

Introduction

This report provides guidance on achieving semantic interoperability for *in vitro* diagnostic (IVD) test results. The challenges associated with interoperability, describing current and past efforts, and presenting benefits associated with achieving semantic interoperability are discussed.

The report identifies common terminology required for the following data elements of an IVD test result to enable semantic interoperability:

- Test ordering or reporting identification
- Observation values
- Units of measure
- Specimen identification
- IVD reagent kit and instrument identification

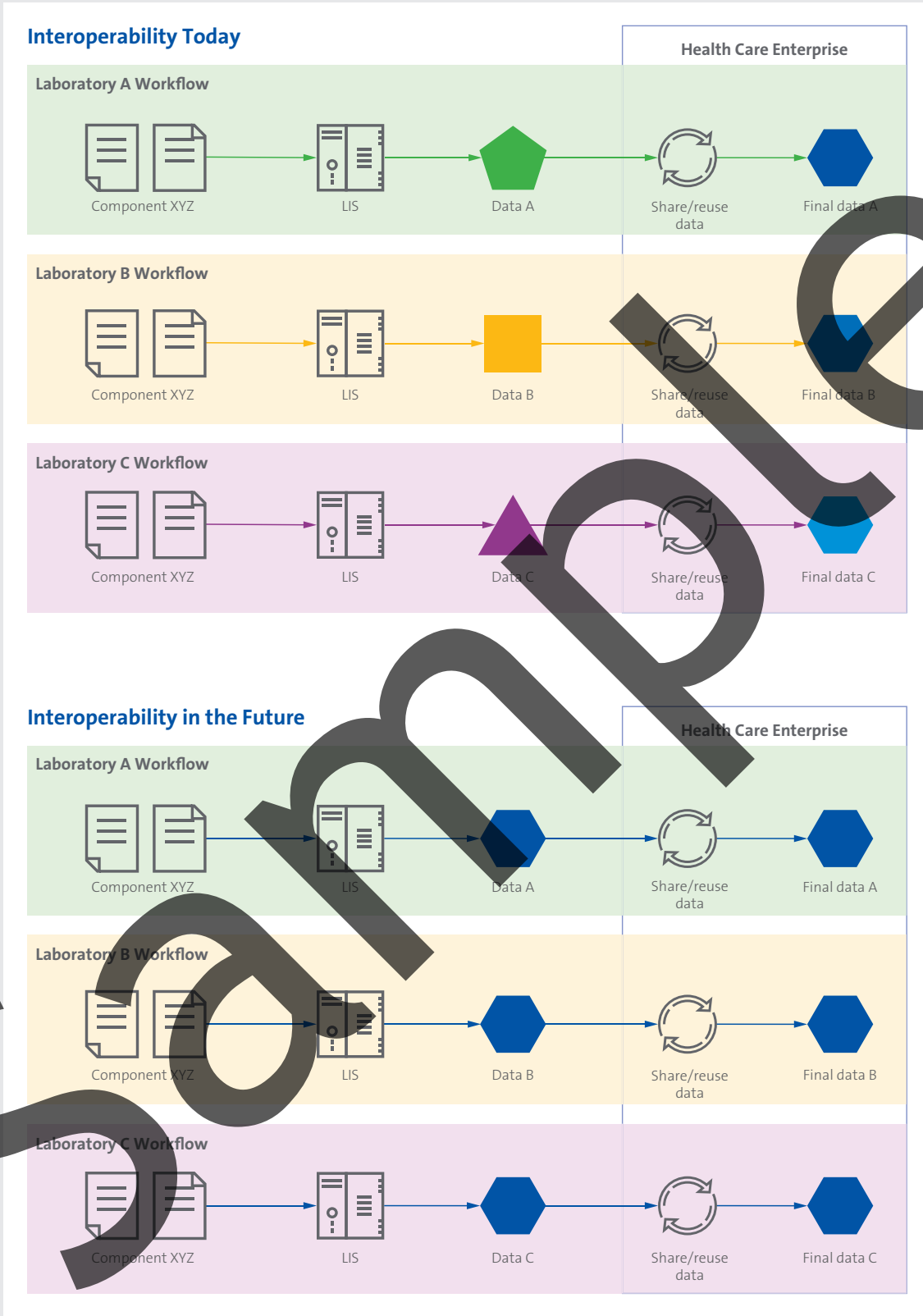
The following standards and representations can be used to provide common terminology, consistent test result data, and consistent transmission for these data elements:

