COVID-19 Evidence Accelerator Collaborative

Diagnostics Evidence Accelerator #15

Thursday, *October 1, 2020, 12:00-1:00PM ET*

Call Summary

Introduction to Diagnostics Evidence Accelerator Meeting 15

This week's Diagnostics Evidence Accelerator meeting consisted of 4 presentations.

1. Leveraging the Diagnostics Evidence Accelerator (Jeff Shuren, FDA/CDRH)
2. LOINC Codes and SARS-CoV-2 (Swapna Abhyankar, Regenstrief Institute)
3. Role of LabHubs (Ross Cantor, LifePoint Informatics)
4. Parallel Analysis Project One Update (Carla Rodriguez-Watson, Foundation and Gina Valo, FDA)

Leveraging the Diagnostics Evidence Accelerator (Jeff Shuren, FDA/CDRH)

FDA's Center for Devices and Radiological Health (CDRH) is committed to supporting the Diagnostics Evidence Accelerator as a resource for expanding real-world evidence (RWE) for medical technologies. There are many limitations that clinical trials present for pre-market and post-market surveillance. Those limitations can be low patient enrollment due to the lack of incentives, continuous modification of technology, and the time period it takes to conduct the trial. Also, the exclusion and inclusion criteria do not include the population that would use the device in the real world. As there are technological advancement, traditional regulatory framework do not include the rapid changes. The research community should move to a continuous learning model which leverages the use of critical RWE.

At the beginning of COVID-19, CDRH used Emergency Use Authorizations (EUA) to develop recommendations to validate diagnostic tests. The goal for CDRH was to expedite test access for patient, therefore, relying on RWE became critically important. The Diagnostics Evidence Accelerator has many potential benefits to be used on other devices, not just COVID-19 testing. This can be accomplished by improving the national infrastructure for generating clinical evidence for diagnostic test performance. In collaboration with MedEpiNet, CDRH engages with 12 national coordinated registry consortia and 4 international registry consortia to collaborate on a variety of medical technology. Therefore, CDRH's goal is to connect the smaller pipes and eventually connect the larger pipe to advance the learning health care system we need to implement public health.

LOINC Codes and SARS-CoV-2 (Swapna Abhyankar, Regenstrief Institute)

Logical Observation Identifiers Names and Codes (LOINC©) originated in 1994 by Clement McDonald, MD. There are 4 types of LOINC terms: laboratory; clinical; HIPAA attachments; and standardized survey instruments. There are currently more than 95,000 LOINC terms. Each term aims to achieve a level of

detail that will map one to one to an individual observation on a laboratory or other clinical report. LOINC terms do not include details such as instrument used in testing, details about the sample or collection site, the priority of testing, and the size of sample collected.

Term creation is driven by global user requests and the submission queue is publicly available. The term creation process consists of initial intake of a submission, pre-QA processing, QA review, post-QA processing, post-LOINC creation tasks, sending Completed Term Report to submitter, and public distribution of LOINCs. The SARS-CoV-2 term creation process is the same, except it is on an accelerated timeline. The turnaround time for regular codes is 130 days; turnaround time is one week for SARS-CoV-2 terms. The LOINC team is working closely with FDA, CDC, public health, and other stakeholders on how to best to model these concepts.

The significant difference between SARS-CoV-2 and typical microbiology tests and term requests is that there are still many unknowns about SARS-CoV-2, and tests and LOINC codes are being developed as we are still learning about COVID-19. The usual pathway for developing a LOINC code is as follows: 1) new disease is identified; 2) organism identified; 3) understanding of an organism and disease process; 4) test development; and 5) LOINC code development. However, for SARS-CoV-2, the test and LOINC code development is occurring in parallel with new information discovery about the disease process.

For SARS-CoV-2 term creation, the LOINC team relies on the information in the EUA for development of codes. They are also looking at modeling in the context of existing LOINC terminology. For molecular testing, there are a range of existing terms for generic and specific targets, specimens, and methods. For serology testing, there is a limited range of targets, specimens and methods. Out of 7,000+ existing LOINC serology terms, only 103 active terms specify the protein antigen that the antibody binds to. Before SARS-CoV-2, there was not a requirement by the FDA for manufacturers to specify the targeted gene but for SARS-CoV-2 it is required, therefore, the LOINC codes include the gene target. Serology tests do not require manufacturers to name the specific antigen targeted by the antibodies but rather to describe the type of antibody (e.g., IgG, IgM) and whether the types can be distinguished, and the LOINC serology codes mirror these requirements.

