SHIELD
Systemic Harmonization and Interoperability Enhancement for Lab Data

FDA U.S. FOOD & DRUG ADMINISTRATION

A Pragmatic Approach to Harmonizing *in vitro* Diagnostic (IVD) Laboratory Data:

Semantic Interoperability Consensus Standard Development, Adoption and Implementation

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Center for Devices and Radiological Health
Food and Drug Administration

CIIC Meeting, January 10-12, 2018

SHIELD Mission

(Systemic Harmonization & Interoperability Enhancement for Lab Data)

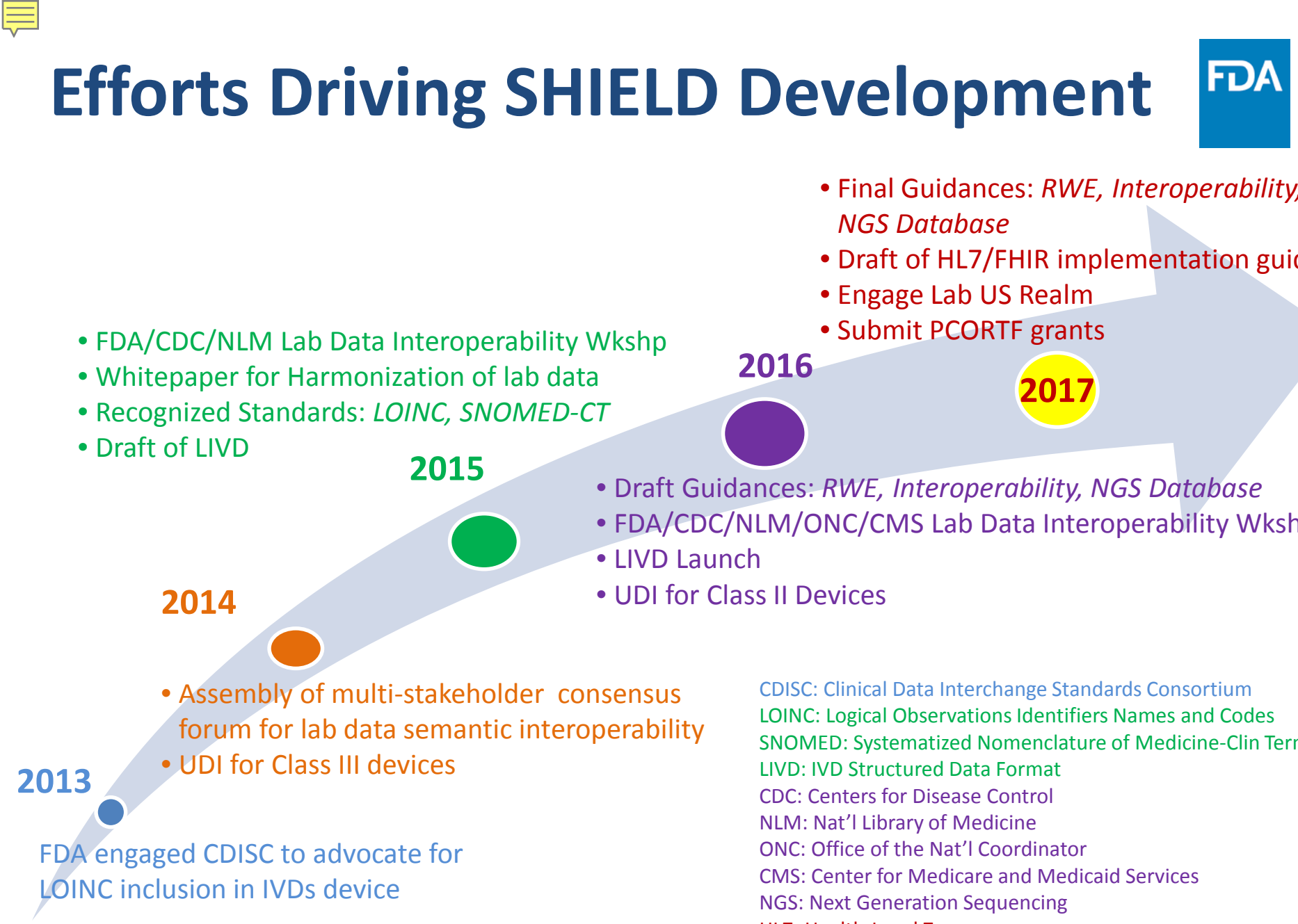
SHIELD supports efforts to harmonize and harness *in vitro* diagnostic (IVD) data sources to:

- support regulatory decisions and sponsor actions throughout the Total Product Life Cycle (TPLC),
- reduce burdens to the healthcare ecosystem and
- promote development of innovative solutions to public health challenges.

