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Systemic Harmonization and Interoperability Enhancement for Laboratory Data (SHIELD) Community Roadmap

Key considerations for building a harmonized laboratory data ecosystem

**Presented by the SHIELD Community**

*This roadmap document integrates the work of many volunteers who contributed in their personal capacity. The views expressed in this roadmap are the contributor’s own and do not necessarily represent the views of any contributor’s employer, the Food and Drug Administration, the Office of the National Coordinator, the Department of Health and Human Services, or the United States government.*

**2022**

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# Acknowledgments

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This roadmap document integrates the work of many volunteers who contributed in their personal capacity. The views expressed in this roadmap are the contributor’s own and do not necessarily represent the views of any contributor’s employer, the Food and Drug Administration (FDA), the Office of the National Coordinator for Health Information Technology (ONC), the Department of Health and Human Services (HHS), or the United States government.

This SHIELD Community Roadmap is dedicated to the memory of Michael Stephan Waters (1973-2020) and honors the work he envisioned by conceptualizing and founding Systemic Harmonization and Interoperability Enhancement for Laboratory Data (SHIELD).1

# Executive Summary

Clinical laboratory data – orders, results, values, and interpretations – are among the most important types of data for clinical care, public health, and the development of drugs and medical devices. Of all clinical data exchange transactions in the country, laboratory data make up the largest share and have the longest history of being digitized. American Society for Testing and Materials’ (ASTM’s) *Standard Specification for Transferring Clinical Laboratory Data Messages Between Independent Computer Systems*, printed in 1988, is the world’s first published balloted consensus standard for clinical data.

It is thus paradoxical that laboratory data, despite their importance and high usage, represent a failure of clinical interoperability. Health data messaging (Health Level Seven (HL7®) and coding standards exist (Logical Observation Identifiers Names and Codes (LOINC®), Systematized Nomenclature of Medicine -- Clinical Terms (SNOMED CT®), and others), but consistent and accurate industrywide adoption of such standards on both sides of data exchange transactions has yet to be established due to the high fragmentation of the clinical laboratory market in the United States. The lack of interoperability in the healthcare ecosystem has been discussed in a number of publications.28

The United States pays a high but largely hidden price for the lack of nationwide laboratory interoperability in terms of safety, quality, innovation, and efficiency. Medical errors stemming from misinterpretation of laboratory data pose a safety risk to patients. As clinical laboratory data become more easily exchanged2 (e.g., using Fast Healthcare Interoperability Resources® [FHIR]), the risk of commingling data with underspecified semantic meaning could compromise patient safety more in the near future. Laboratory data interoperability is not simply the transmission of test result values without error, it also requires the consistent transmission of data elements that allow for meaningful interpretation and use of the laboratory result. Laboratory test results require additional data elements besides the result (e.g., units of measure, reference range values, specimen type, methodology) to be correctly interpreted and to meet interoperability standards and requirements. A new approach to interoperability standards is required for standardized digital representation of laboratory tests to allow for accurate interpretation and equivalence determination and a shared understanding of the laboratory data as it moves across the healthcare ecosystem. The inability to fully utilize laboratory data for quality measurement, clinical decision support, and population health management undercuts the quality-of-care delivery.

Real-world evidence (RWE) for discovery and post-market surveillance are severely hampered by poor data quality. Local test codes, tests names, normal range values, formats of test results and associated units all vary by individual laboratories. The limitations created by lack of interoperability include surveillance used to respond to the COVID-19 pandemic and other public health reportable conditions. Additionally, the resources devoted to laboratory data mapping and curation at each point of the data exchange are compounded across the entire value chain, imposing costs on the U.S. healthcare system. Accurate mapping of local laboratory codes to standardized terminologies would enable semantic interoperability in data sharing and aggregation across systems for a variety of purposes. However, existing literature documents the poor outcomes associated with creating terminology mappings without guidance, prior education, or an easily accessible authoritative source of truth. One study showed laboratories had an overall rate of 80.4% for correct LOINC code selection for coagulation and cardiac markers assays.3 Another study showed a 41% mismatch rate between diagnostic test manufacturers’ recommended LOINC codes and the LOINC codes used at five major medical center laboratories for the same test.4 A study of 68 oncology sites showed a representation agreement rate of 22-68% for 6 medications and 6 laboratory tests for which well-accepted standards exist.5

Systemic Harmonization and Interoperability Enhancement for Laboratory Data (SHIELD)1 is a public-private initiative to develop and launch collaborative policies and business models to overcome laboratory interoperability barriers. Due to the complexity of the U.S. laboratory market today, SHIELD has embraced an ecosystem perspective that recognizes no single government agency or industry actor has the authority or market influence to meaningfully impact the state of laboratory interoperability. SHIELD’s goal is to achieve laboratory data interoperability by *describing the same test the same way, every time.*

This objective is realized when a specific laboratory test result performed on one In-Vitro Diagnostic (IVD) platform and the same laboratory test performed on a different IVD platform can be viewed as performed on the identical IVD platform. This outcome means the data are precisely equivalent and can be safely intermingled to achieve complete clinical interoperability. A more limited, but necessary, stage of laboratory data is that laboratory test data performed on a particular IVD platform can be associated electronically with laboratory test data performed on the same IVD platform at any healthcare institution with 100% accuracy, this is referred to as structural interoperability.

The SHIELD collaborative emerged out of multi-agency workshops in 2015 and 2016, and a Food and Drug Administration (FDA) solicitation of funds to Patient-Centered Outcomes Research (PCOR) in 2017. SHIELD currently brings together stakeholders including IVD manufacturers, commercial and institution-based (e.g., hospital) laboratories, Association of Public Health Laboratories (APHL), standards developers, Pew Charitable Trusts, National Evaluation System for Health Technology (NEST)/Medical Device Innovation Consortium (MDIC), College of American Pathologists (CAP), Medical Device Epidemiology Network (MDEpiNet), American Society of Clinical Labs, numerous federal agencies, and standards organizations.

The SHIELD community took a major step when the Coronavirus Aid, Relief, and Economic Security (CARES) Act required “every laboratory that performs or analyzes a test intended to detect SARS-CoV-2—or to diagnose a possible case of COVID-19” —to report the result values of every test to state and local public health agencies. This SHIELD Community Roadmap builds on that advance for interoperability.

SHIELD’s value proposition follows the use cases of protecting patient safety, improving clinical care, reduced lab data user burden, and making RWE less expensive and timely. The Laboratory Interoperability Repository (LIDR) is envisioned as a centralized repository of codes that serves as an easily accessible authoritative source for the standardized digital representation of laboratory tests. LIDR will hopefully allow mapping to standard coding systems to be automated, at the minimum, by moving the mapping process upstream to assay manufacturers as well as providing mapping reference and tooling. This will reduce the burden on individual laboratories to perform mapping.

