New hope for lab data interoperability

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November 2021—Interoperability, a problem of long standing in health care, has a new push and new prospects.

Interoperability has become a front-burner issue because it has become increasingly urgent to bring the standardized communication of health care data up to speed. Since the 2009 Affordable Care Act, significant resources have been directed to bringing widespread use of electronic health record systems. But interoperability among those EHRs has been held up by the lack of mechanisms and standards to ensure interoperability of laboratory data, which has drawn special concern during the pandemic.

An initiative led by federal agencies could turn that shortage of standards for laboratory data around. The key is a public/private initiative called SHIELD (Systemic Harmonization and Interoperability Enhancement for Laboratory Data), launched in 2016 by the Food and Drug Administration. Starting early in 2022, the profile of lab data interoperability should rise as SHIELD takes major public steps forward.

Led by Gregory Pappas, MD, PhD, associate director of national device surveillance for the FDA's Center for Devices and Radiological Health, SHIELD has brought together more than 70 stakeholders, among them the CAP, federal agencies (NIH, ONC, CMS, VA), public health (CDC), IVD manufacturers, EHR vendors, and others to determine how to standardize coding of IVD laboratory tests and results. The goal of SHIELD is to improve the quality, utility, and portability of IVD laboratory data through the harmonized implementation of semantic data standards. CAP members were appointed to seven of the SHIELD project's eight subcommittees, with two CAP Informatics Committee members included in SHIELD's implementation subcommittee.

"When we look at the clinical side, we can move the laboratory data around very nicely with EHRs in a single institution," says Walter Scott Campbell, PhD, MBA, an implementation subcommittee member and director of pathology laboratory informatics at the University of Nebraska Medical Center. Laboratories, in fact, were the groundbreakers in figuring out how to do that as far back as the 1970s, to make their jobs much easier, he says. "But now you have laboratory data coming in from multiple places via disparate EHRs and laboratories." Instruments from two different vendors can supply two different results of the same test within the same institution.

Dr. Campbell

SHIELD describes interoperability as the ability to "Describe the same test the same way, every time." An interoperable coded message, the FDA says, occurs when a specific IVD asks a question of a specimen taken from a human body, gets an answer to that question, and the entire process can be represented by standardized semantic codes.

How usefully one test can be compared with another is the problem now, Dr. Campbell explains. D-dimer tests at two different laboratories, for instance, could have a five- to 10-fold difference in the breakpoint to identify whether a patient has a clot.

That's one example, Dr. Campbell and other members of the CAP Informatics Committee suggest, of why the absence of interoperability is critical and why CAP members are helping the SHIELD team make interoperability

happen. The situation is not necessarily worse than it was 20 years ago. But “I think we all expected to have it worked out by now,” he says. “In so many ways it’s as difficult as it’s ever been and perhaps even more complex because we do more complex things.”

“Laboratory data is really confusing in a certain way, because you could pick any part of the laboratory and say you need to peel back the onion about 14 layers to get to exactly what you are trying to say with that test,” Dr. Campbell says. “What we—especially the CAP members—have been trying to do as part of SHIELD is to create a unique ‘fingerprint’ for any test performed on any piece of equipment with any test kits or reagents that go with it.”

Harmonization, in which an internationally agreed-upon standard would normalize references to any particular test, is also a part of SHIELD, and harmonization would be sufficient to ensure comparability of those test results. INR is one example of a harmonized test, but fewer than 100 other tests are clinically completely harmonized, he points out.

Part of SHIELD is to come up with a reference standard when there is no internationally agreed-upon harmonization. “It’s to answer the need to let clinicians know that two results can be safely compared or safely put in the same row in an EHR. While there’s still risk in this approach, you’re starting to minimize the risk,” Dr. Campbell says.

Such interoperability could benefit the IVD vendors. “If vendors are able to come into an environment where they know there is a standard way to communicate their information, that takes a burden off them,” he says. “They can say this is how you bring our device on and incorporate the information from our device. And we don’t have to customize that for every hospital in every different information technology environment.”

The FDA, too, has a specific interest in interoperability. “They want to be able to see these types of data in such a way that they can give provisional approvals to manufacturers.” Typically, Dr. Campbell notes, the time from invention to implementation in the medical space is 10 to 15 years. “Interoperability is one way the FDA might shorten that time frame.”