SHIELD Stakeholders:

FDA (CDRH, CDER, CBER), CDC, NIH, ONC, CMS, IVD Manufacturers, EHR Vendors, Laboratories, Standards Developers, Academia

Efforts Driving SHIELD Development



CDISC: Clinical Data Interchange Standards Consortium
LOINC: Logical Observations Identifiers Names and Codes
SNOMED: Systematized Nomenclature of Medicine-Clin Terms
LIVD: IVD Structured Data Format
CDC: Centers for Disease Control
NLM: Nat'l Library of Medicine
ONC: Office of the Nat'l Coordinator
CMS: Center for Medicare and Medicaid Services
NGS: Next Generation Sequencing
HL7: Health-Level 7
FHIR: Fast Healthcare Interchange Resource
PCORTF: Patient-Centered Outcome Research Trust Fund

Semantic Interoperability Importance

1. ***Laboratory consistency:***
   - Decision support/knowledge generation
   - Public health reporting
   - Real-time epidemiology *(including outbreaks)*
   - Laboratory cost savings
   - Signal detection
2. ***Adverse events:***
   - Reduction in coding errors
3. ***FDA:***
   - Post-market information *(w/ Unique Device Identifiers (UDI))*
   - Earlier IVD clearance
4. ***Other…***

Semantic Interoperability Importance

Significant Laboratory Cost Savings

American Clinical Laboratory Association

	Estimated 10 providers per group practice			Estimated 20 providers per group practice		
	Initial Development	Annual Maintenance	Cost for first 5 years	Initial Development	Annual Maintenance	Cost for first 5 years
Current manual Process	$3,226,083,120	$322,608,312	$4,516,516,368	$1,613,041,560	$161,304,156	$2,258,258,184
With eDOS	$806,520,780	$80,652,078	$1,129,129,092	$403,260,390	$40,326,039	$564,564,546

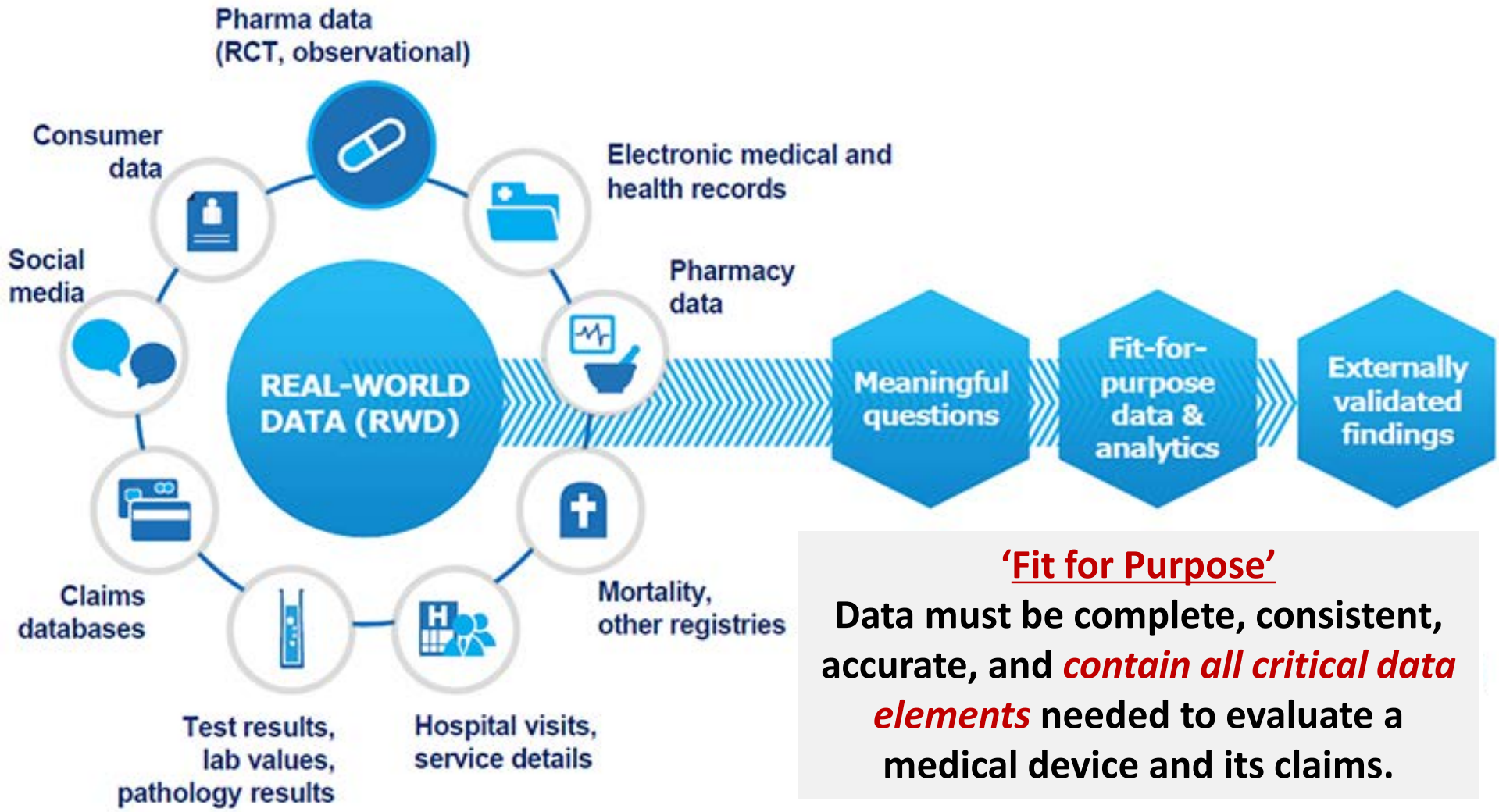
https://www.acla.com/acla-shares-edos-cost-saving-estimate-with-office-of-the-national-coordinator-for-health-it/

Reduction in Adverse Events

Device: Immunoassay System Analyzer
Problem: Low tropoinin test results
Adverse Events: 1 death; 120 patients mistreated

*"false negative troponin… **120 patients were negatively impacted** … results were sent to the LIS as ng/mL, but… the LIS was configured to report… units of ng/L… results… were reported out of the LIS labeled as ng/L; thus resulting in erroneously low patient results."*

Finding Utility from RWD/RWE



'Fit for Purpose'

Data must be complete, consistent, accurate, and *contain all critical data elements* needed to evaluate a medical device and its claims.