The IVD and Clinical Information System (CIS) industries strive to meet the needs of customers and promote the healthcare of the population through the provision of safe and effective products. Addressing the barriers to laboratory interoperability such as lack of standardization will have a significant positive impact on clinical laboratory operations, as it will significantly reduce the time and cost involved with deploying, connecting, and updating instruments in the laboratory. This will eliminate the need for vendor-customized connectivity implementations and favor vendors that adopt the specifications and pass the savings on to their customers. The creation of an IVD data hub provides an incentive for the IVD industry by providing a pathway for using RWE as a viable alternative to clinical trials to support regulatory decision making.

# Introduction

## SHIELD’s Vision and Mission

## *SHIELD’s Vision:*

## Enable consistent and uniform communication of high-quality laboratory IVD test data that are computer and human actionable to promote safe, high quality and equitable patient outcomes. In short, SHIELD’s vision is to: “Describe the same test the same way everywhere in the health care ecosystem”.

***SHIELD’s Mission:***

To achieve its vision, the SHIELD Community’s mission consists of the following key components:

* Consistent, standards-based identification and description of IVD laboratory data and their attributes which contributes to its semantic harmonization
* Secure, standards-based description of patient information in a manner that allows effective utilization while protecting patient privacy
* Consistent, standards-based interoperability across all applicable information technology systems from the point of order through all downstream uses, both within and between entities in the health care ecosystem
* Understandable, reproducible, and useable results for both human and computerized systems
* Support universal implementation of the above across all entities within the US health care ecosystem

## History

SHIELD started well before the COVID-19 pandemic and emerged out of multi-agency workshops in 2015 and 2016. An FDA solicitation of funds to Patient Centered Outcome Research (PCOR) in 2017 that focused on ways to facilitate the adoption and implementation of clinical data interoperability standards to enable consistent, accurate, and harmonized descriptions of IVD tests and result values.1

SHIELD stakeholders include IVD manufacturers, commercial and clinical center laboratories, professional organizations, EHR vendors, Pew Charitable Trusts, numerous federal agencies, standards development organizations, and patient advocates. The technical work to create harmonized standards for a variety of laboratory tests was conducted at regularly scheduled teleconferences, and those meetings continue. SHIELD received funding in 2018 from the Patient-Centered Outcomes Research Trust Fund administered by United States Department of Health and Human Services (HHS) Office of the Assistant Secretary for Planning and Evaluation.6 Support has also been provided by the FDA Medical Countermeasures for Emerging Infectious Diseases and the Presidential Advisory Council for Combating Antibiotic-Resistant Bacteria (PACCARB).7,8

As part of the national response to the COVID-19 pandemic, the Coronavirus Aid, Relief, and Economic Security Act (CARES) Act requires “every laboratory that performs or analyzes a test that is intended to detect SARS-CoV-2 or to diagnose a possible case of COVID-19” to report the result values from each test to state and local public health agencies. These agencies then forward the information to the Centers for Disease Control and Prevention (CDC) and HHS. Most SARS-CoV-2 assays were authorized for use via emergency use authorization (EUA). The LOINC® In Vitro Diagnostics (LIVD) specification, which was named as the source of truth in the HHS announcement for laboratory data reporting requirements for SARS-CoV-2 tests on June 4, 20208, is published through CDC for purposes of codifying SARS-CoV-2 tests, results and specimen types for public health reporting.9 By providing this single authoritative source of codes for COVID-19 reporting, SHIELD reduced the burden on laboratories that were struggling with testing volume, supply shortages, staffing shortages, and financial constraints. SHIELD also aids public health agencies that were overwhelmed with contact tracing, and reconfiguring their systems to receive new data elements and to sending those data elements on to federal agencies (replacement of correct reagents in short supply, etc.)

In general, the lack of precisely codified laboratory test and result values remains a major obstacle to data collection and analysis to support the detection of and response to high-consequence public health threats. Accurate and timely information on national patterns of infections, supply shortages, and quality of tests require that laboratories use standardized coding across the country and that the information provided by this codification is retained across the healthcare ecosystem, including a link to the clinical profile of the patients and to fatal outcomes. The pandemic highlighted a significant weakness in the management of healthcare data in the United States. This weakness in laboratory data pervades the entire U.S. healthcare system and is not constrained to infectious disease. It is manifested in day-to-day delivery of healthcare, and it affects patients daily.

## Development of This Roadmap

This SHIELD Community Roadmap, built on many years of work, was fast-tracked by the pandemic response. As a public-private initiative, SHIELD provided a consensus among partners on the nature and consequences of the lack of interoperability of laboratory data. The Roadmap was developed through the work of many volunteers, representing various healthcare, life science industries, and thought leaders in laboratory interoperability. This ensured a strong representation from a variety of stakeholders and breadth of knowledge and ideas. Committees are listed below along with their primary aims and tasks.

## SHIELD Committees

|  |  |  |
| --- | --- | --- |
| Committee | | Responsibilities |
| Coordination | * Provide general oversight and coordination with other committees * Work with each committee on areas of overlap to define limits and articulation of parts of the Roadmap | |
| Communication | * Roadmap presentations and materials needed to promote national involvement and implementation through national meetings, trainings, and newsletters | |
| Strategic Alignments | * Increase communication between federal agencies and SHIELD partners * Identify and assess further opportunities for improving the adoption of SHIELD initiatives | |
| LOINC® In Vitro Diagnostics File Expansion | * Define the initial design and develop a sustainability and steady state Roadmap for LOINC® In Vitro Diagnostics specifically and for other SHIELD standards in the future | |
| Implementation | * Support the active implementation of SHIELD standards, create an environment of buy-in of all stakeholders * Build and provide technical assistance (TA) where needed * Create the implementation Roadmap | |
| Tooling, Tech, knowledge management | * Create and implement a knowledge management architecture and tooling for the purpose of enabling highly reliable semantic interoperability to improve laboratory technologies and codification of data exchange structures | |
| Industry | * Provide cross-cutting support for articulating the role of industry in the various parts of the SHIELD Community Roadmap | |
| Effectiveness | * Provide measurement services by developing comprehensive evaluation plans * Plan and perform data collection, comprehensive analysis, and identity impacts | |

## The Roadmap’s Scope

Clinical interoperability is the ability of two or more systems to exchange information (laboratory results) and to use equivalent results for trending purposes, clinical decision support and machine learning algorithms. Although this Roadmap intends to focus on best practices and considerations for addressing clinical and semantic interoperability of IVD test results in the United States, it is structured to be compatible with laboratory data standards used worldwide. This document is not intended to guide clinical practice, including test ordering and application of IVD test results to patient care. This is intended as best practice information for the healthcare industry, not binding.

