FDA nudges standards adoption in electronic reporting

Anne Paxton

March 2019—An interesting medical informatics moment occurred post-9/11 with the delivery of anthrax-poisoned letters to several congressional and news media offices.

“There was not a single anthrax test order communicated to the CDC electronically,” says Steven H. Hinrichs, MD, chair of the Department of Pathology and Microbiology at the University of Nebraska Medical Center and director of the Nebraska Public Health Laboratory. “Everything was on paper. That was when it was finally understood what public health needed to do.”

Soon after, the Centers for Disease Control and Prevention set up the National Electronic Disease Surveillance System as its first effort to do electronic reporting and made great progress by providing a tool to share and analyze information, Dr. Hinrichs says.

But adopting a common vocabulary is central to electronic reporting. To date, standardized, commonly shared codes for electronic reporting across the health system have remained out of reach, as federal agencies and the diagnostics industry jockey for authority over standard-setting.

With a recent action, however, the Food and Drug Administration has raised hopes of new momentum in the electronic reporting standardization quest. On June 15, 2018, the agency published a final guidance document on LOINC (Logical Observation Identifiers Names and Codes), a universal code system for identifying laboratory and clinical observations.

In the document, “LOINC for In Vitro Diagnostic Tests,” the FDA encourages adoption of a consensus standard: the IVD Industry Connectivity Consortium’s LIVD (LOINC to IVD) format for distributing LOINC codes. “The FDA recognizes LIVD as a consensus standard that contributes to greater semantic interoperability within and across laboratories,” the consortium said in announcing the guidance. LIVD ensures that laboratory personnel will select the appropriate LOINC codes for IVD tests used by their laboratory. It also allows laboratory information systems to automatically map the correct IVD vendor test result to a LOINC code, according to the consortium.

‘I am so anxious for progress [on interoperability] that any move forward is progress.’ **—Steven Hinrichs, MD**

This FDA recognition is a strong start toward a unified data system, Dr. Hinrichs says, and other experts agree. Hung S. Luu, PharmD, MD, director of clinical pathology at Children’s Health and chief of service for pathology at Children’s Medical Center Plano, UT Southwestern Medical Center, applauds the FDA guidance as an advance toward standardization. “The fact that the FDA has

recognized there is a need for greater participation on the part of the vendors in assigning LOINC codes to their tests is a very recent development. We haven't seen anything like that for the past 10 years, so this is brand new," Dr. Luu says, adding that public health laboratories are probably ahead of everyone else in wanting unified data.

Unified data for all was the aim when, in 2011, the Office of the National Coordinator for Health Information Technology and the Centers for Medicare and Medicaid Services began phasing in minimum U.S. government-set standards for electronic health records through meaningful use, relabeled as interoperability in 2018. But actual interoperability has not been achieved.

It's a problem, Dr. Hinrichs says, because a common vocabulary is critical to providing care and maximizing the usefulness of health care data, and it can optimize the value of medical research. "If researchers think they are looking at apples but they're looking at oranges because they are using English words as opposed to standard codes that have all been linked and curated, then the research itself is questionable," he says.

LOINC is only part of the solution to standardizing electronic reporting because, aside from being a voluntary standard, it is designed mainly for test orders; the standard for reporting test results is SNOMED CT. "LOINC provides codes for the questions," Dr. Luu says. "It is just a way of assigning a number to a test so you can track it, the way a barcode does."

"SNOMED is the computable language of the result in all of its complexity," Dr. Hinrichs says, meaning that computers can understand and analyze SNOMED vocabulary. While efforts are underway to reengineer LOINC, it's a language that falls short of SNOMED, in his view. "LOINC will not be a satisfactory solution long term because it does not have sufficient structure to address the complexity of results, particularly as you integrate anatomic pathology or next-generation sequencing with LOINC."

