Semantic Harmonization and Interoperability Enhancement for Laboratory Data (SHIELD):

A Pragmatic Approach to Accessing *in vitro* Diagnostic (IVD) Real-World Evidence (RWE)

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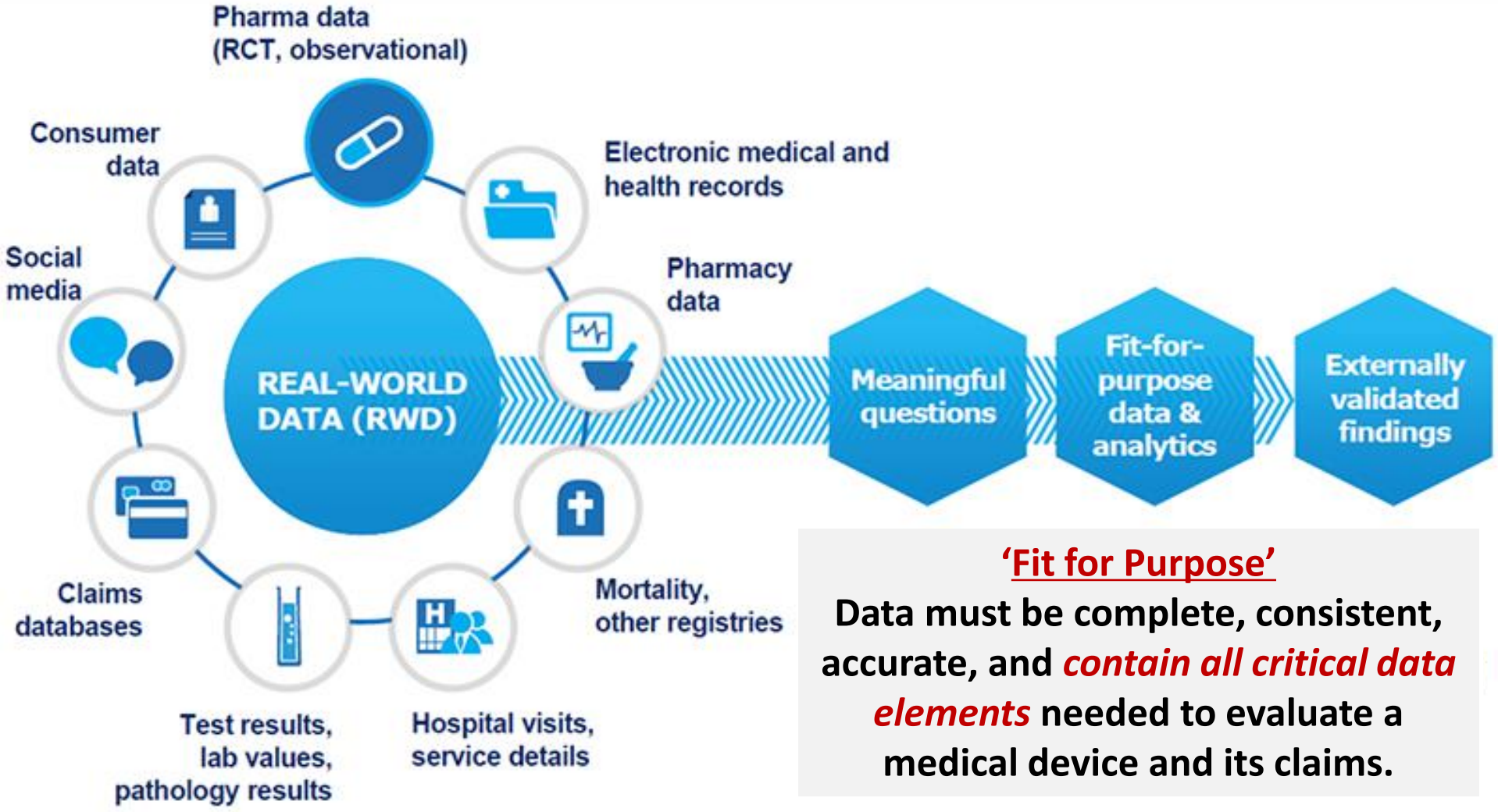
Finding Utility from RWE