This Roadmap does not directly address Laboratory Developed Tests (LDTs). Instead, the strategies identify tests that may be applied to LDTs for reporting purposes; but key LDT regulatory issues are distinct from those of commercial tests and require inclusion of appropriate stakeholders for successful resolution. Incorporating LDT into this proposal, including recruitment of additional stakeholders, would add significant complexity and extend project timelines substantially.

## National Laboratory Landscape

This description of the national laboratory landscape provides further understanding of the dimensions of the SHIELD Community Roadmap’s suggested transformation. As of October 1, 2021, there exist 320,865 Clinical Laboratory Improvement Amendments (CLIA) certified laboratories that perform approximately 14.4 billion laboratory tests annually.10 In response to the COVID-19 pandemic, 49,601 new laboratories became CLIA-certified. Most of these new laboratories were in physician office laboratories, pharmacies, assisted living facilities, home health agencies and nursing homes.

The overwhelming majority of testing volume for clinical use is attributable to relatively few high-volume hospitals and independent commercial laboratories. 6.3 billion laboratory tests are performed by hospitals, of which 80% of this volume was produced by 20% of hospitals (1,860 of 9,339 total hospitals). Independent laboratories produced an additional 4.7 billion laboratory tests with 95% of that volume produced by 5% of independent commercial laboratories. Labcorp and Quest Diagnostics generated 20% and 22% of the total independent commercial laboratory test volume, respectively. These findings show that targeting key high-volume hospitals and commercial laboratories for the initial implementation of SHIELD standards would potentially have a disproportionate impact on clinical interoperability in the United States.

Amidst a global pandemic, the need for efficient exchange of electronic health information between hospitals and public health agencies rose to a critical level in the context of public health agencies’ needs for more detailed information on SARS CoV-2 testing. The CDC has onboarded state and jurisdictional health departments to provide more detailed COVID-19 electronic laboratory reporting.12 As of April 21, 2021, 56 states and territories have converted to electronic laboratory reporting to CDC.

A 2019 ONC data brief11 uses nationally representative survey data from the 2019 American Hospital Association information technology (IT) supplement to describe the number and types of challenges hospitals experienced when electronically reporting to public health agencies and how these challenges varied by state and hospital characteristics. In 2019, half of all hospitals reported a lack of capacity to electronically exchange information with public health agencies - seven in ten hospitals experienced one or more challenges related to public health reporting, and small, rural, independent, and critical access hospitals were more likely to experience a public health reporting challenge compared to their counterparts. The types of public health reporting challenges experienced by hospitals varied substantially at the state level.

# Why Laboratory Data Interoperability Is Critical

## Patient Safety

Medical error is one of the leading causes of death in the United States. The precise contribution of coding errors on which this Roadmap is focused on is unknown, but the potential is significant.13,14,15,16 It is estimated that as many as 98,000 Americans die each year due to preventable medical errors in hospitals. Others suffer disability or permanent functional impairment. Hundreds of thousands more experience the risks associated with unnecessary tests, procedures, and hospitalizations.17 Medical errors have been associated with the erroneous data exchange between IVD testing devices and the LIS. The following two case studies demonstrate the impact on patient safety when laboratory data interoperability is absent.

**Case 1**

An immunoassay analyzer was configured to report results of a test as ng/mL, but the LIS was configured to display units and apply a reference range in ng/L. This misalignment of laboratory test data representation between IVD systems and Laboratory Information Systems resulted in erroneously low values that yielded false negative conclusions for several hundred patients and may have contributed to one known death. An investigation determined that the cause of the incorrect units of measure was incorrect configuration of the Laboratory Information System, not incorrect reporting from the analyzer. The actual error was in the default sample type mapping, which led to an incorrect calculation and result unit’s assignment in the Laboratory Information System. There was also inadequate evidence that the customer performed analyzer to Laboratory Information Systems testing and verification prior to processing live patient samples.

**Case 2**

A 45-year-old female patient was transferred from a community hospital to the intensive care unit of a tertiary care facility with symptoms of chest pain and low oxygen saturation. Prior to the transfer, imaging and laboratory studies were performed at the community hospital to rule out suspected pulmonary embolism. A chest X-ray was equivocal, but a D-dimer assay was reported as 0.583 Fibrinogen Equivalent Units (FEU) µg/mL, which was within the normal range at the site and indicated a low probability of thrombosis. When the patient was transferred, the laboratory results performed at the community hospital were imported into the EHR of the receiving facility and became available to the new clinical team.

They noted the D-dimer result as higher than their cutoff value of 0.5 FEU µg/mL without realizing that it had originated from an outside hospital using instrumentation different from their hospital laboratory. The D-dimer assays used at the two facilities produced numerically different results and had different cutoff values for predicting the likelihood of thrombosis, despite having the same LOINC® and similar units of measure. The misinterpreted D-dimer result led the clinical team to believe the patient likely had a pulmonary embolism, and she was started on empiric heparin therapy. The patient underwent computed tomography (CT) pulmonary angiography to definitively diagnose pulmonary embolism. The CT scan did not show any evidence of pulmonary embolism but did show bilateral lung infiltrates consistent with pneumonia. The patient also underwent Doppler ultrasound blood flow studies of the arms and legs to rule out deep venous thrombosis. A repeat D-dimer was performed in the tertiary care facility’s laboratory and showed a value of 0.376 FEU µg/mL, below the institutional cutoff for thrombosis. Heparin therapy was discontinued, and the patient was treated for her pneumonia. Two days later, however, her platelet count dropped precipitously from 347 x 109/L at admission to 80 × 109/L. The patient was diagnosed with heparin-induced thrombocytopenia and required treatment with continuous intravenous infusion of argatroban.

The two cases reported in this section are based on actual events and illustrate the substantial harm that can result from misinterpreting clinical laboratory results. In the first case, patients received incorrect diagnoses leading to suboptimal care that may have contributed to at least one death. In the second case, the patient underwent unnecessary laboratory testing and imaging, had effective treatment delayed, and developed a serious iatrogenic condition from unnecessary treatment. Accurate transfer of clinical data among systems as patients move through different phases of healthcare is critical for safe and effective treatment. Current EHRs and IVD design do not contain strong protections against such errors. In the past, laboratory results were exchanged by paper or facsimile, and physicians were more likely to be alerted to the fact that the results were generated from an external laboratory as the name and address of the performing laboratory were required to be displayed on result reports and the provider could take that fact into consideration when making clinical decisions. However, reading results from paper or from faxes limited the ability of providers from having a full longitudinal history of patient results, especially if that history involved decades of information.