Having LOINC and SNOMED working together from the start would help a great deal, in his view. "When the CDC had to make the next-generation test for influenza, we saw that as a great opportunity to provide coding with the test up front, so all the public health partners would use the same codes for all the influenza tests out there. There are molecular tests, antigen tests, and antibody tests for influenza, so if you don't code them correctly, you don't know what actual information the test is providing." The influenza pandemic in 2008 and 2009 was the first time that new laboratory tests had LOINC and SNOMED codes linked to them. "Instead of having every laboratory in the country go and find out which LOINC or SNOMED codes to use, those codes were provided up front," Dr. Hinrichs says.

But coding other areas of testing is less advanced. "What we have now is post-coordinated coding," he says. "This means that after I see a test result, I put a code on it. It would be much better if the laboratory test result could be encoded prior to its being transmitted. LOINC needs to incorporate the full richness of result reporting, and it would be much better if both LOINC and SNOMED codes were incorporated into package inserts."

The diagnostics industry has expressed opposition to mandates by the FDA on interoperability requirements. AdvaMed told the FDA in 2015 that requiring LOINC codes on instruments or product inserts would be difficult for manufacturers to implement, posed an excessive regulatory and administrative burden, and could freeze product innovation. However, up-front coding and package inserts are what the laboratory community wants, Dr. Hinrichs says. "We realize the commercial entities are not willing to do it at this point, but that is what we are asking for."

The FDA guidance on LOINC does highlight the importance of having a common vocabulary to identify IVD test results, says Ed Heierman, PhD, chief technology officer for the IVD Industry Connectivity Consortium and a product software architect for Abbott. "That is what initiated the FDA workshops and the industry collaboration to establish the need for a common vocabulary. As an industry, we wanted all the manufacturers of IVD instruments to provide LOINC for the tests their instruments perform." And among the manufacturers, "There was alignment on the importance of providing LOINC codes because that's what allows upstream laboratory systems or systems

performing automated analysis to know that they could compare a result from instrument A with a result from instrument B."

The seeds were planted with the Office of the National Coordinator for Health IT and meaningful use, he says, because there were items of meaningful use that required certain vocabularies, with LOINC among them. "So laboratories were already facing the requirement of 'I have to start publishing results that come out of my laboratory and identifying them with LOINC.' The vendors like Epic that are providing the EHR and EMR, the IVD instrument manufacturers, and the LIS and middleware vendors—ultimately all of these entities will have to handle that requirement."

Dr. Heierman

The FDA's SHIELD program (Systemic Harmonization and Interoperability Enhancement for Lab Data) is the next evolution of the workshops that led to LIVD on which the FDA LOINC guidance document is based, Dr. Heierman says. "SHIELD is focused on real-world evidence and real-world data. That means being able to collect real data from a population of patients or regions of the country or even specific instruments to perform a big-data analysis. You need these test results in a consistent format that is aligned on vocabulary."

But whether it is big data, or the health record of an individual who may have received multiple IVD test results from different facilities, or information about a particular instrument to help move along its approval process, "You can see that having data use a common vocabulary is a way the diagnostics industry—the government agencies, the laboratories, and the manufacturers—can open up a lot of possibilities," Dr. Heierman says.

A mandate from the FDA is not the way forward, he contends. There is leeway in the FDA's guidance document, and Dr. Heierman thinks that is helping manufacturers with publishing LOINC codes. "After thoughtful discussion, we made an intentional decision to keep the LOINC codes out of the package inserts, and one of the biggest reasons is it is not as useful for laboratories that need to use it to identify the appropriate LOINC code because it is in a PDF or paper format. It is not in an electronic format that their laboratory systems can consume."

Updating digital content will be much more efficient than updating package inserts, Dr. Heierman says. "Long term, we are looking toward systems that are automated. So [the decision against package insert LOINC codes] has taken away an obstacle that might have slowed some of this down."

Dr. Heierman is hopeful that the manufacturers, having made progress by collaborating voluntarily, can get industry as a whole to promote and adopt standardized codes instead of waiting for FDA regulations. "I think this is a case where the industry can solve it itself, and I believe that is what the FDA would prefer. The support from the FDA came in the LOINC guidance document they published recommending LIVD as a way to LOINC mapping. As to how it is done, they have left that open."

