Importance of Logical Identifiers, Names and Codes (LOINC®) in Developing *in vitro* Diagnostic (IVD) Infrastructure to Support a National Evaluation System for health Technology (NEST)

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Overall Goals

FDA

Support efforts to harness non-traditional data sources (e.g., data collected from clinical experience) to:

- **support regulatory decision making,**

- **reduce burdens to the healthcare ecosystem and**

- **promote development of innovative solutions to public health challenges.**

Supporting Meaningful Data Access: IVD Code Harmonization (Semantic Interoperability)

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Semantic interoperability for IVD tests, is essential to enabling multi-source laboratory data access and advancing health information technology.

- The ***unambiguous and consistent representation of laboratory tests (and results)*** can drive the development of decision support tools and disease monitoring systems, provide 'real-world evidence' of safety and effectiveness and far more.

- **Focus on the adoption of Logical Observations, Identifiers, Names and Codes (LOINC®)**

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...*

Outline

FDA

1. Using Real-World Data/Evidence (RWD/RWE) to support regulatory decision making for *in vitro* Diagnostic (IVD) devices

2. Value of a National Evaluation System for health Technology (NEST)

3. Developing IVD infrastructure to support NEST

4. Collaborating to develop valuable/sustainable infrastructure for stakeholders (Better/ Cheaper/ Faster)

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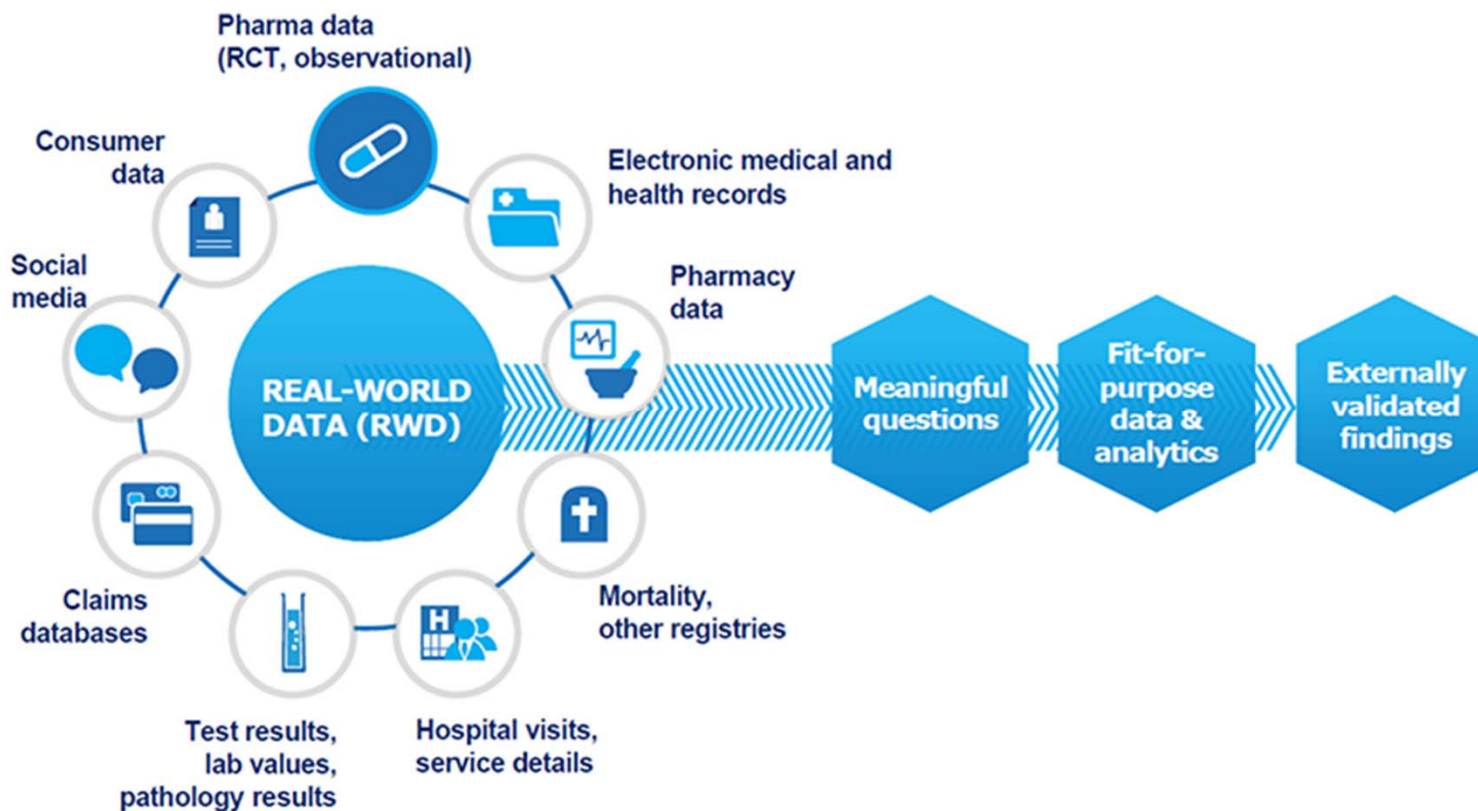
What is RWD/RWE?