KEY: Coordination/Harmonization (Interoperability)

Finding /RWE

Harrison playing Solo.

'Fit for Purpose'

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KEY: Coordina nteroperability)

Perspective on IVDs

- *In vitro* diagnostics (IVDs) products are… intended for use in diagnosis of disease or other conditions... [21 CFR 809.3]

- Fundamentally, IVDs ask a 'question' of a specimen taken from a human body.

- The result that follows is the 'answer' to that question.

Some Nuances Unique to IVDs

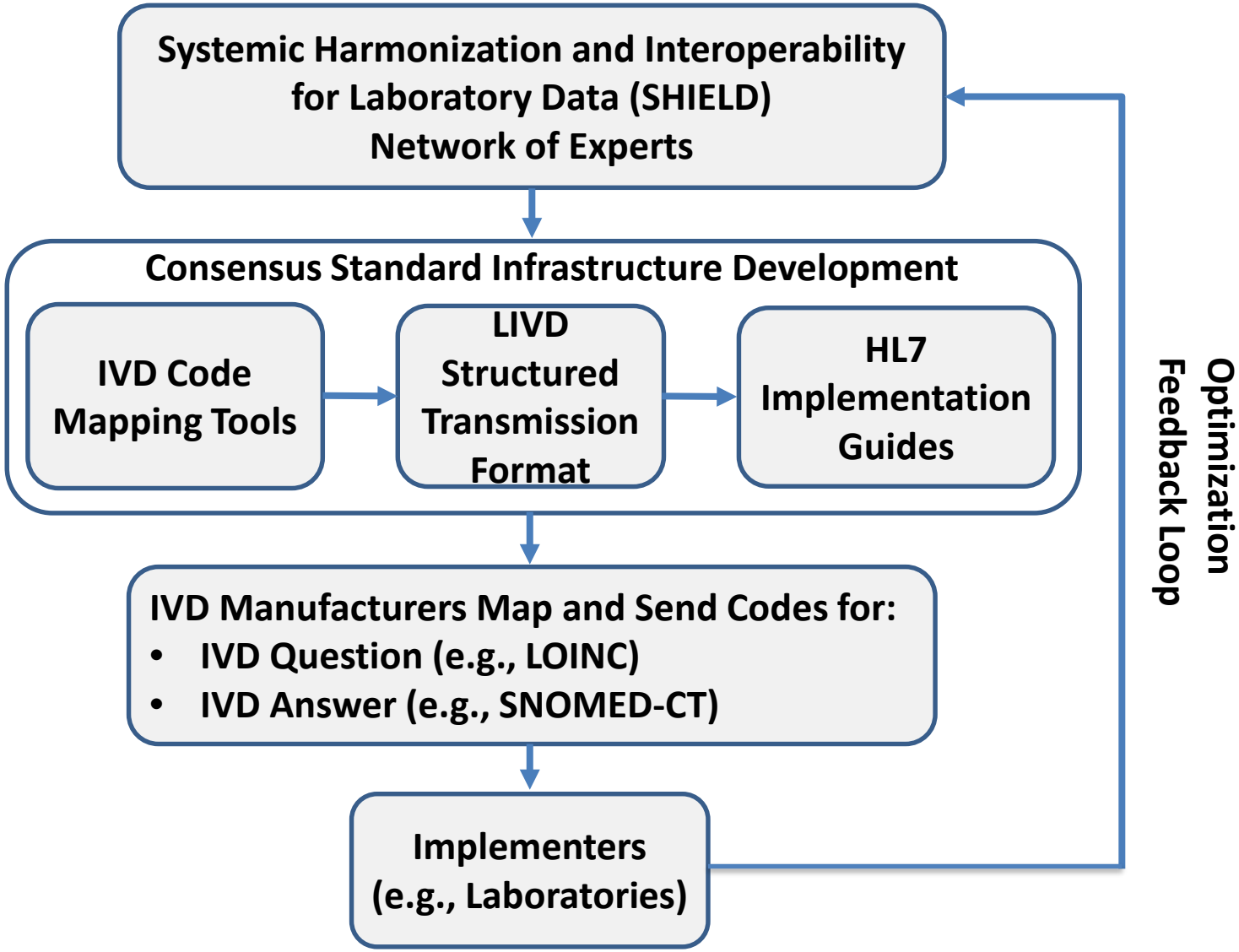
- Labs operate under the Clinical Laboratory Improvement Amendments (CLIA) regulations
- CMS oversees labs through the College of American Pathologists (CAP) lab accreditation program Labs regularly conduct proficiency testing of CAP panels and submit results to CAP (for most tests)
- Labs conform to Good Laboratory Practices (GLP; 21 CFR 58 & 42 CFR 493)
- Labs have to validate off-label use and Laboratory Developed Tests (LDTs)

SHIELD Infrastructure

Function	*Candidate Coding*	*Elements (partial list)*	*Transmission Format*
Describe IVD device/method type ***Question***	LOINC (Logical Observations Identifiers Names and Codes)	Component Property Time System Scale Method	Structured Data Format -LIVD
Describe IVD device/method result ***Answer***	SNOMED-CT *(or appropriate alternative)* (Systematized Nomenclature of Medicine – Clinical Terms)	Detected Not Detected Inconclusive Test Not Completed	Structured Data Format –LIVD II
	UCUM (Unified Code for Units of Measure)	Units of Measures (e.g. grams, etc.)	Structured Data Format –LIVD II
Unique Device Identification ***Who's asking?***	UDI (FDA Unique Device Identification System)	Device Identifier Elements of UDI	Structured Data Format -LIVD

Associated data populated into Laboratory Information Systems (LISs) can be queried. Fast Healthcare Interchange Resource (FHIR) implementation guide is near completion.