The closer to the source of the data the standard code can be included, the better for interoperability and patient care. The LOINC team is working with members of the SHIELD initiative, including FDA, CDC, and APHL, on the LIVD file for SARS-CoV-2. This file includes order and result LOINC codes for nearly all of the SARS-CoV-2 tests approved by the FDA under EUA and is updated weekly. It also includes SNOMED CT codes for specimen types and qualitative results. Additional fields for test kit name ID and equipment ID have recently been added to the file.

Role of Lab Hubs (Ross Cantor, LifePoint Informatics)

LifePoint Informatics provides software solutions and technical expertise for hundreds of healthcare and laboratory organizations. For COVID-19, they have provided patients direct access to results through patient portals and mobile applications. The focus of the presentation was to discuss the reporting of COVID-19 data elements to state health organization which will accelerate RWE. They build a single integration to performing laboratory information system (LIS) or remote devices such as those utilized as part of the RADx initiative. Through this single connection, they centralize and normalize the data to be able to distribute the data to various entities. They can report COVID-19 results and testing data for other infectious diseases to all 50 states. They host the data on their web portal, so providers that do not have access to the EMR systems can access data.

The challenges for Labs reporting are multiple point-to-point connections, various connectivity methods, implementation processes, format, scalability, and maintenance. States also have similar challenges , in that there can be hundreds laboratory connections that come into the state. Laboratories are reporting to the state via HL7 Electronic Laboratory Reporting (ELR), .csv files, or faxes. Each of those methods provide different challenges to the state. States have to ensure that the data are complete. The largest roadblock to the state will be variability as each state has their own method of connectivity, result format and implementation process. Also, resource constraints, technical capability, and scalability cause major challenges. Most labs have do not have fields to collect all of the necessary data elements. Labs have to create different workflows that is not part of their original workflow which presents challenges for the lab. Lifepoint bridges the gap in data collection by including the records and device information that are required by the state.

The advantages to a LabHub are efficiency where a single connection for both labs and states reduces development time and maintenance and post live changes. Lifepoint and Labhubs ensure regulatory requirements are met, data are improved through advanced LOINC Mapping (phrase/natural language processing, filling gaps, combining with instrument data, unique IDs, translation tables, etc.), and there is a rapid deployment though connections can be implemented in weeks to months vs months to years. Using Labhubs like Lifepoint to consolidate lab results, add missing data and rapidly deploy state health integrations, in turn could provide a single connection to aggregators or federal organization which could be deployed in months not years. This will increase data collection quality and improve the use of RWE.

Parallel Analysis Project One Update (Carla Rodriguez-Watson, Foundation and Gina Valo, FDA)

The constraint that we as researchers face are that existing identifiers are created for unique and specific purposes, therefore we need to be able to use them for a broader purpose. Also, new identifiers lead to greater simplicity and complexity. Complex systems of hardware, software, and middleware create bespoke configurations for every organization and use case. These configurations are brittle and inflexible relative to the speed of innovation. In order to solve these constriants, we need to gather RWD and be able to connect all the data pipes.

From the Chat Box

- A participant stated that there is an urgency to understand and remove unnecessary roadblocks. One of the known problems with LOINC is the many-many terms (there are about 915 codes for glucose alone), and many correct mappings are not interoperable.
- We lack unique identifiers for distinct COVID-19 diagnostic tests, and there is no interoperable, harmonized coding system to capture what is being measured, the interfering substances, and the limits of detection so that health professionals can easily access and interpret the laboratory findings.
- A caller urged that we need to understand the performance of each lot of the more than 850 different COVID-19 diagnostics in use worldwide.
- An accelerator stated that test performance for COVID-19 (RT-PCR at least) depends upon sample site, transport medium, sampling device, etc. Applying traditional meta-analysis techniques to the data is also challenging, because of possibly unrecognized heterogeneity and the limitations of power in tests to identify heterogeneity.

- An participant provided the link to LIVD codes: https://www.cdc.gov/csels/dls/sars-cov-2-livd-codes.html
- An accelerator states that she has done mapping of EUA numbers to the LIVD file - if this is useful to anyone please contact me to request it. Her email its gina.valo@fda.hhs.gov.
- The challenge is how much to put in an individual LOINC code versus utilizing other means of conveying the same information. For example, we have terms to report limits of detection, device information such as lot number, serial number, model, etc. Much of this information can be sent in various parts of the HL7 message. At some point, if we have millions of LOINC codes that are specific to all of these details, then they will no longer be useful for patient care without having another mechanism for aggregating the results within/across patients.
- Many legacy systems have severe limitations so the ability of LifePoint and other systems to facilitate flow of information are applauded.

Next Steps

- Continue making data connections through the Evidence Accelerator

Next Meeting: Thursday October 15, 2020 12-1 pm ET