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Real-World Data (RWD)*

Data relating to patient health status and/or the delivery of health care *routinely collected from a variety of sources*

Real-World Evidence (RWE)*

Clinical evidence regarding the usage and potential benefits or risks of a medical product *derived from analysis of RWD*
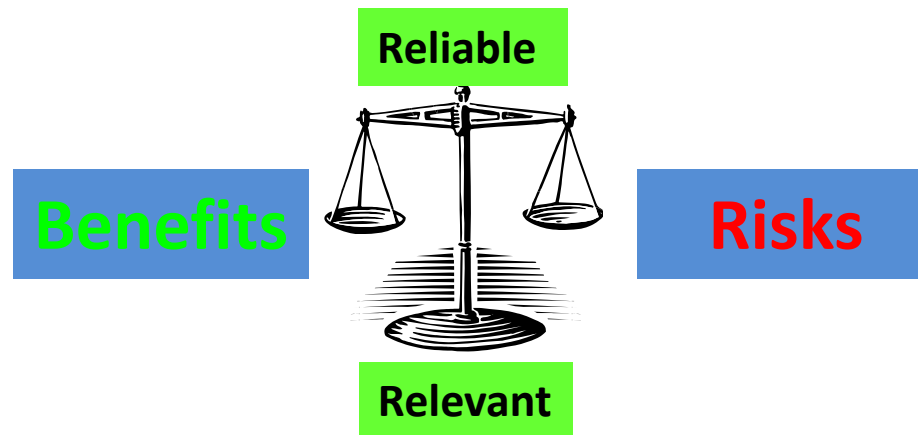
Good Decisions Require Good Data

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'Fit for Purpose' –

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

Reliable

Benefits   Risks

Relevant

Safety

Are there reasonable assurances, based on valid scientific evidence that probable benefits to health from use of the device ***outweigh any probable risks?***
[860.7(d)(1)]