His institution’s experience with research shows another value of SHIELD. “As a researcher, I want to know that I can logically aggregate and make decisions from these very large observational data we are looking at” in patient-centered outcomes research. “We’re dumping our EHR data into shared data repositories and trying to apply data standards and metadata to that. But when you get into lab data, as we’re starting to find out, not all apples are the same type of apple.”

Whether the goal is to aggregate data sets to make decisions about cancer or COVID-19, “laboratory data are important. Laboratory data related to cardiac function and respiratory function are particularly important in COVID. These types of labs in particular are often not normalized, but we’re aggregating them. Now, are we at risk of reaching incorrect conclusions from our research data? I would argue we are.”

The role of COVID-19 testing during the pandemic shed clarity on this problem, Dr. Campbell says. “If you’ve got an Abbott machine, and you’ve got a Beckman Coulter, and somebody else has a Roche, how do we know we’re getting positive results for COVID-19 and that each device is as reliable as the next device? We were pushing technology and tests out as fast as we could, and we saw with the antigen tests a lot of questioning about whether you can know you’re not getting false-positives or false-negatives. It underscores that we’re not tracking enough information to really know that ourselves, let alone to exchange information” with other institutions.

These limitations could stall the development of rich and beneficial technologies. For example, “There’s no way we can support enough clinical trials to vet all the different versions of liquid biopsy—a promising new technology. It would take you forever and be really expensive to fund the clinical trials necessary to get the evidence we need. But if we can begin to provide an environment to enable us to start collecting this type of information in vivo, we might be able to get to conclusions faster.”

“We’ve been living this data nightmare for a very long time. In general, it’s gotten pretty small and a pandemic is pretty big. And we’re moving lots of data about lots of things that we didn’t know and people in the government didn’t know.” All of that shows, he says, “that we were weak in terms of the type of information we capture. So how do you start to look at this data world in a different way? I think CMS has been trying to come up with answers but not realizing how disjointed our systems are.”

But with the FDA providing its backing and clout through SHIELD, the laboratory world may be nearer to gaining a system of standardized coding. “The FDA would love to see a pilot started, running, and generating momentum at the end of three years and somehow be more broadly adopted in the next five to six years,” Dr. Campbell says. The pilot could be no greater than two separate institutions such as the University of Nebraska Medical Center and the nearby VA Nebraska-Western Iowa Health Care System.

With the differences between the two institutions, he says, “you’ve got a microcosm of what the rest of our world is going through in the U.S.—two major EHR vendors, different laboratory information systems, a whole cast of characters of in vitro devices.” Together the university and the VA could function more like a prototype project for interoperability, and perhaps that prototype would be enough to test an interoperability plan without 10 or 20 pilots at different hospitals at much greater cost.

Dr. Campbell is of the view that SHIELD has developed its concept into a tangible, doable, sustainable model: “We’ve put the right frameworks together to get on the right pathway to data interoperability in the laboratory.”

The SHIELD initiative is poised to start making its recommendations public in 2022. The SHIELD subcommittees have submitted their recommendations to a small working group, which is compiling those submissions into a draft to go out for public comment before publication. “The authors are working on a short timeline. To finish by the end of the first quarter of next year is probably realistic,” says Monica E. de Baca, MD, a member of the CAP Board of Governors and the CAP Informatics Committee.

Dr. de Baca

Once the interoperability specifications are fairly far along, the project will likely turn to a pilot IVD data hub project. “Depending on how the pilot evolves, there would be a subsequent expansion into a national IVD data hub. It is my understanding,” Dr. de Baca says, “that, in theory, that is something there is agreement on among HHS, FDA, ONC, CDC, and others.”

Trained in both ophthalmology and in pathology, Dr. de Baca has a clear window on the comparative stakes of following proper procedures in those specialties. Her perspective on interoperability is based on the Hippocratic Oath.

As a surgeon, she says, “the risk of harm I could do was limited to the number of patients I could directly treat on a given day. Now I’m a pathologist and coming through the laboratory are thousands of patients’ samples; my understanding of the data, data flow, and downstream data usage can affect each sample. As a result, in the clinical laboratory there is the potential of harm to thousands of patients a day. It’s our job to focus on quality and safety—to make sure we know the risks, foresee potential data errors, and mitigate error that could cause harm.”