Accurate data integration in current EHRs and IVD systems are not always linked to obvious provenance cues, and, therefore, there is a real risk of inaccurate electronic integration and unsafe interpretation of laboratory test data, especially when the data originate from multiple sources. With laboratory directors and clinicians increasingly under pressure to limit redundancy and waste in testing--and the ease with which laboratory data can be exchanged between clinical entities--the opportunity for medical errors based on laboratory data is increasing.

## Interoperability for Clinical Care

Laboratory test and result data are cornerstones of patient care and provide critical objective information that supports clinical decisions. Beginning in the 1970s, clinical laboratories developed and adopted information technology and automation technologies to deliver laboratory test data efficiently and safely to the clinician in the volumes required to meet demand. Until EHRs technology’s adoption, laboratory test results were communicated by phone, fax, or paper. CMS’ *Promoting Interoperability Programs* legislation and subsequent adoption of EHRs in the U.S. healthcare industry facilitated the electronic transmission of laboratory data into EHRs as discrete data in some areas but has not achieved clinical interoperability yet.28

These data could be managed by EHRs to improve patient care, reduce costs and medical errors, apply artificial intelligence to health information, improve public health surveillance, and accelerate translational research based on Real World Evidence (RWE). Certainly, gains have been made in terms of electronic data exchange of laboratory test data for public health reporting. Unfortunately, the electronic exchange and storage of laboratory test data do not always translate to clinically useful or safely interoperable laboratory data.

The need to repeat laboratory testing as patients move between providers is well understood and documented. Laboratory data interoperability will enable laboratory test results that are shared between providers to be appropriately interpreted. Foundational efforts in laboratory informatics made laboratory test result data readily machine processable but not always comparable to similar data generated by disparate laboratories with different IVD analyzers. Differences in IVD vendor products’ analytical techniques, combinations of reagents (i.e., test kits) and calibration techniques of laboratory equipment vary between IVD platforms, testing kits and local laboratory practices. As these differences are not reflected in current electronic laboratory data exchanges this can result in patient safety issues, increased costs, deficient translational research conclusions, and poor, ineffective public health surveillance/public health responses.

Correct interpretation of laboratory test data is highly dependent upon multiple factors. These include reference ranges, units of measure of reported results, and the assumption that a result for a particular clinical test is clinically equivalent to a subsequent measure for the same test. Ranges of normality are routinely reported with a single test result and are easily interpreted by the clinician. When clinician(s) in different locations receive results for the same type of laboratory test, there are no systems in place to ensure that results from one test/location are comparable to another test/location and the data is limited to a few chronic disease biomarkers. Data necessary to equate and interpret laboratory data originating from differing locations or performed on differing IVD platforms are not communicated to and/or are suppressed in the EHRs which can impact patient care and safety. SHIELD offers the mechanisms to address these laboratory data exchange circumstances.

Interoperability is essential to promoting accuracy and consistent descriptions of IVD test results within EHRs. By improving the interoperability of laboratory data among healthcare organizations and other authorized entities, test results can be used to better support clinical decisions and enable RWE and reliability monitoring for FDA-approved IVD tests. SHIELD supports the provision of vetted and harmonized codes from manufacturers and industry to laboratories. It is expected that this will enable consistent representation in Laboratory Information Systems and EHR systems, achieving cross-institutional interoperability.

## Real-World Evidence (RWE) and Public Health Emergency Response Requires Laboratory Interoperability

RWE, data collected as part of routine clinical care, represents an enormous untapped potential resource for secondary use cases such as public health surveillance, clinical translational research, regulatory and quality improvement, and post-market surveillance of IVD vendor assays. An enormous amount of laboratory test data is generated in support of patient healthcare across the country using a wide variety of in vitro diagnostics test systems. The data are represented using different data structures and codes, depending on the healthcare system and the Laboratory Information Systems and EHRs used. Even though the same component may be measured using the same reagents and In-Vitro Diagnostics (IVD) system, the result’s digital representation may differ significantly across organizations, Laboratory Information Systems, and EHR systems. For the data to be used effectively for patient care, providing computerized decision support, public health reporting, or in research across institutions, they can first be converted to a common representation, a process which at present is manually performed.

A national interoperable health system could allow for diagnostic information to be used to better support clinical decision-making and enable RWE relevance and reliability. Despite more than a decade of federal investment in RWE, there are still many barriers to effective use, including lack of data interoperability. The vision of a national interoperable health system remains elusive. SHIELD specifically seeks to address the foundational conditions preventing laboratory data interoperability through the creation of unique laboratory test data fingerprints for any laboratory test performed on a particular IVD and set of reagents and test kits.

The ideal state is one in which the digital representation of laboratory test results is the same across all healthcare systems and provides sufficient information for the determination of comparability of results. In this ideal state, data could retain the same digital representation (same structure and same codes) upon transmission across different healthcare systems, LIS, and EHR systems as the data had upon initial creation and storage. There is currently no single standard terminology that fully describes laboratory data sufficiently to support clinical interoperability. Laboratory concepts can be represented by a standardized set of uniform codes and descriptions that fully explain the laboratory test. The same test can be described by the same set of standardized codes in every instance. This “fingerprint” of structure and standardized codes would allow for support of clinical interoperability and RWE without the need for manual conversion or transformation.

Currently a variety of data hubs and registries, maintained by clinical specialty societies, and private sector data aggregators are collecting data to provide RWE for a variety of uses, including assessment of quality of care, research, and to support regulatory decision-making.18 The cost and time needed to curate data coming in from clinics and laboratories are major barriers to the use of RWE. SHIELD harmonized standards could improve the quality of data following into these aggregation efforts and decrease the amount of money and time needed to produce reports.

High-quality data are critical to public health decision-making. The pandemic has made it clear that there can be improvement to public health data.19 The CARES Act and the response by the HHS secretary was an important step toward improving interoperability of laboratory data.

# Principles for Laboratory Interoperability

## This Roadmap explains principles for laboratory interoperability and includes data alignment, data semantics, data transport, result harmonization, and trackability as well as provenance. Data Alignment

The SARS-CoV-2 pandemic exposed the deficiencies in data elements exchanged and provided with the test results generated by multiple IVD platforms. HHS mandates require that laboratories provide information about each SARS-CoV-2 test result order in a standard form. Additionally, HHS has mandated that results must be delivered in a standardized form and a device identifier of the IVD platform to be included with the results.\* These data elements were neither defined nor curated for the U.S. healthcare system, and the CDC’s efforts to provide tables with such data remain an ongoing endeavor. The existing approach was minimally sufficient to address an international emergency, but it is not a sustainable and reliable approach. A concerted effort to define, collect, store, distribute, and curate the necessary, standardized data elements to include with each IVD test result is a potential solution for addressing this deficiency in data and about the data (metadata) to include with each laboratory test result generated for any test on any IVD platform within the United States.