Effectiveness

Is there reasonable assurance, based on **valid scientific evidence** that the use of the device in the target population will provide ***clinically significant results?***
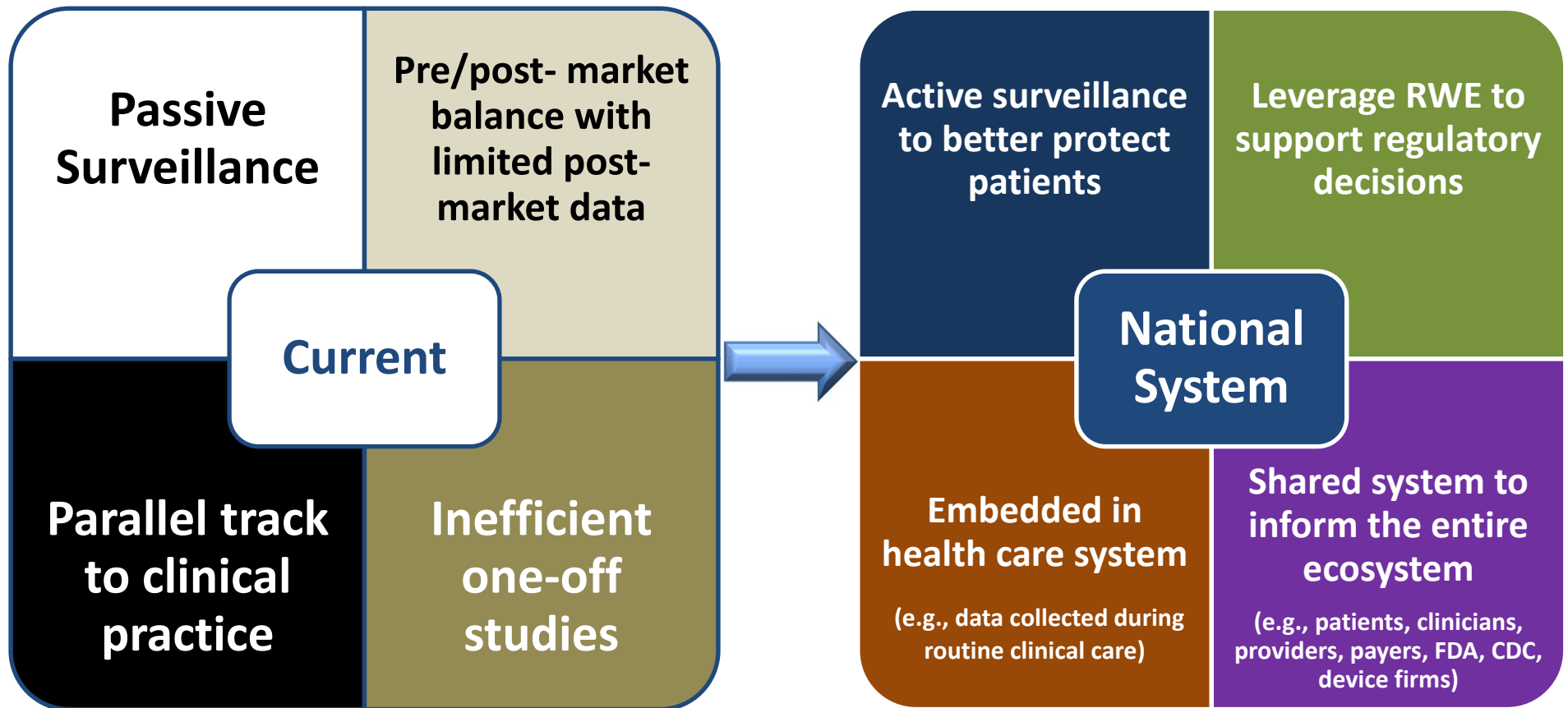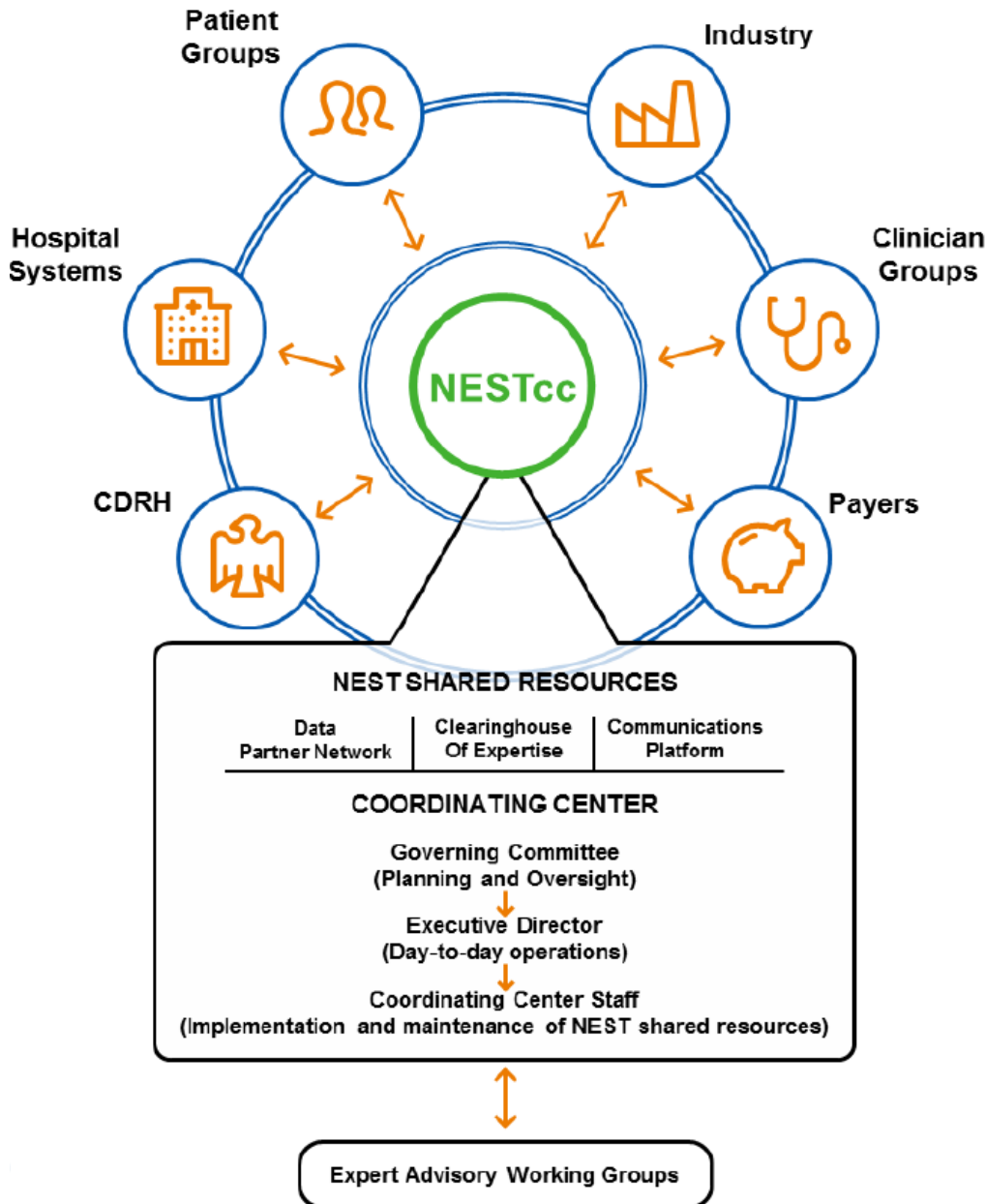*[860.7(e)(1)]*