There are multiple goals for SHIELD, says Dr. de Baca, founder of MDPath LLC and director of hematopathology, Pacific Pathology Partners, Seattle. The major objective is the creation of the IVD data hub, which would enable the FDA and industry to work together to use real-world evidence as a pathway for industry to earn FDA approval. But “SHIELD offers the possibility of complete clinical interoperability—that data from any one patient can be used for

that patient, in as many ways as possible, in as many places as possible, knowing there is as much retained context as possible and as little error as possible."

Luckily that goal is now in sight, she believes, because the federal government has decided that it isn't going to happen without new force, and the FDA is supplying that force by leading SHIELD.

From the 40,000-foot level, Dr. de Baca says, "We still don't have seamless functional data flow among institutions allowing colleagues at other sites access to actionable information they can implement to help a mutual patient. What does this mean practically? If you're on an anticoagulant and you land in a hospital 500 miles from home in a coma and with a broken leg, currently it is unlikely that the institution can access your data from your home institution or, if they can see it, know that the PT/PTT they see on their screen is absolutely equivalent to the values they'd have measured in their laboratory. If data assumptions lead to incorrect therapy, the results could be devastating."

In short, she says, communication is always "hugely contextual." If spoken conversations are context free, they become "merely a meaningless word or a string of words—or in the case of laboratory data, communicating a series of numbers could, in the wrong context, become very dangerous."

The notion of a conversion factor is too limited to bring about interoperability because of the complexity of the variables involved, in her view. By way of analogy, "When cooking, it's not just looking at a recipe written in French, and it says X grams of butter. I must know that French butter is cultured, has a different fat content, and is unsalted as opposed to my butter, which may or may not be cultured or have salt. Conversions or harmonizations—similar but not equal concepts—where possible, both require context."

Numerous sets of standards already exist, such as SNOMED CT, HL7, and DICOM, Dr. de Baca says. "In very broad strokes, SHIELD will create a guideline that considers existing standards and provides guidance about what items must be included for each test, each set of reagents, and for each instrument," thereby ensuring that the context required to know what is behind each piece of information as it comes through is provided.

In an earlier time, interoperability would have been the single paper-based chart—a binder with paper documents from all patient interactions, with all the information in it for the treatment team to see. "Information provenance was much more limited. Now we have both more input sources and more complex downstream data needs. The number of tangles in our ball of yarn gets bigger," Dr. de Baca says, noting, "It is ever more apparent that we need to evolve to meet the data demands."

The pandemic put a spotlight on that need, she says. "There was an imperative to use laboratory test result data for national epidemiology in a way that hasn't ever existed. With COVID-19, every one of our systems became overwhelmed, ironically, while living in an information society. People expect information flow to occur the way they *think* it should. The pandemic showed our expectations and reality aren't aligned—we have some serious Rubicons we need to cross."

Although currently fewer than 100 laboratory tests have complete clinical interoperability, the prospects for the remainder of the tests to reach that stage are good, she believes. "Someday we're going to get there. The question is what's our definition of 'someday.' The SHIELD initiative gives me hope that the horizon to someday just got closer."

Most of the western countries are using LOINC or SNOMED for coding, and "there is recognition that no one code is adequate to fully convey the depth of meaning required to have interoperability of laboratory data," says Hung S. Luu, PharmD, MD, a member of the CAP Informatics Committee and SHIELD implementation subcommittee. "That's why the SHIELD initiative going forward is different from that," he says.

Dr. Luu

But one of the main obstacles to achieving interoperability is the lack of understanding, shared by analysts and others, of laboratory processes and the fact that for the vast majority of tests you can get different results that are not interchangeable, says Dr. Luu, director of clinical pathology at Children's Health in Dallas. Prior initiatives sometimes included people who understood one piece of the puzzle but may not have understood the other complexities that needed to be solved, he says.

The past five years, however, have led to a tipping point because the ability to exchange data between institutions has progressed immensely. Meanwhile, data aggregation has shifted from mainly a public health perspective—i.e. how many people tested positive for flu, whether it was via a molecular instrument or point-of-care device—to a clinical care issue.