CDC’s *Clinical Standardization Programs* demonstrated that laboratory data can be harmonized, and clinical data can efficiently be combined for generalizable clinical decision-making, such as developing harmonized reference intervals by combining data from large cohorts on which evidence-based clinical practice guidelines were created. These success stories provide evidence for benefits of data harmonization.

## Data Semantics

Data semantics confer the meaning of the data being exchanged. In laboratory data, it is encouraged to identify the specific analyte evaluated, the specimen evaluated, the method used to interrogate the analyte, the time, and additional information. Such information is to be communicated using national/international data standards. In the United States, the standard prescribed by ONC for use in laboratory data is LOINC®. Since 1994, LOINC®’s mission has been to provide a standard catalog of measurements, including laboratory tests, clinical measures such as vital signs and anthropometric measures, standardized survey instruments, and more.2

LOINC® is complex to code and requires time and training. With hundreds of thousands of laboratories using thousands of assays, and often using different reporting models for similar testing, this creates a significant burden on individuals tasked with coding to LOINC® who do not have the underlying knowledge of laboratory testing or lack experience with LOINC®. Although the bulk of high-frequency testing is more facile, LOINC® supports the requirements of different labs for more complex testing by providing variant result models for similar tests. One example is the provision of LOINC® codes that specify method details and other LOINC® codes that do not. This has resulted in the possibility of different laboratories correctly coding the same test to a different LOINC®, one that includes method and another that does not. This type of problem is not new and multiple attempts to reconcile these differences range from the use of thesauri similar to the Unified Medical Language System (UMLS) curated by the National Library of Medicine (NLM) or via extending existing models as was done for the collaborative effort between Regenstrief Institute and SNOMED International. The goal is for these systems to work toward a shared common, computable concept model. However, none of these options are sufficient in themselves to fully meet the semantic needs for laboratory data interoperability. Additional defining attributes for laboratory data to ensure interoperability are necessary that are beyond the scope of UMLS and LOINC®/SNOMED CT®.

\*Replication of the U.S Department of Health and Human Services Mandate.

While LOINC® is currently in use in the U.S. laboratory domain, complexities noted above can lead to mapping mismatches. Mapping mismatches are well documented in the informatics literature and are confirmed as part of SHIELD test site evaluation. In addition, a survey performed by College of American Pathologists asked the laboratories for their associated LOINC® code for a particular test.3 This demonstrated incorrect LOINC® assignment for critical laboratory tests. The results show an approximately 80% agreement of LOINC® term assignment between laboratories. Use of LOINC® as a primary key on which to align laboratory test data with a mismatch rate of 20% is unacceptable for patient safety and subsequent secondary data uses.

Further complicating the sole use of LOINC® for laboratory data interoperability stems from the incompatibility of IVD analyzer precision that precludes blending of laboratory data derived from different IVD platforms. As a result, even when LOINC® terms are correctly assigned to represent a particular test and test data are generated by differing IVD platforms, these laboratory data are not always interoperable for clinical purposes. The College of American Pathologists laboratory proficiency data provides one acute example of correct LOINC® encoded D-dimer test data generated by multiple different IVD analyzers. Review of laboratory test data indicates an eight-fold difference in the clinically actionable data point, depending on IVD analyzer employed. In other words, all IVD derived data for the D-dimer test were correct, but the critical value indicative of a thrombus greatly differed depending on device. By design, best practices suggest that additional data, and metadata such as specific device, precise units of measure, specific methodology, and reagents to be included along with the LOINC® for the results to be correctly interpreted. HL7 V2.X and HL7 FHIR® both accommodate this additional information, but the importance of including the detailed data and metadata is currently not emphasized in existing interoperability models.

The approach will address LOINC® alignment issues, but it does not address the advantages of supplementation of LOINC® to support secondary, but essential, uses of laboratory data, including translational research or public health surveillance. LOINC® currently does not provide an extensible basis to determine levels of similarity between LOINC® terms. Although LOINC® has a rich semantic model of parts that are used as pieces to build LOINC® terms, LOINC® has so far chosen not to distribute robust internal hierarchical structures of those parts (except in certain areas such as clinical documents). Rather, LOINC® has favored the approach of providing mappings of its component parts to external terminology systems. Examples of these external terminology systems include chemical entities of biological interest, The National Center for Biotechnology Information genes and taxonomy of microorganisms, the Human Genome Organization (HUGO) gene nomenclature committee, and of course, SNOMED CT®.

Through such mappings, LOINC® can be bound to a model that ascribes meaning to LOINC® terms and integrates LOINC® encoded data with other essential domains of human health, specifically medicinal products, diagnoses, medical procedures, non-laboratory-based diagnostics, and others represented by U.S.-supported and/or international data standards. Fortunately for the U.S. healthcare domain, this work began in 2014 through a cooperative agreement between LOINC® and SNOMED CT®, from which grew the mappings of LOINC® parts to SNOMED CT® concept codes. SNOMED CT® is an advanced, medical terminology standard that covers all aspects of human health in great depth and employs basic and advanced concept models consistent with the gold standard for medical terminologies defined by Cimino in his *Desiderata for controlled medical terminologies in the 21 century* .20 The cooperative agreement acknowledged the breadth of laboratory concepts in LOINC® and both the superior concept modeling represented in SNOMED CT® and the extensive representation of non-laboratory medical concepts contained in SNOMED CT®. The cooperative agreement resulted in SNOMED CT® models for 20,000 LOINC® laboratory concepts. Unfortunately, the cooperative agreement stalled due to institutional and political resistance at varying levels.

To achieve the mission and vision put forth by SHIELD, best practices suggest that these data standards be harmonized, integrated, and disseminated into a unified format. Reliance on any single one of these standards for laboratory data interoperability will result in a substandard and problematic implementation and will impede the desired levels of SHIELD’s success. The encouraged response is to *integrate* efforts between standard development organizations (SDO) in the U.S. domain.

Despite the setback, SNOMED CT® and researchers in the Veteran Affairs (VA) and University of Nebraska Medical Center (UNMC) continued the development work to extend the level of laboratory concept coverage in the SNOMED CT® domain. Further, SNOMED CT® developed a broadly accepted model for medicinal products that the National Library of Medicine (NLM) assisted to develop. This model is readily extensible to RxNorm to cover U.S. pharmacopeia, including branded drugs. Both the VA and UNMC have successfully integrated these three national data standards (LOINC®, SNOMED CT® and RxNorm) into a unified, controlled medical terminology that leverages these advancements while protecting relevant licensing and proprietary interests for each standards body. The result is a cogent, logical, and controlled medical terminology that incorporates and binds the critical human health domains represented in EHRs and will support the data science needs for public health surveillance and translational research efforts envisioned by SHIELD. As such, this unified LOINC®-, RxNorm-, and SNOMED CT®-controlled medical terminology can be incorporated into the SHIELD strategy.