Building Valuable Infrastructure



Ongoing SHIELD Efforts

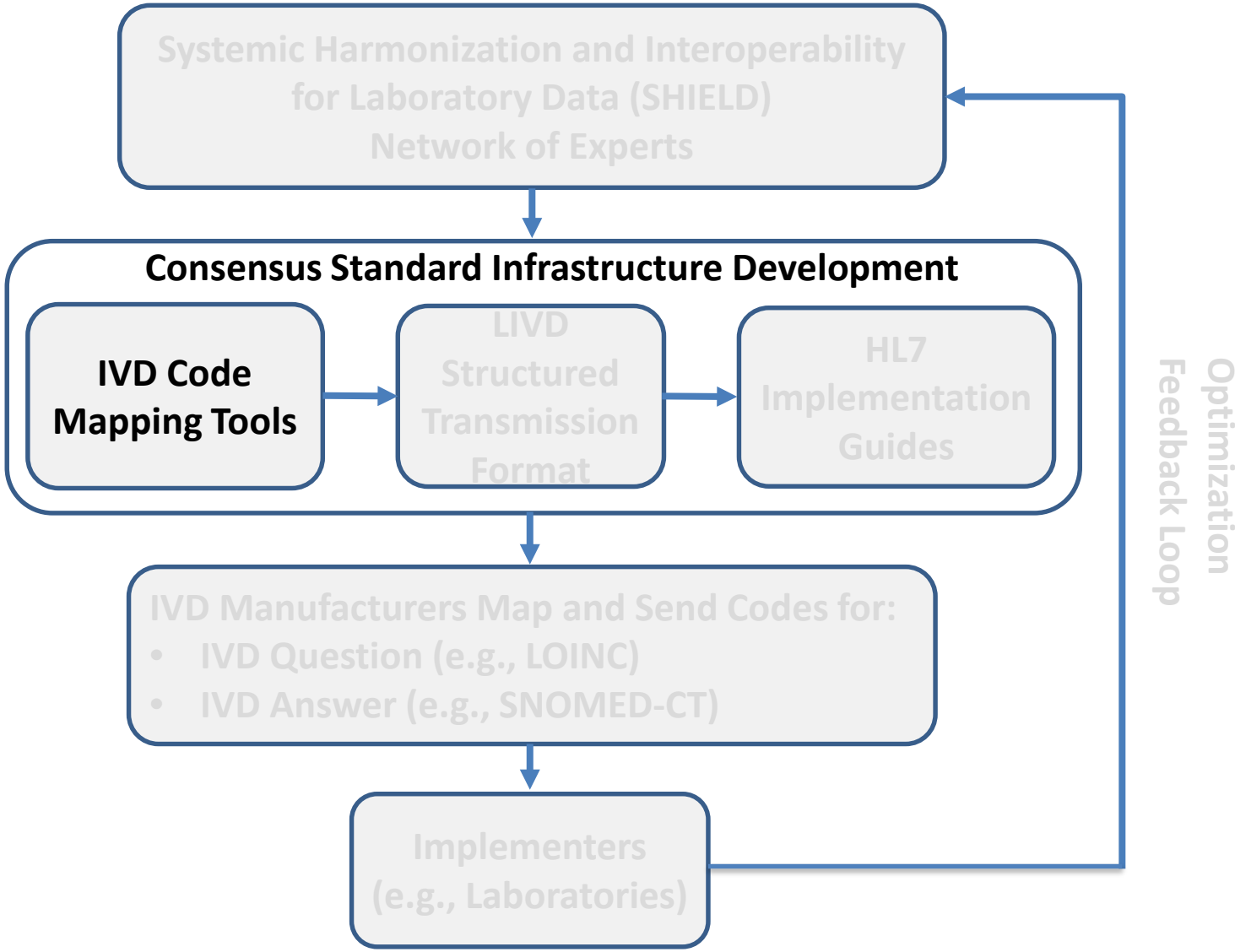
1. Developing tools for the application of semantic standards in structured data formats through:
   - step-by-step manual defining how to map LOINC to IVD devices
   - MDIC/Industry/Laboratory/Government Clinical IVD Semantic Interoperability Meeting – Value Sets (LIVD II)

2. FDA is developing regulatory guidance and inter-Office/Center infrastructure to determine how/when regulatory grade Real-World Evidence (RWE) can be leveraged in regulatory decisions.