- Logical Observation Identifiers Names and Codes (LOINC^{®a})¹
- Unified Codes for Units of Measure (UCUM)²
- Systematized Nomenclature of Medicine—Clinical Terms (SNOMED CT^{®b})³
- Japan Laboratory Analysis Code version 10 (JLAC10)⁴
- International Classification of Diseases (ICD)⁵
- Nomenclature for Properties and Units (NPU)⁶
- Integrating the Healthcare Enterprise (IHE) Laboratory Analytical Workflow (LAW) profile⁷ (CLSI document AUTO16^{®8})
- LOINC[®] *In Vitro* Diagnostic (LIVD)⁹
- Health Level Seven version 2 (HL7^{®c} v2)¹⁰
- HL7[®] Fast Healthcare Interoperability Resources (FHIR^{®c}) standard¹¹

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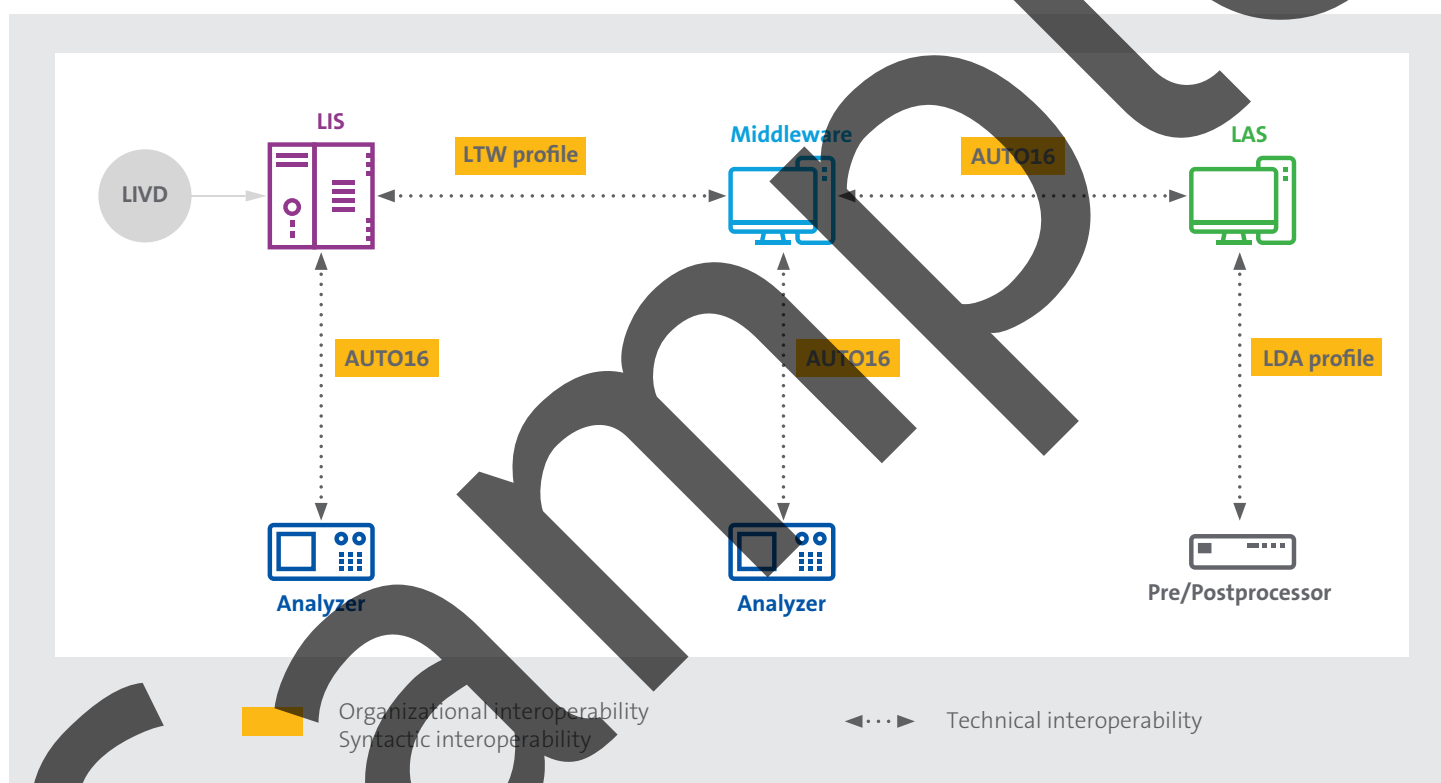


Abbreviation: LIS, laboratory information system.