## Data Transport

Data transport of required data elements necessary and sufficient to realize laboratory data interoperability can be divided into two sections. First, the data exchange between IVD platform and the laboratory information system can be defined, required, and implemented. Specifically, the IHE LAW data exchange standard (aka CLSI AUTO-16) provides direction to IVD maker and software vendors regarding the data elements necessary to electronically exchange between an IVD platform and information system, including device identifiers and test kit identifiers.

However, very few IVD manufacturers and Laboratory Information Systems vendors have developed the capability to adhere to this standard, because a feature not purchased by the market will not be sustainable. Laboratory data exchange between clinical information systems is defined and promoted by HL7 and ONC. Including data elements necessary for partial and complete clinical interoperability for laboratory data into the HL7 exchange standards and by ONC directive will provide the necessary structure and guidance to meet this component of laboratory data interoperability.

## Result Harmonization

In vitro diagnostic (IVD) vendor products’ analytical techniques, reagents, and equipment calibration vary between IVD platforms and testing kits. These methodological differences can produce significant variation in results for similar laboratory tests across different IVD vendor platforms. Some clinical laboratory tests have undergone calibration by manufacturers using standardized methods and internationally certified reference materials. However, despite these efforts, significant differences among manufacturers and platforms still exist. To address the situation, the CDC’s Clinical Standardization Programs (CSP) tests for verification that measurement results are appropriately harmonized, and it makes information about harmonized tests publicly available. Harmonized tests can be considered sufficiently equivalent for the purposes of patient care, and they allow for the development and promulgation of national clinical guidelines using laboratory cutoffs that are not method dependent. Test harmonization has been an active area of development in laboratory medicine. The CDC’s CSP has provided leadership and support to several professional organizations in their harmonization efforts, such as the International Consortium for Harmonization of Clinical Laboratory Results and the Joint Committee for Traceability in Laboratory Medicine. It made major contributions to two standards that define acceptable harmonization methods (International Organization for Standardization [ISO] 17511:2020 and 21151:2020). The CDC’s CSP efforts are aligned with those standards. Until recently, harmonization has been regarded as primarily an internal laboratory concern, and therefore, laboratory test data communication standards do not define fields specifically for the harmonization status of a test.

SHIELD recognizes that harmonization is critical in determining whether a test result can be fully integrated and is clinically interoperable with results from other locations. In addition to display of results, clinical interoperability would allow automated application of national clinical guidelines, decision support based on test result values, safe use of data by machine learning algorithms, and inclusion of data in aggregates that are analyzed statistically. SHIELD regards harmonization as important for the realization of its goals. SHIELD promotes the continued harmonization of tests across IVD vendor platforms and plans to define data elements that allow the harmonization status of tests to be communicated as part of the path to interoperability.

## Trackability and Provenance

We propose that for information on the original performing laboratory to be captured and transmitted to all downstream systems to allow for trackability and determination of provenance for public health and post-market surveillance of IVD vendor assays. While the name and address of the performing laboratory is a required element of the result report, this information can potentially become separated from the test result as the laboratory result data is transmitted and incorporated into multiple LIS or EHR systems. An example is esoteric or highly specialized testing that is frequently performed at a few select sites in a large referral laboratory operation. The specimen may be received at a referral laboratory network site local to the referring client and then sent to the specialty testing locale for actual performance of the test. The result report would contain the name and address of the receiving local site despite the actual testing having been performed at the specialty testing site. The information on the specialty testing site may be included in the result report as a result comment at the request of the client. This situation was especially prevalent in the early days of the COVID19 pandemic when test availability was limited. Trackability is a critical best practice for the RWE use case, as required by regulatory frameworks describing data quality.

# The Business Cases

## Industry Value Proposition

**Laboratories and healthcare institutions.** Both laboratories and healthcare institutions bear large, ongoing costs in dollars and personnel to maintain encoded laboratory test compendiums and dictionaries. Initial and ongoing costs for data encoding necessary to support interoperability are high but have not achieved levels of laboratory data interoperability greater than 80% accuracy. Current terminology knowledge and proliferation mechanisms are not achieving desired results. We propose the development of an authoritative source to inform end users how to populate their data dictionaries.

* SHIELD addresses this directly through the creation of the Laboratory Interoperability Data Repository reference service. Laboratory Interoperability Data Repository (LIDR) will provide a vetted and prescriptive reference for assignment of codes for all laboratory test attributes using code systems such as LOINC®, SNOMED CT and HL7 concepts. However, LIDR also acknowledges gaps that may exist with the prevalent code systems that cannot currently address laboratory data that are specific to IVD instrumentation, test harmonization status (i.e., metrology), and variations of reagents/test kits on data interoperability. LIDR extends the reference standard beyond LOINC® and other prevalent terminologies and incorporates those additional data elements and standards necessary to enable full laboratory data interoperability.
* The Laboratory Interoperability Data Repository reference service provision eliminates the variation of laboratory test compendium encoding by individual laboratories and healthcare institutions. It removes the burden of terminology maintenance from the end-users and promotes consistency of terminology and data representation nationally.

**CIS vendors.** CIS vendors include both EHRs and LIS. CIS vendors did not develop their products with national/international data standards into their core designs. Data standards are an *add-on* to CIS’ information model to comply with *meaningful use*, which supports improvements in healthcare quality and safety by the implementation of certified EHRs. Further, CIS vendors place the burden of data standards alignment and dictionary population onto the client. This action propagates the current situation.

* Additionally, some vendors have created their own data terminologies as a response to a perceived lack of movement on a cohesive national interoperability strategy. While this may be initially enticing to their customers and serves to bind them to vendor specific products versus technology-agnostic alternatives, the deviation to a vendor-norm further fragments the overall healthcare data environment as each vendor takes its own data alignment approach, which is not in the national interest. The lack of interoperability with other vendor platforms will prove problematic in an increasingly mobile healthcare ecosystem and will eventually require vendors to expend resources to provide interoperability solutions to disparate competitor systems. SHIELD provides the authorative source for IVD produced laboratory data. This eliminates the need for vendors and their clients to normalize their data from vendor specific terminologies to national/international standards in their own ecosystems and across vendor ecosystems. SHIELD and LIDR may reduce potential CIS liability associated with adverse patient results due to data mismatches.

**Device integration and CIS systems.** Integration of IVD instrumentation with CIS platforms is essential for laboratory automation and efficient laboratory operations. However, the absence of consistent standard adoption for device-to-CIS integration requires that both IVD and CIS vendors maintain and support a wide array of integration and interface technologies. This drives cost into each party’s business operations. SHIELD promotes the use of IHE standards for IVD/CIS integration. This is supported by the IVD community and IVD Industry Connectivity Consortium (IICC). CIS vendors will need incentives, perhaps, as interface services are revenue-producing, although support costs may offset some profits.