Involved Stakeholders:

FDA (CDRH, CDER, CBER), CDC, NIH, ONC, CMS, IVD Manufacturers, EHR Vendors, Laboratories, CAP, Standards Developers, Academia

Building Valuable Infrastructure



IVD Test LOINC Code Harmonization

Manufacturer	Assay	Assay Test Result (according to PI)	LOINC Code (Vendor)	LOINCs used by labs (lab name)	APHL recommended LOINC
M1	HIV Ag/Ab Combo	Reactive Nonreactive	56888-1	56888-1 (L1, L2)	56888-1
M1	HIV O Plus	Reactive Nonreactive	57975-5 =HIV 1+O+2 Ab Fld Ql		48345-3
M2	HIV-1 Western Blot (CLIA high complexity assay)	Positive Negative Indeterminate			PLT599
M3	HIV-1 RNA Qualitative Assay	Reactive Nonreactive Invalid	5018-7 = HIV1 RNA XXX Ql PCR 5017-9 = HIV1 RNA Bld Ql PCR		25835-0
M4	HIV-1 DNA and RNA Qualitative Detection by PCR, Plasma			48023-6 =HIV 1 proviral DNA SerPl Ql PCR (L1)	79379-4

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M2	HIV-1 Western Blot (CLIA high complexity assay)	Positive Negative Indeter			PLT599
M3	HIV-1 RNA Qualitative Assay	Reac Nonre Inva	5018-7 = HIV1 RNA XXX Ql PCR 5017-9 = HIV1 RNA Bld Ql PCR		25835-0
M4	HIV-1 DNA and RNA Qualitative Detection by PCR, Plasma			48023-6 =HIV 1 proviral DNA SerPl Ql PCR (L1)	79379-4

IVD Infectious Diseases LOINC Mapping Manual

Logical Observation Identifiers Names and Codes (LOINC®)

Guide for Using LOINC Microbiology Terms

IVD Infectious Diseases LOINC Mapping Manual

Components*:

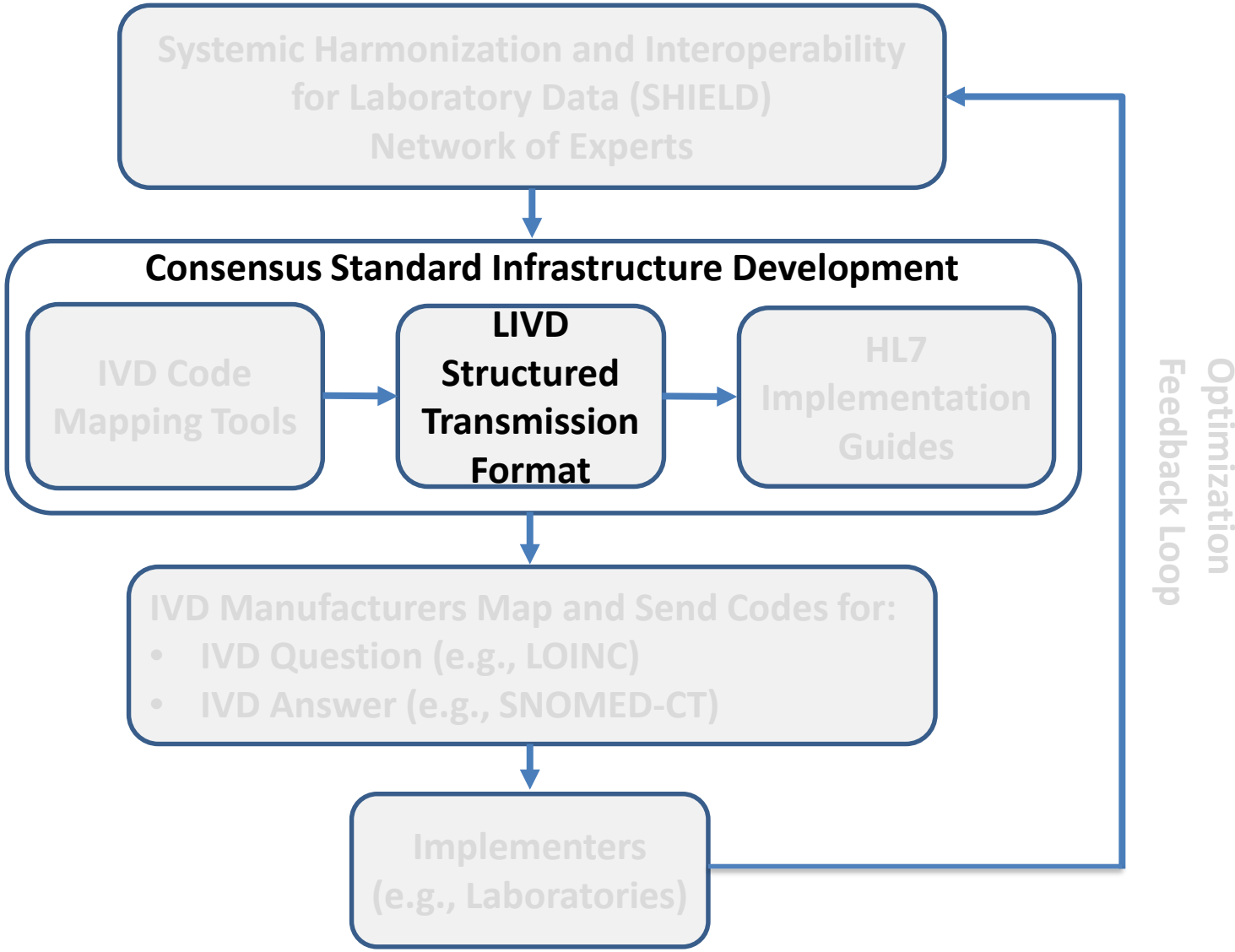
- Background/ Appendix
- Microscopic Examination
- Cultures
- Susceptibility Testing
- Resistance Testing
- Antigen Tests
- Nucleic Acid Tests
- Serology Testing

Includes but is not limited to.