'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)

Successful Pre/Post-Market Examples

(partial summary from tracked submissions leveraging RWE)

RWE Use

New pre-market indications

PMA approval

de novo granting

510(k) clearance

Pivotal trials

Post-market surveillance

Pre- and post-market controls

indication expansion (primary and secondary)

post-market studies

evaluate labeling claims and secondary effectiveness outcomes

HDE-to-PMA conversion

Response to a final classification order

Bayesian analysis with RWE

RWE Data Sources

Electronic Health Records (EHRs)

Sponsor registries

National registries

Hospitalization records

Public databases

CMS claims database

OUS device data

RWE Post-market study

Remote-monitoring

Retrospective studies

OUS Clinical case summaries and chart data

National Death Index

Device-generated data

Medical records

Private databases

Real-world Literature

State-run routine screening programs

International biobanks

Optimizing RWE Utility/Value

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.

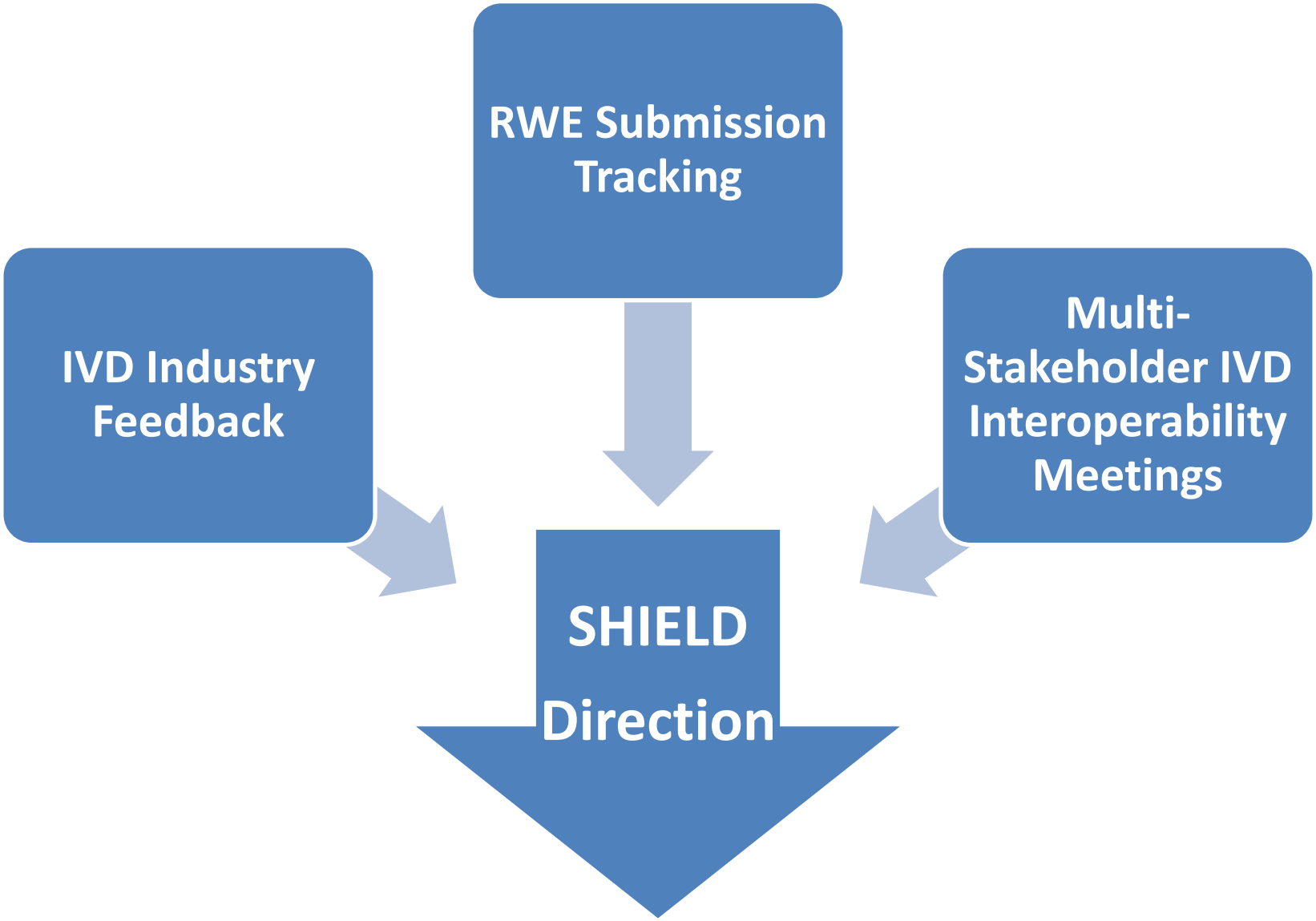
Problems:

- 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.

Building Valuable Infrastructure



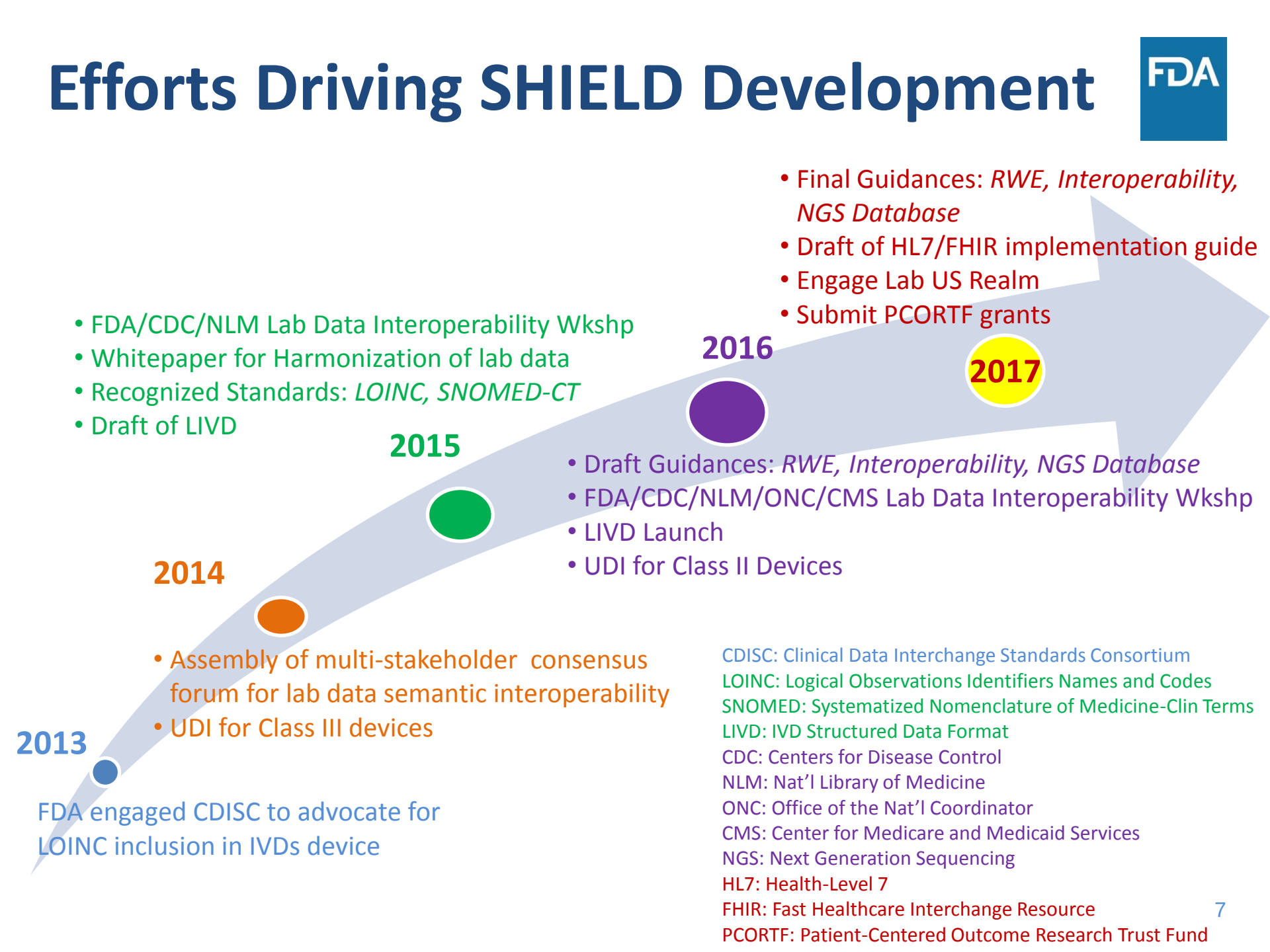
SHIELD Mission

(Systemic Harmonization & Interoperability Enhancement for Lab Data)

Support efforts to harness non-traditional *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.

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

What IVDs Do?

- *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.

Semantic Interoperability Standards*

LOINC® *– Logical Identifiers, Names and Codes*

SNOMED-CT *– Systematized Nomenclature of Medicine – Clinical Terms*

UCUM *– Unified Code for Units of Measure*

UDI *– Unique Device Identification*

LIVD *– Digital Format for Publication of LOINC Vendor IVD Test Results*

HL7/FHIR *– Health Level 7; Fast Healthcare Interchange Resource*

**All internationally used (except LIVD) and aligned with several critical standards/nomenclatures (e.g., ISO; ANSI; GMDN)*

SHIELD Infrastructure

Function	*Candidate Coding*	*Elements (partial list)*	*Transmission Format*
Describe IVD device/method type	LOINC (Logical Observations Identifiers Names and Codes)	Component Property Time System Scale Method	Structured Data Format -LIVD
Describe IVD device/method result	SNOMED-CT (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	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.

