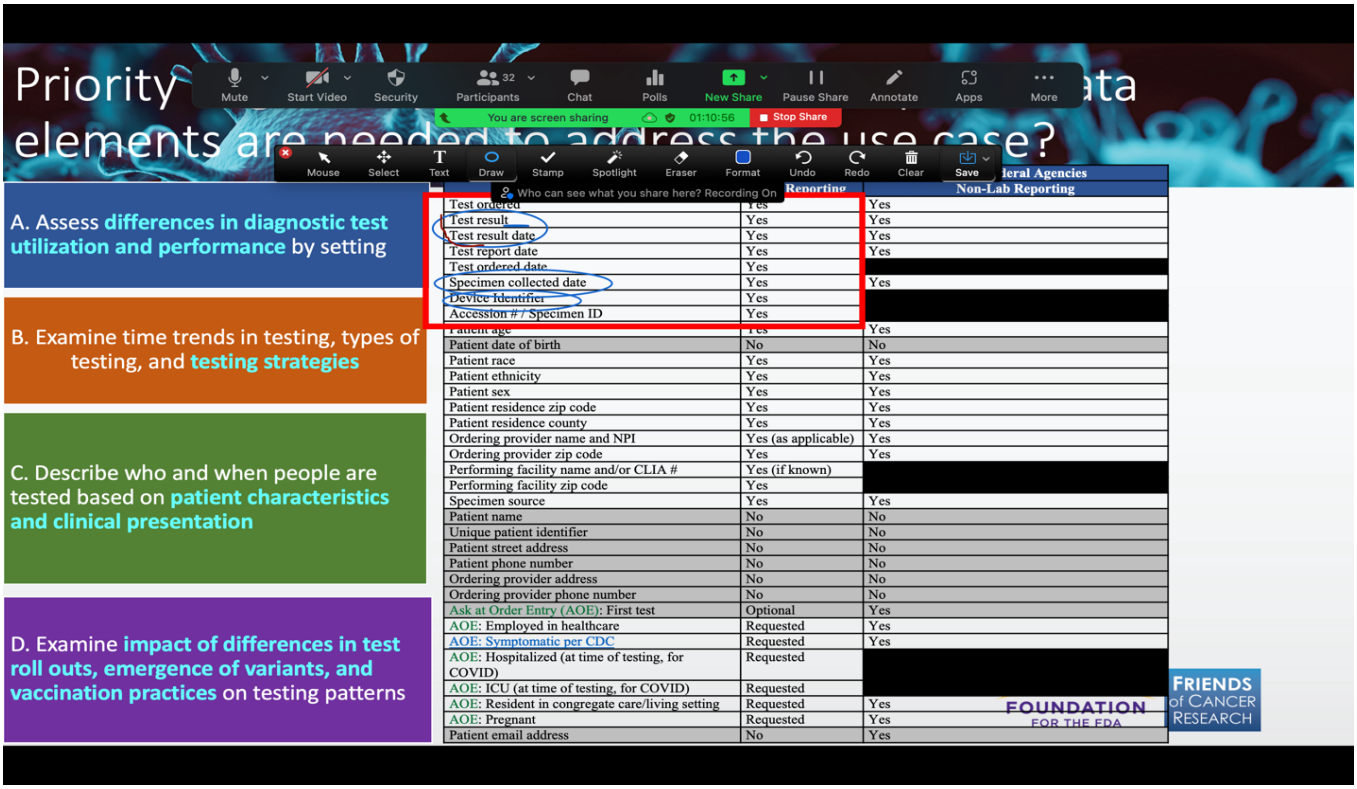

Figure 4:Potential data elements (circled in blue) that are beneficial in defining the use cases.

Next Steps

- Continue making data connections through the Evidence Accelerator and through www.EvidenceAccelerator.org.

Next Meeting: Thursday, November 4, 2021 12-1 pm ET