Best practices suggest that vendors (IVD and CIS) would engineer their products to adhere to standards promoted by SHIELD and other community stakeholders for data flow, however, there may be reluctance to do so without compelling customer demand or regulatory requirements. Regulatory requirements may be met with resistance if unfunded.

The hope is that end-users are provided CIS and IVD products with SHIELD functionality, reducing financial barriers to adoption. It is intended that supportive tooling developed by the SHIELD community as part of the pilots are freely available and support implementations with limited end-user investment.

# Recommendations

## Recommendation 1: Establish the Laboratory Interoperability Data Repository (LIDR) and related infrastructure

The suggested best practices for Laboratory Interoperability Data Repository are as follows:

* Establish the knowledge architecture by describing how coding can be harmonized.
* IVD manufacturers to assign codes according to SHIELD’s direction, including coding with their products and submission to a repository.
* Develop a repository for the coding similar to how UDIs are collected and made available through a body such as the NLM.
* Develop a process to improve the quality of the data in Laboratory Interoperability Data Repository is appropriate for use in the healthcare continuum.

**Best Practices.** The following are best practices for the establishment of the Laboratory Interoperability Data Repository:

* Develop a freely accessible knowledge management architecture for laboratorians, clinicians, researchers, and regulators, which is needed to promote clinical interoperability, enabling the determination of equivalency between different test results to decide whether they can be safely used for trending, data aggregation, post-market efficacy studies, and research.
* Determine the usefulness of clinical interventions to improve patient care, based on relevant laboratory knowledge and reporting data, such as public health reporting and clinical surveillance.
* Harmonize how meaningful laboratory terminology standards, such as SNOMED CT® and LOINC®, are used.
* Enhance the reproducibility of data exchange structures used to express laboratory procedures and outcomes, such as Clinical Data Interchange Standards Consortium (CDISC), FHIR, and IHE LAW.
* Promote the understandability of the laboratory test knowledge as interpreted and processed by supporting health IT systems such as LIS, Laboratory Information Management Systems (LIMS), and EHRs.

**Identification of the Data Elements that are needed for Clinical Interoperability**. SHIELD aims to determine the data elements and select the appropriate standard representation, creating a harmonized set of elements that can be moved between data systems in the lifecycle of a test result from creation of the test kit to the results being available in the IVD data hub. Clinical interoperability is suggested for the interpretation of individual test results that are temporally related, but most likely derived, from different source systems. Only results from equivalent assays can be safely trended.

For tests to be equivalents and interchangeable, the following conditions are suggested:

* 1. Same test (defined as the same analyte/observable performed on the same specimen type)
  2. Same instrument platform
  3. Same test kit

OR

1. Same test
2. The IVD manufacturer has calibrated its assay to an internationally certified and standardized material, and this calibration and measurement reliability test has been independently verified for example by the CDC, which website lists all labs and assays that demonstrate equivalence and calibration to an international standard.

Only assays that have undergone this harmonization process can be considered equivalent, regardless of platform and/or test kit.

* As additional elements are identified, a data model expansion process will be established for the LIVD file format and the Laboratory Interoperability Data Repository.

For clinical interoperability to be achieved, it is necessary for the information for equivalence determination of tests (e.g., specimen information, instrument and kit information) to be readily available at the time of mapping the external result into the native EHRs. These are currently the minimum elements that need to be included in the data exchange for every test (code system suggested for use in the United States):

* IVD test performed identifier including the test analyte/observable (LOINC®)
  + Specimen information
  + Specimen type (SNOMED CT®) at minimum
  + Specimen source site (SNOMED CT®)
  + Specimen source site topography (SNOMED CT®)
  + Specimen collection method (SNOMED CT®)
  + Specimen additives (SNOMED CT®)
* **Test kit identification.** (Unique Identification for the test kit could be UDI for FDA-approved tests or another unique identification system for other types of tests such as EUA and LDTs.) This can be in the package insert to allow for a guaranteed match between the test being set up in the laboratory and the entry in Laboratory Interoperability Data Repository for commercially available tests (not LDTs).
* **Equipment identification.** (Unique identification for the instrument should be its UDI.)
* Harmonization indicator for assays that have undergone successful manufacturer harmonization with calibration to an internationally certified and standardized material
* Results
* Quantitative results need to include units of measure (UCUM)
* Qualitative result value set (SNOMED CT®)

## Recommendation 2: Ensure the Flow of the Knowledge Throughout the Healthcare System

The development of a data hub for quality-controlled laboratory data relies on transfer of laboratory data from IVD to LIS, LIMS and EHR without the loss of clinical meaning and data integrity. It is suggested to identify the applicable standards for each specific use case, including adjustments to the standards, if needed. Additionally, participation is suggested in connectathons to test the updated specifications and system integration across all stakeholders of the healthcare ecosystem. Enable the adoption of these SHIELD identified standards.

**Best Practices.** SHIELD encourages the development of structured representations for specific laboratory entities (orders, tests) and related patient and instrument data that is unambiguously understood across the healthcare ecosystem. Examples are represented below:

* What must be supported by systems at the class level and what is optional?
* What data must be sent?
* Which data elements belong in each class and must be supported?
* When the data should be sent and how it should be accessible?
* What systems support it and in what?
* What standards can be used (V2, FHIR and Consolidated Clinical Document Architecture (CCDA))

## Recommendation 3: Tooling and Knowledge Management

Every laboratory health IT system lacks a standardized approach, tooling, and the mechanisms necessary to manage various amounts of clinical and device-specific information in safe and interoperable ways. Often, this causes laboratory systems to describe the outcome of identical tests with different and diverging results. In addition, extraordinary amounts of ad-hoc manual procedures are necessary to overcome clinical patient record inconsistencies and reporting differences when participating with public health initiatives. These problems, caused by a void in laboratory semantic interoperability, manifest within clinical care settings as inefficiencies and have a potential negative impact on patient care and safety. Therefore, it is suggested that the entire laboratory ecosystem implement standardized tooling and mechanisms to support more automated and consistent management of fundamental laboratory knowledge.

**Best Practices.** Develop a knowledge management architecture and tools that enable highly reliable laboratory semantic interoperability and promote its adoption and provide real-world value to laboratory systems and clinical care through improvements resulting in:

* The harmonization of how meaningful laboratory terminology standards, such as SNOMED CT® and LOINC® are used.
* The reproducibility of data exchange structures used to express laboratory procedures and outcomes, such as CDISC, FHIR, and IHE LAW.
* The understandability of the laboratory test knowledge as interpreted and processed by supporting health IT systems, such as LIS, LIMS, and EHRs.
* The usefulness of clinical interventions to improve patient care based on relevant laboratory knowledge and reporting data, such as public health reporting and clinical surveillance and research.