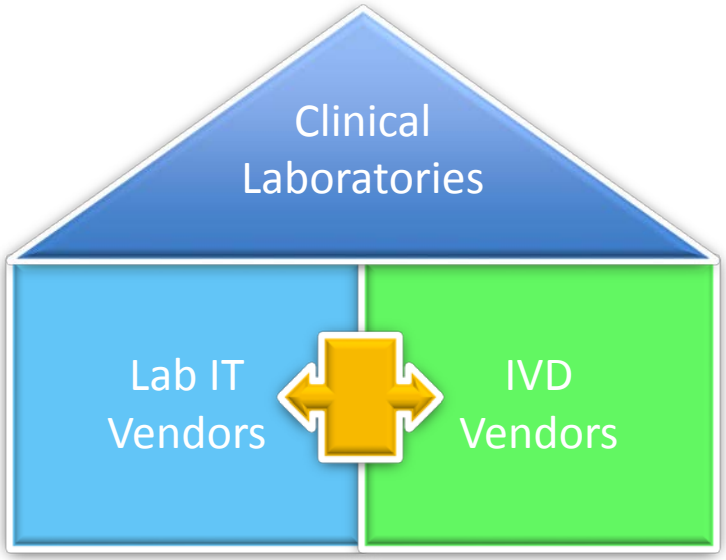
Features*:

- Mapping Examples
  - Examples in the manual
  - Link to externally populated
- How to deal with:
  - Qualitative/ Quantitative Assays
  - Multiplex Assays
- Mapping Validation

Building Valuable Infrastructure



Digital Format for LOINC to IVD (LIVD)



MEDICAL DEVICE INNOVATION CONSORTIUM

Clinical Dx IVD Semantic Interoperability Meeting

Friday, July 22, 2016

IVD Industry Connectivity Consortium (IICC) Mission:

- Modernize connectivity between laboratory IT systems and analyzers
- Enable clinical laboratories to achieve more and spend less

Members: Abbott Laboratories, A&T, Beckman Coulter, Beckton Dickinson, bioMérieux, Data Innovations, Hitachi, IZASA SA, Orchard Software, Ortho Clinical Diagnostics, Roche Diagnostics, Samsung, Siemens Healthcare Diagnostics, Sunquest Information Systems, and Systelab Technologies SA.

Digital Format for LOINC to IVD (LIVD)

Column Header	Comments
Publication Version ID	
Manufacturer	Sortable column could be used if spreadsheet form multiple manufacturers are combined into one
Model	
Equipment UID	Leave empty if no universal ID
Equipment UID Type	
Vendor Analyte Code	
Vendor Analyte Name	
Vendor Specimen Description	
Vendor Result Description	
Vendor Reference ID	Leave empty if no additional vendor reference
Vendor Comment	Leave empty if no vendor comment
LOINC Code	Leave empty if no LOINC mapping
LOINC Long Name	Leave empty if no LOINC mapping
Component	Leave empty if no LOINC mapping
Property	Leave empty if no LOINC mapping
Time	Leave empty if no LOINC mapping
System	Leave empty if no LOINC mapping
Scale	Leave empty if no LOINC mapping
Method	Leave empty if no LOINC mapping

HL7 is creating a Data Analysis Model (DAM) for LIVD

LIVD Contributors

Authors

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Participating Organizations

Abbott Laboratories
Advanced Medical Technology Association (AdvaMed)
Association of Public Health Laboratories (APHL)
BD Life Sciences
bioMerieux
Cerner Corporation
Epic
Geisinger Health Systems
HL7 Orders and Observations Working Group
IHE Pathology and Laboratory Medicine (PaLM) Technical Committee
Intelligent Medical Objects, Inc
IVD Industry Connectivity Consortium (IICC)
Medical Device Innovation Consortium (MDIC)
National Laboratory of Medicine
Orchard Software
Phast
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Swiss Laboratory Interoperability Interest Group (Joint Venture of FAMH.ch, IHE-Suisse.ch, HL7.ch, SULM.ch)
U.S. Centers for Disease Control and Prevention (CDC)
U.S. Food and Drug Administration (FDA)
Vernetzt, LLC

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LAUNCHED JUNE 1st, 2017

http://ivdconnectivity.org/livd/

Participating

Abbott Laborat
Advanced Medical Technology Association (AdvaMed)
Association of Public Health Laboratories (APHL)
BD Life Sciences
bioMerieux
Cerner Corporation
Epic
Geisinger Health Systems
HL7 Orders and Observations
IHE Pathology and Laborator
Technical Committee
Intelligent Medical Objects, Inc

m (IICC)
Medical Device Innovation Consortium (MDIC)
National Laboratory of Medicine
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U.S. Centers for Disease Control and Prevention (CDC)
U.S. Food and Drug Administration (FDA)