The manufacturers are taking the FDA recommendations to heart, he says. "The recommendations are almost as strong as a mandate but without the regulations behind them. The manufacturers are producing mapping tables for LOINC and giving thought to how the content can be automated. We are trying to remove the burden of laboratories having to figure out the LOINC code by giving them instead information to accurately and efficiently perform mappings: If we are running this test from this manufacturer and our lab is configured this way, this is the right LOINC code."

The diagnostics manufacturers have embraced the FDA guidance because they were the primary players at the table, Dr. Hinrichs says. "They were very much against having standardized codes in the package inserts."

However, “I am so anxious for progress [on interoperability] that any move forward is progress. I wish it would happen faster and, of course, that is where federal mandates can accelerate things.”

A study by Dr. Luu, based on responses to a questionnaire attached to a CAP Survey, confirms that laboratories find LOINC far from perfect for practical use. “We found that there is a lot of variation in how laboratories are assigning LOINC codes to their testing,” often with different LOINC codes being used for the same assay. “Part of the reason is that it takes quite a bit of expertise and an understanding of the local menu and hierarchies for LOINC, and I think that is very confusing for U.S. laboratories,” says Dr. Luu, who is the CAP’s liaison to the LOINC effort. “Even for a given manufacturer, laboratories are assigning different codes to them. In some cases they are incorrect. In some cases they are different in level of specificity.”

The questionnaire findings revealed only two-thirds of respondents were using LOINC. For those who do, his study’s look at activated partial thromboplastin time (APTT) showed the majority of laboratories were using code 14979-9 for that assay, which corresponds to APTT in platelet poor plasma by coagulation assay. Others used other LOINC codes such as 3173-2, which is the code for APTT in blood by coagulation assay.

“That’s not technically wrong, but one term is more specific and the other term is more general, so they’re not going to map to each other,” Dr. Luu explains. “The whole purpose of LOINC is to aggregate all these data. So all of these laboratories, if they were in a common database, would not be mapping to the same place. It would not be recognized as the same result.”

This is one example of the fact that “laboratories are struggling because there are so many options and it is unclear to them which to choose,” he says. “This has not gone unnoticed by the FDA, and the FDA put a memo out in November 2017 [“Recommendations for the Submission of LOINC Codes in Regulatory Applications to the U.S. Food and Drug Administration”] indicating that starting on March 15, 2020, it is going to require that regulated research, such as research that results in an application to the FDA for new drug applications, abbreviated new drug applications, and biologics license applications must include LOINC codes for the testing.”

The industry is not ready for that, Dr. Luu says. In fact, the FDA already recognized this by pushing out the original rollout date to 2020. But the industry has had some degree of response to the FDA request for assigning LOINC codes to their tests. “The IICC has developed the LIVD standard where if a lab consumer asks their laboratory instrument sales representative, the lab can be provided with a spreadsheet of the tests on the instrument that are pre-mapped to LOINC codes. That does remove some of the variability,” he says.

The FDA’s SHIELD program is trying to harmonize not only the LOINC codes across manufacturers but also the result codes that come with them, Dr. Luu adds. The FDA has also commissioned manuals that will provide a step-by-step coding of LOINC terms for microbiology. At the CDC, the opioid epidemic has stoked interest in unified data for multiple laboratories; the agency also wants to aggregate and look at microbiology data and susceptibility patterns nationwide.

‘Being able to pool data across laboratories, whether for research or public health, is the future of

medicine.'

—Hung Luu, PharmD, MD

In the private sector, Epic Systems has launched a program called Cosmos, creating a voluntary process whereby if a user of its software chooses to join a cooperative, the user would upload de-identified lab results to a database and the results would be accessible across all participating labs. All who choose to upload their results would have access to everyone else's results. "You can imagine that if this takes off, you would have this massive wealth of testing data that you could dissect and break down, for a given diagnosis, what are the most commonly ordered lab tests, how do turnaround times compare, those kinds of things," Dr. Luu says.

This falls apart, however, "if codes are not assigned consistently. You may have inaccurate data because people are using the wrong LOINC codes." Dr. Luu does not expect this initiative to take off rapidly unless there is synergy at the instrument-vendor level whereby the linkage of LOINC with tests becomes more automated, ensuring that the mapping is not the responsibility of the small labs.