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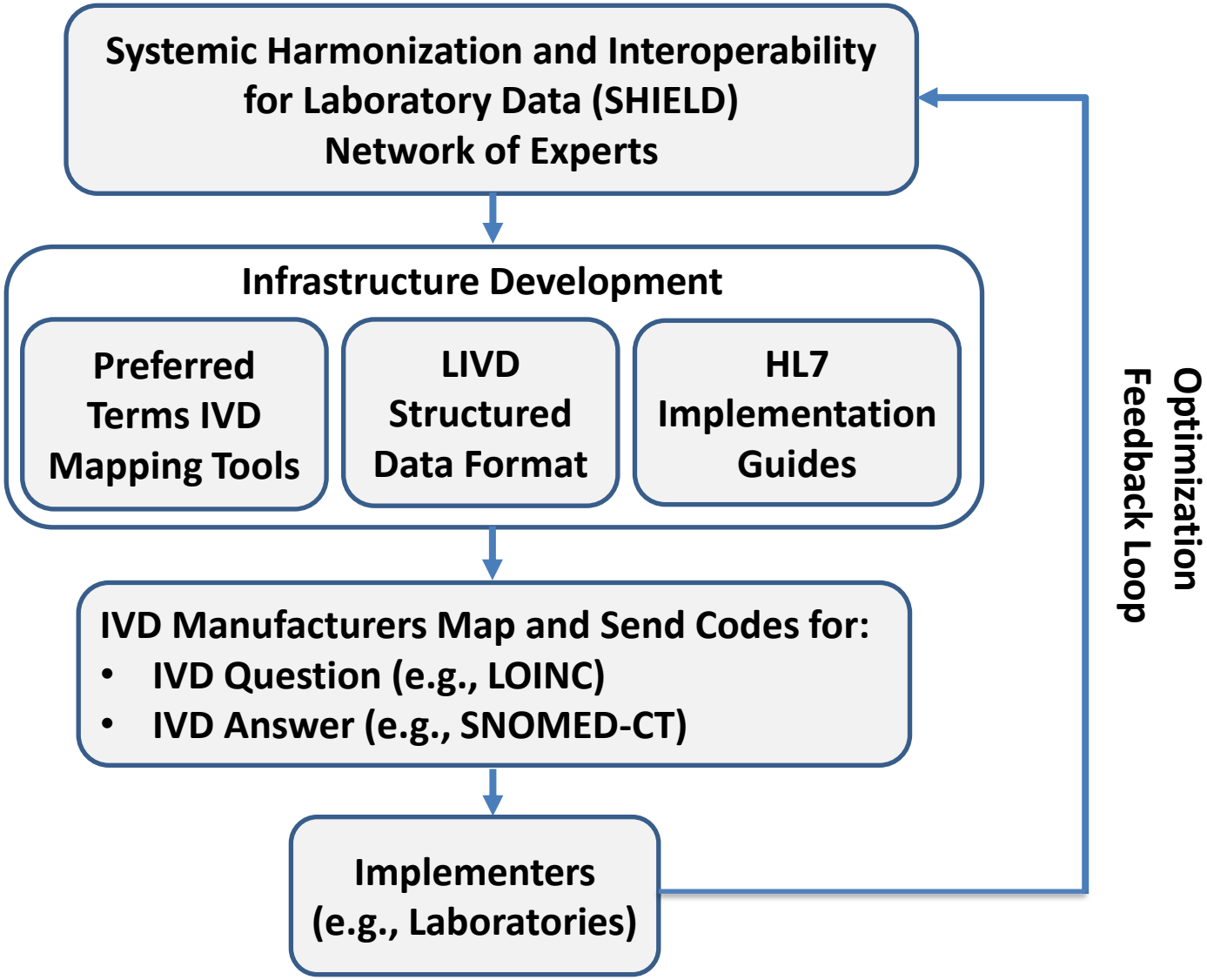

Lab Data Interoperability/RWE/TPLC

SHIELD Aims to:

Improve decision support, real-time epidemiology, healthcare cost savings, access Real-World Evidence (RWE) throughout the Total Product Life Cycle (TPLC) and more…

OIR is currently:

- Engaging in cross-center multi-stakeholder consensus efforts to aid the adoption of semantic interoperability and structured data format standards into lab workflow.
  - Unambiguous step-by-step manual defining how to map LOINC to IVD devices
  - Clinical IVD Semantic Interoperability Meeting – Value Sets *(Jan. 22-23, 2018)*
  - Actively writing grants to support laboratory data interoperability efforts

- Providing guidance on how to leverage RWE and safely disseminate data harmonization information to increase access to meaningful RWE.

Critical Involved Stakeholders:

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

IVD Infectious Diseases LOINC Mapping Manual

Objective:

Collaborate with stakeholders in the development of an ***unambiguous step-by-step manual defining how to map LOINC to IVD devices*** intended to identify and evaluate infectious disease agents.

Proposal:

- Develop a standardized document/manual to include:
  - processes, examples of all types of Microbiology IVDs, tools for LOINC adoption in microbiology
  - Mechanisms to solicit new LOINC codes
- Pilot manual clinical laboratories
- Coordinate with key stakeholders to attain input (Industry, EHR vendors, CDC, ONC, CMS, etc.).
- Post manual feedback, revision, implementation, support

Help Us to Help You

To focus efforts pragmatically, please let us how we can support your efforts to leverage RWE by:

- Sending a *pre-submission** describing how you would like to leverage RWE in a regulatory submission.
- Get involved in multi-stakeholder efforts to adopt/develop and pilot data harmonization standards.

Questions/Comments?

Contact: Michael.Waters@FDA.hhs.gov


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