Figure 1. Comparison of Interoperability Today and in the Future

Standard Supporting Workflow and Data Transfer in the Health Care Ecosystem

This section concentrates on the syntactic and workflow aspects to meet the need for syntactic and semantic standards to support the IVD test result value’s journey through the digital health care ecosystem. CLSI document AUTO16⁸ defines a connectivity standard based on the LAW profile of the IHE organization, which originated from the work of the IICC. In addition to the LAW profile, which covers workflow and syntax to and from the analyzer, CLSI document AUTO16⁸ includes implementation and integration guidance, security considerations, examples, and other supplemental information. AUTO16⁸/LAW (standard messages specifications) and LIVD⁹ (standard “IVD test to LOINC[®]” mappings specifications) are used to assist in the transmission of IVD test results in a standard way to the LIS, which meets the criteria mentioned in the Challenge section: “The objective is to apply data standards in the microtier that are consistent with those specified within the mesotier and macrotier, thus achieving IVD test result semantic interoperability.” AUTO16⁸/LAW and LIVD are two first steps to support the semantic interoperability of IVD tests and test results (see Figure 6).



Abbreviations: LAS, laboratory automation system; LAW, laboratory analytical workflow; LDA, laboratory device automation; LIS, laboratory information system; LIVD, LOINC[®] *in vitro* diagnostic; LTW, laboratory testing workflow.

Figure 6. Relationship of AUTO16/LAW and LIVD

AUTO16⁸/LAW and LIVD provide transport specifications of data elements described in the Data Elements and Their Representations in Standards section above, and the message content supports LOINC[®], SNOMED CT[®], UCUM, and UDIs (DI and PI). LIVD is a standard “IVD test to LOINC[®]” mappings specification that is intended to be used by manufacturers to publish mapping tables. Laboratory personnel use the tables to encode their IVD test data with LOINC[®] and establish UDIs for IVD analyzers and test kits in their laboratory IVD test result messages. The sections below provide further details on LAW and LIVD.

Examples of the Value of Semantic Interoperability

This section identifies several examples of semantic interoperability for laboratory IVD test data when the same test is described the same way across all health care ecosystems. This section describes errors associated with a lack of interoperability and a few interventions designed to mitigate the problem. These examples from industry and public health reporting/surveillance represent highly specific use cases constrained by the lack of consistent implementation of standards for reporting laboratory test results. If the laboratory community were to implement the concepts discussed in this report, it might still be insufficient to preclude several errors in laboratory data interpretation without traceability. Much work is needed to reach agreement on the best process to achieve this goal.

Use of Real-World Evidence in a US Food and Drug Administration Premarket *De Novo* Application for Computer-Assisted Triage Software

RWD were used to decrease the cost and time for FDA's premarket approval of a *de novo* application. The computer-assisted triage software notifies an on-call neurosurgeon or specialist of a potential stroke in patients. Traditionally, the application would require a multireader multicase (MRMC) study to demonstrate the safety and effectiveness of the device. MRMC clinical studies are expensive and time consuming, typically including hundreds of patient cases read by 20 to 30 reviewers over numerous sessions to evaluate the device's performance. For this computer-aided triage device, RWE was used in lieu of the MRMC studies. The triage software is designed to improve the time to notification or treatment of patients in time-sensitive scenarios without affecting reader performance. The applicant compared RWE (time to notification under the current standard of care) with the measured time to notification for the subject device. Stand-alone testing estimated the performance of the subject device to a test dataset with known ground truth to measure the sensitivity and specificity of the device in the intended patient population. These data were then used to justify the device benefit of effective triage (ie, timely care of the patient), and a *de novo* was granted.⁸² Cost saving and faster approvals could result in devices being available sooner, and the cost saving might be reflected in the cost of the device. Although this approval was for a radiology device, similar benefits may be applicable to laboratory IVD devices.

Detection of Medical Errors

Incompatibility of data exchange between an IVD testing device and the LIS resulted in erroneous reporting of false-negative results (low values) in the patient's EHRs and may have been the contributing factor in one death. An immunoassay analyzer was configured to report the results as nanograms per milliliter, but the LIS was configured to report units of nanograms per liter.⁸³ Another factor was that although the LIS's primary sample type was set as serum, the analyzed specimen was plasma. When test orders on serum specimens were requested on the immunoassay analyzer, incorrect results and values with default units of nanograms per liter were transmitted to the LIS. If the IVD device had been capable of transmitting the manufacturer-defined data (serum specimen reported with nanograms per milliliter) to the LIS, this type of translation error might have been avoided. The customer should perform LIS vs analyzer result analysis and verification before processing live patient samples and perform quality checks of data, processes, systems, and interfaces before tests go live and at regular intervals to catch any issues when updates occur up or downstream that may affect patient results.