But he sees high levels of cooperation in the industry. "I have been extremely surprised by the development of LIVD. This already shows what can be accomplished if the different vendors come together."

LOINC and SNOMED evolved separately, and W. Scott Campbell, PhD, MBA, director of pathology informatics and public health informatics and senior director of research information technologies at the University of Nebraska Medical Center, believes that legacy has created political difficulties affecting the potential usefulness of the FDA guidance. "The LOINC folks drove the conversation with the FDA, and it was not until just before they issued the first round of recommendations that the other standards organizations, mainly SNOMED, were brought into the conversation. So the conversation was well intended but not well informed."

Dr. Campbell

SNOMED, Dr. Campbell says, has a much more robust information content model underneath it—"We call it description logic in the IT world"—and allows for more in-depth linkages of data than LOINC, though LOINC is good at defining the terms of what is being measured, the units being used, and so on.

"The problem is LOINC does not help tell us how the parts relate to one another. That has been a problem since day one," he says. He notes that there are more than 600 LOINC codes for serum glucose measurements but no way to logically aggregate "like" terms. Without such a mechanism, for example, a clinician cannot easily determine if a diabetic patient has had any form of blood sugar testing done, regardless of result interpretation, without enumerating the entire list of LOINC terms.

The United Kingdom and Scandinavian countries have rejected LOINC, Dr. Campbell says, because of its insufficient granularity and insufficient description of relationships among concepts. "The U.K. has been a SNOMED country for 20 years," he says, "so they would have to retool their electronic health record infrastructure to accommodate LOINC as a standard." But any company trying to sell something to the United States is going to have to use LOINC in the laboratory world, he points out.

Ideally, Dr. Campbell says, there should be grouping concepts that bring together logically the LOINC codes for separate flu tests, if they are testing the same thing. Infectious diseases, in fact, are a good example of why national and international cooperation to coordinate LOINC and SNOMED is increasing. "Influenza has no borders

and no respect for borders, so it's important that we get a read on these things and share our information across the globe," he says.

Between Georgia and Nebraska alone, the lack of standardization presents problems. "In the public health space as well as in the hospital space, it's a huge deal if we cannot figure out that two states are experiencing the same kind of flu, as Georgia and Nebraska were. Data indicating that different strains are showing up can easily be masked because we have chosen different terminology and there's no way to blend that data. This is still an issue," Dr. Campbell says.

His colleagues have addressed the terminology gap by developing a format known as LOINC-on-OWL, taking every laboratory term represented in LOINC, marrying it to the SNOMED concept model, and applying all the logical rules that apply in SNOMED to LOINC. "This allows us now to easily look at lab data and nonlab data and realize real conclusions. How many times have patients shown up in the emergency department, had an opioid test performed, and had a positive test result? Those things could not have been determined prior to this because there was no connectivity between LOINC terms and SNOMED or other medical information."

This "universal translator" that he and his colleagues have developed lets LOINC and SNOMED work together, and the challenge now, Dr. Campbell says, is just a matter of getting everyone to agree on implementing it.

"We need to recognize that LOINC is not going away in North America. It is part of the fiber of our health care infrastructure. LOINC is almost 100 percent supported by the U.S. government and SNOMED by roughly half that percentage. We should be telling our leaders that these two need to talk, for public safety and public health, for general patient care, and finally so we can collaborate with our international partners on translational science and new discoveries."

Dr. Luu is reserved in predicting success in the near term. In assessing the 2018–19 flu season, for example, the medical community could experience a repeat of the familiar pattern of having too much fragmentation of data to have a clear picture of the outbreak, he says. But there is hope, he adds, and the government clearly sees standardization as a priority.

"Unified data is the future," Dr. Luu says. "Being able to pool data across laboratories, whether for research or to better address public health issues, is the future of medicine. What we need to realize is that the tools we have currently are imperfect. I don't know if that means improving LOINC or partnering LOINC with SNOMED or playing to the strengths of different coding systems. But improvement definitely needs to be made to realize the benefits of unified data. That is clear to everyone."

Anne Paxton is a writer and attorney in Seattle.