FDA Perspective on LOINC for IVDs

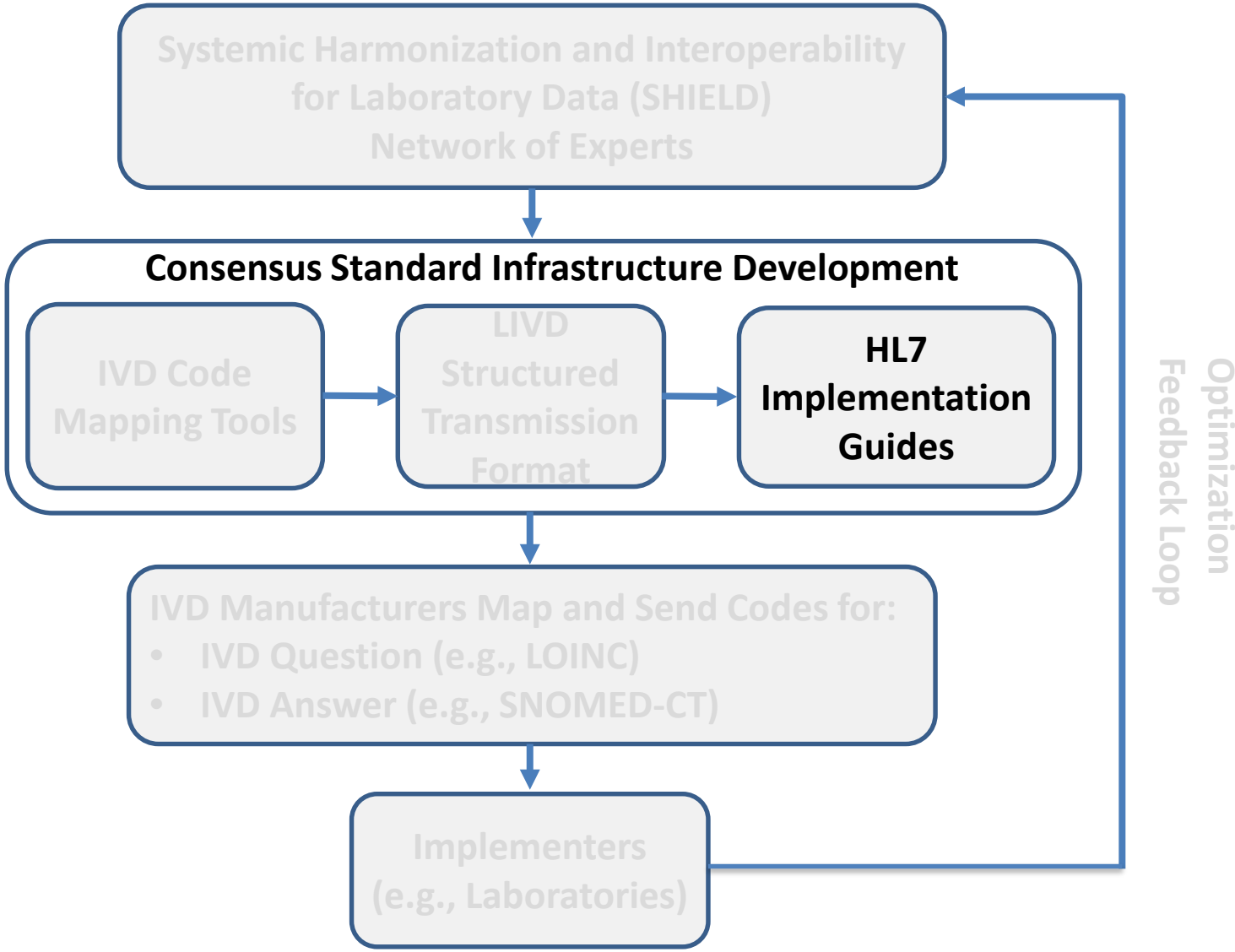
1. **Any similar coding system for characterizing IVDs (e.g., LOINC) is voluntary and will not be required or reviewed by FDA**
   (distinct from the required FDA-accredited UDI system*)

2. **FDA strongly encourages use of FDA-recognized consensus standard structured data format to communicate IVD descriptive coding.**
   - Distribution of LOINC coding *by manufacturers* that suggests an unapproved/uncleared Indication for Use (i.e., off-label use) could result in the device being considered adulterated and/or misbranded.
   - Laboratories and/or other users must fulfill their obligations, including (but not limited to) any statutes, regulations, and validation procedures that must be complied with when making the results from the off-label uses available to those requesting the test.

3. **A 3rd party resource for codes (and coding) could aid in harmonization efforts (*e.g., Regenstrief*)**

*https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/UniqueDeviceIdentification/