It is best practice for all laboratory knowledge management tools and standards to have the integrity and agility necessary to provide meaningful and equitable contributions to laboratory information and management systems, local EHRs, and public health reporting initiatives. In addition, Veteran’s Administration has well-established existing resources, ideas, and thoughts regarding how to design and implement clinical knowledge management ecosystems effectively. Integration of this content into the overall SHIELD Community Roadmap is suggested to produce a solution that is flexible enough to respond to unforeseen pandemics, medical innovations, and emerging pathology research. Below are technologies and specifications which can be tailored to achieve SHIELD’s encouraged goals and best practices.

* **Integrated Knowledge Architecture** – integrates disparate knowledge sources and preserves the meaning of information for the interoperability of EHR-data (i.e., semantic interoperability) that are critical to delivering safe patient care and leveraging standards-based clinical decision support. The integrated knowledge architecture, described in the HL7 Terminology Knowledge Architecture informative ballot21, employs the separation of concerns design principle, whereby a system is divided into distinct sections, such that each section can address separate concerns.
* **Analysis Normal Form (ANF)** – is a model for improved data representation designed to prevent terminology misrepresentations, reduce data variation, increase data integrity, and enhance clinical decision support to ensure patients receive proper care. ANF enhances data association and querying, improving analytical and searching capabilities, and promoting usability and shareability of analytical outcomes.22
* **Terminology Knowledge Architecture** – is a logical architecturedesigned to allow integrating clinical terminology and local concepts to increase the data quality of interoperable clinical information. 21 Quality clinical data enable healthcare systems across the enterprise to conduct robust and meaningful data analysis and improve overall interoperability, which enhances the quality of care across all medical facilities.
* **Highly Reliable Knowledge Management** – employs principles derived from Highly Reliable Organizations that reduce the frequency and severity of system failures leading to preventable patient harm. These principles mitigate difficulties with recognizing equivalence between different standards, representing clinically significant concepts that are needed, preventing the inclusion of errors in clinical data, and ensuring the safe and reliable evolution of terminology standards, solutions, and processes as new technologies and policies emerge.

## Recommendation 4: Creation of an In Vitro Diagnostics Data Hub

RWE has been suggested for use in the post-market evaluation of IVD.23 The provision of an IVD data hub would support the movement toward interoperability in two ways. First, it would create an incentive for IVD manufacturers to assign coding to their products following the guidelines called for in Step 1. Second, the creation of a sustainable national data hub with many laboratory contributions would support data aggregation and use. This multipurpose resource could serve many stakeholders needs provided appropriate safeguards around patient privacy are in place.

The IVD data hub could be modeled after existing data hubs or registries of national clinical subspeciality societies. Data hubs or registries, as a self-sustaining, private-sector activity, will support IVD industry development and provide evidence for the FDA’s evaluation of safety and efficacy. Successful data hubs have developed around surgical and medical products to provide RWE to multiple stakeholders. The registries business model is to collect data once and use them many times. A large literature has developed around Coordinated Registry Networks (CRN) through MDEpiNet, a public-private partnership advancing RWE solutions for stakeholders in the device space.24 A major cost of data hubs is curation of RWD collected as part of routine clinical care (EHR, claims). Historically laboratory data curation has been very time consuming and expensive because of lack of interoperability. Lowering the cost of curation creates a business model for an IVD data hub.

The IVD data hub can be comprised of many clinical laboratories contributing data that is interoperable due to implementation of SHIELD harmonized standards. IVD manufacturers will be able to obtain RWE for research, development, and regulatory decision-making. Although data needs for IVD are less intensive than that of implantable devices, the cost and time needed to produce evidence remain a barrier to manufacturers. An IVD data hub, as a national utility serving the needs of multiple stakeholders can be adapted as a viable business plan to and from other data hubs. An IVD data hub has been suggested to support the transitioning COVID-19 diagnostics from EUA to De Novo or 510(k) marketing authorization using RWE.

**Best Practices.** The following best practices may be considered in the development of an IVD Data Hub:

* Use RWE to evaluate IVDs that have been approved under EUA to consider and facilitate transition to de novo or 510(k) marketing authorization.
* Create an RWE resource for IVD manufacturers.
* Implement SHIELD harmonized standards into clinical laboratories (number to be determined by design specifications) to support evidence needs of IVD manufacturers and others.
* Identify manufacturers with IVD currently marketed under an EUA to collect real-world data (RWD) to support conversion from EUA to de novo or 510(k) marketing authorization as collaborations.
* Identify RWE data sources in clinical systems to evaluate IVD currently marketed under an EUA.
* Develop agreed-upon methods to analyze RWE to evaluate IVD currently marketed under an EUA.
* Widely share learnings for the practical use of RWE in the FDA premarket submission review process.

## Recommendation 5: Communication and Branding

Operationalize coordination, planning, management, and execution of multiple related initiatives across organizations utilizing the appropriate level of support to realize shared vision of laboratory interoperability. Additionally, have transparently targeted stakeholder and data-informed communication with clear channels of engagement and purposeful knowledge sharing.

**Best Practices.**

* Develop a communication component to support implementation of Goal 1 and Goal 2.
* Sustain communications to support ongoing needs for laboratory interoperability.

## Consideration 6: Alignment of Stakeholders

Align government agencies and private-sector partners on a single way forward. Federal agencies are critical to the transformation needed to bring about laboratory data interoperability. An ongoing effort among federal agencies to ensure laboratory interoperability and develop interoperability in other areas is offered. SHIELD encourages forming a forum for ongoing private-sector stakeholder engagement.

**Best Practices.**

* Coordinate the multiple government agency actions while respecting each unique authority and separate funding efforts. Strategic alignment will support policies and programs that promote laboratory interoperability. Develop an ongoing engagement of government agencies for promotion of interoperability of healthcare data.
* Sustain a forum of private-sector partners necessary to ensure laboratory interoperability.
* It is encouraged that this open and evolving forum ensure that private-sector stakeholders have access to transparent information about government efforts to promote interoperability, and the forum should provide ongoing feedback for the broad enterprise.

The strategies and related action needed to transform the U.S. laboratory system would be monitored for accountability. Stakeholders are encouraged to take action to ensure accountability. The plan would provide a framework to track milestones and metrics, to analyze case studies, and to provide critical feedback to all stakeholders to ensure that laboratory interoperability progress is being made.

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This roadmap document integrates the work of many volunteers who contributed in their personal capacity. The views expressed in this roadmap are the contributor’s own and do not necessarily represent the views of any contributor’s employer, the Food and Drug Administration, the Office of the National Coordinator, the Department of Health and Human Services, or the United States government.

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