"SHIELD has done an immense amount of good work at getting people to the table. The vendors are now more engaged than they've ever been," Dr. Luu says. "Five or 10 years ago, sending data from institution to institution as easily as it is done today wasn't imagined." Now, "Most of the people on SHIELD recognize that the future of medicine should be harmonized values." The pandemic, too, has been helpful by pulling together different players who might not have interacted before, he adds.

Strangely, when lab results were delivered via paper or fax, it was easier to pinpoint the lab that produced them. The new absence of test provenance in digital test results has created a problem in an era in which results come from a wide range of sources, Dr. Luu says. Formerly, "You had a standardized format with required elements. Now, with digital, it's much harder to determine provenance." The pandemic showed this vividly because as COVID testing got underway, "unless you had a laboratory-developed test of your own, you had to use one of the referral labs." In his case, a test might go to the Quest facility in North Dallas. "That facility would be listed as the performing lab, but the testing for COVID is not performed there. It's performed in North Carolina."

That information is lost—as is the name of the ordering provider most of the time, he says—"because the interface is a blunt instrument." To minimize duplicate testing and conserve reagents, one of Dr. Luu's duties during the early days of the pandemic was to determine if COVID testing performed by outside institutions should be mapped into the Children's Health EHR. Mapping meant the EHR would recognize the external results as equivalent to those performed at Children's Health. The external tests could then be used to fulfill admission and pre-procedural screening requirements. Because "there's no standard out there for what information needs to cross over the vendor interface," he says, an outside COVID test could have minimal metadata and provenance information. One piece of information frequently missing was the specimen type. Often, "I won't know if it is a nasal pharyngeal swab or a saliva specimen, and that has an impact on the sensitivity of a COVID test."

"The true goal of SHIELD, where we're setting up milestones for achievability," Dr. Luu says, "is going to be, first, the interoperability of laboratory data and, second, setting up an IVD data hub to be able to provide real-world evidence for the approval of tests by the FDA, as well as a harmonization indicator to tell laboratories if a test has been harmonized across platforms."

How likely is it that SHIELD could bring about comprehensive harmonization? "Harmonization is a goal of SHIELD and it's definitely on the radar," Dr. Luu says, "but it depends on the vendors, so it's not something that is easily achievable. It's unlikely that the FDA will get more prescriptive about imposing baseline harmonization standards, and SHIELD alone doesn't have the authority to make the manufacturers accomplish harmonization."

First, under ISO guidelines, there must be a standardized reference material that's available for the assay to

calibrate to, and the vendors would have to calibrate their instruments to that reference material. “If the laboratories aren’t clamoring for this, then the vendors don’t see a need.” Moreover, there are some tests for which people have been working on developing a reference material for years without success, he points out.

That limitation would primarily affect the quantitative tests, though. “When you’re talking about infectious diseases and microbiology, harmonization becomes less important,” he says. In general, “The important thing is to make sure we define and code those tests to let a receiver of the result know the platform the test was performed on so they can determine if that is something equivalent to what they’re doing.”

Partial clinical harmonization will probably be achieved first because the information gulfs to be dealt with can be wide. “Obviously we want to walk before we run. Right now, I can’t even tell from the result information crossing over if the D-dimer performed in my lab is performed on the same platform as those from Duke University. The information is just not there.”

Harmonization “is the brass ring,” Dr. Luu says. “It’s where we’re all going to go—hopefully. But probably not in the near future.” By contrast, prospects for interoperability are good. “There is a lot more movement and a lot more investment in interoperability than I’ve ever seen. So, I think this is probably our best chance right now.” But, he says, “we also are trying to make sure that SHIELD minimizes the burden on laboratories so they are not having to invest resources they don’t have into the initiative. We’re trying to streamline the process and make it automated as much as possible so there’s more of a systemic solution in place.”

Along with the Biden White House, Dr. de Baca says, the HHS, FDA, CDC, and other agencies all consider interoperability a priority. “It’s very important to recognize that CAP has been invited to bring the resources and talent our member subject matter experts have to the table. I think pathologists are far and away the best people to help in this conversation,” she says, “and ensure that interoperability can be achieved at the highest quality level—and with patient safety the top priority.”

Anne Paxton is a writer and attorney in Seattle.