Building Valuable Infrastructure



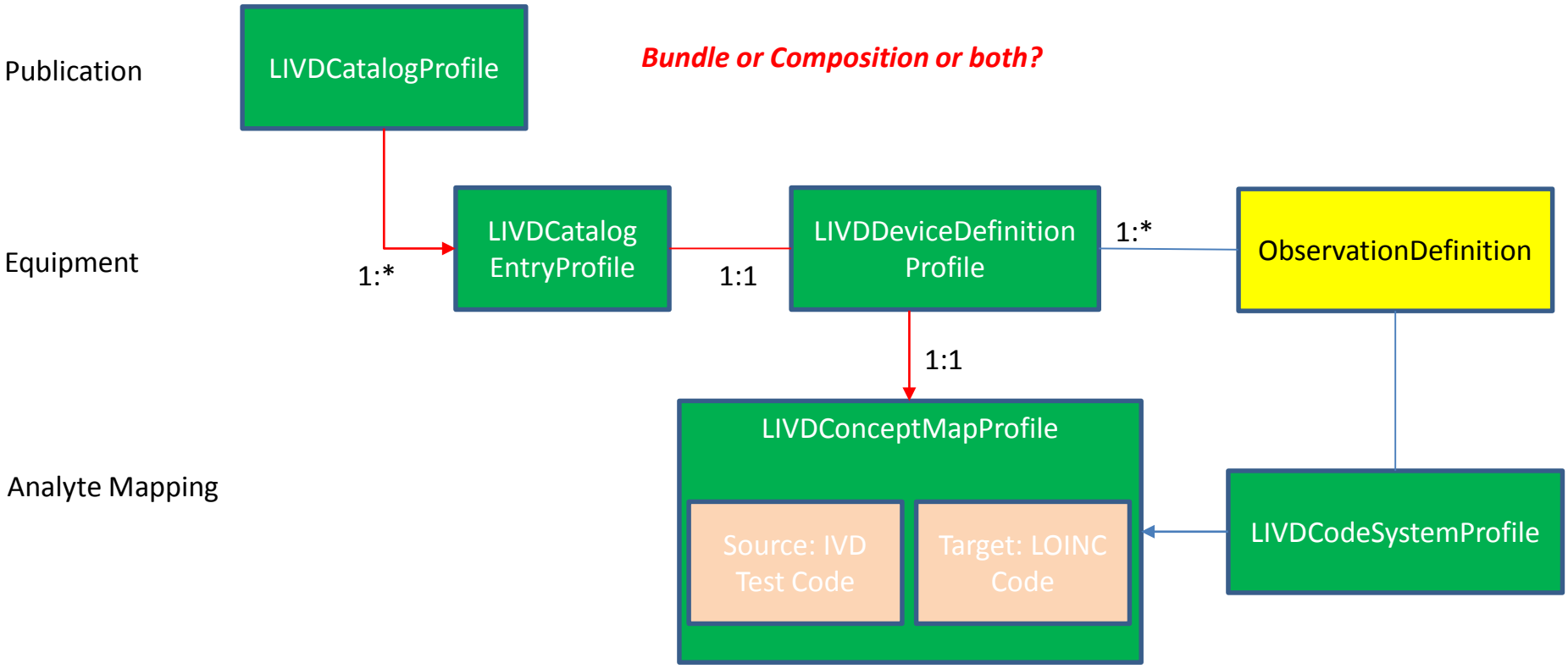
LIVD on FHIR Implementation Guide

- Express the LIVD – Digital Format Publication of LOINC to Vendor IVD Test Results whitepaper in FHIR

- From more general JSON expressions to FHIR resources
  - Propose changes to core resources
  - Create profiles to constrain resources to LIVD requirements
  - Work with the Catalog project

- Future proofing
  - Opportunities to use for service-based APIs.
  - Consistency with other Lab focused FHIR based capabilities.

LIVD on FHIR Summary



Lab US Realm: Foundations*

- Holistic approach to defining requirements during development
- Provides minimum end-to-end interoperability "out of the box"
- Extensible Profile and Component messaging architecture
  - Builds on existing HL7 V2 capabilities, defines explicit use cases and their unique requirements
  - Messages can support multiple (non-conflicting) use cases with no ambiguity for receiving systems interested in only one aspect
  - Allows for incremental interoperability based on need vs. "all systems shall" approach to specifications
- CLIA requirements "baked in" across scope of transactions at core level
  - Orders requirements defined and mapped
  - Results requirements defined and mapped

*2016 ONC Annual Meeting: Committed to Better Health through IT

Clinical IVD Value Set Meeting

FDA

MDIC

SHIELD
Systemic Harmonization and Interoperability Enhancement for Lab Data

Clinical IVD Value Set Harmonization Meeting

Meeting Date and Time

January 22, 2017
8:00am – 5:00 pm EDT

January 23, 2017
8:00am – 12:00 pm EDT

Meeting Location
FDA White Oak Campus
Building 32, Room 1305

10903 New Hampshire Avenue
Silver Spring, MD 20993

Contacts:
Carolyn Hiller, *MDIC Clinical Dx Program Manager*
Office: 952-314-4327

Michael Waters, *SHIELD Team Lead*
Office: 301-796-4653

GOAL: Collaborate to improve laboratory data interoperability to advance patient care. This effort should expedite health care research and practice (e.g., outbreak surveillance; real-world evidence (RWE) generation; decision support etc.) through additional unification of *in vitro* diagnostic (IVD) data. The meeting will address practical limitations of IVD semantic interoperability implementation, with a focus on recommendations for adoption of ordinal value sets (answer lists) for qualitative and semi-quantitative tests and discrete units for quantitative test values. The overarching goal is to improve electronic health record (EHR) interoperability to help protect and preserve public health.

Summary

RWE Opportunity:

- There is a wealth of data siloed in data repositories (e.g., electronic health records - EHRs) that *may* be valuable in regulatory decisions.

Problems:

- Lack of interoperable infrastructure in data repositories is repeatedly cited as a significant impediment to accessing and using RWE.
- Insufficient resources exist to develop infrastructure.

Solutions:

- Improve interoperability by developing infrastructure that will enable RWE access.
- Development by a multi-stakeholder consensus forum, leveraging existing infrastructure.
- Focus efforts on building valuable infrastructure identified by stakeholders.

Conclusions/Requests

- Pragmatic adoption and implementation of semantic interoperability standards for IVDs is essential for enabling the development of 21st century healthcare solutions.
- SHIELD implementation can unlock meaningful RWE siloed in data repositories which *may* be leveraged in regulatory decisions.
- FDA is engaging in multi-agency/stakeholder efforts to assist in the adoption of semantic interoperability standards and structured data formats.
- Collaboration and support is critical to realizing the benefits of these efforts.

Questions/Comments?

Contact: Michael.Waters@FDA.hhs.gov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