8

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National Evaluation System Benefits

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Passive Surveillance	**Pre/post- market balance with limited post-market data**
Parallel track to clinical practice	**Inefficient one-off studies**

Current

➡️

Active surveillance to better protect patients	**Leverage RWE to support regulatory decisions**
Embedded in health care system (e.g., data collected during routine clinical care)	**Shared system to inform the entire ecosystem** (e.g., patients, clinicians, providers, payers, FDA, CDC, device firms)

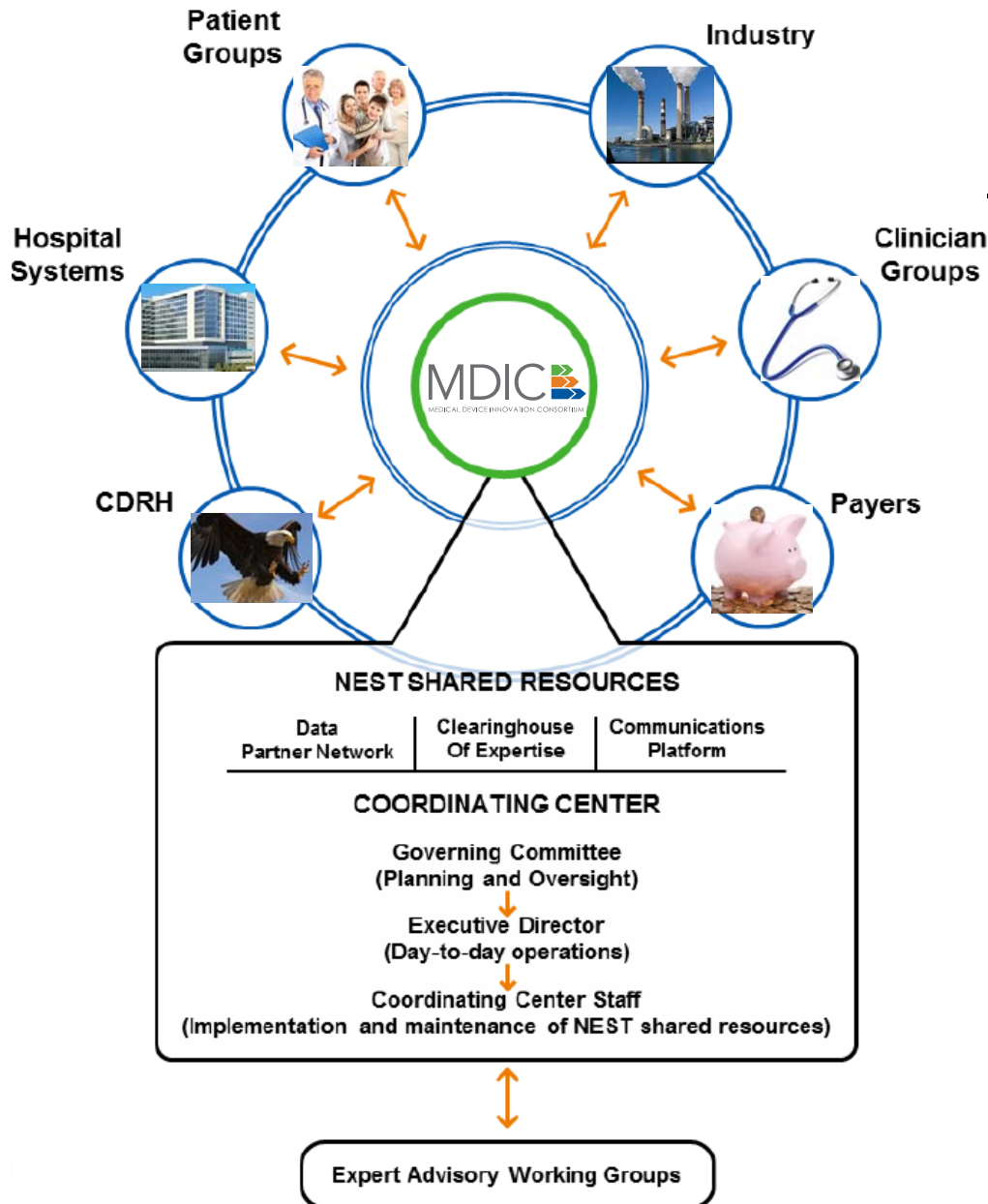**National System**

What is NEST?

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National Evaluation System for healthcare Technology (NEST)

NEST is a strategically-driven, coordinated network of voluntary partnerships to with the combined goal of generating "better evidence more efficiently for medical device evaluation and regulatory decision-making by leveraging RWE throughout the total product lifecycle."*

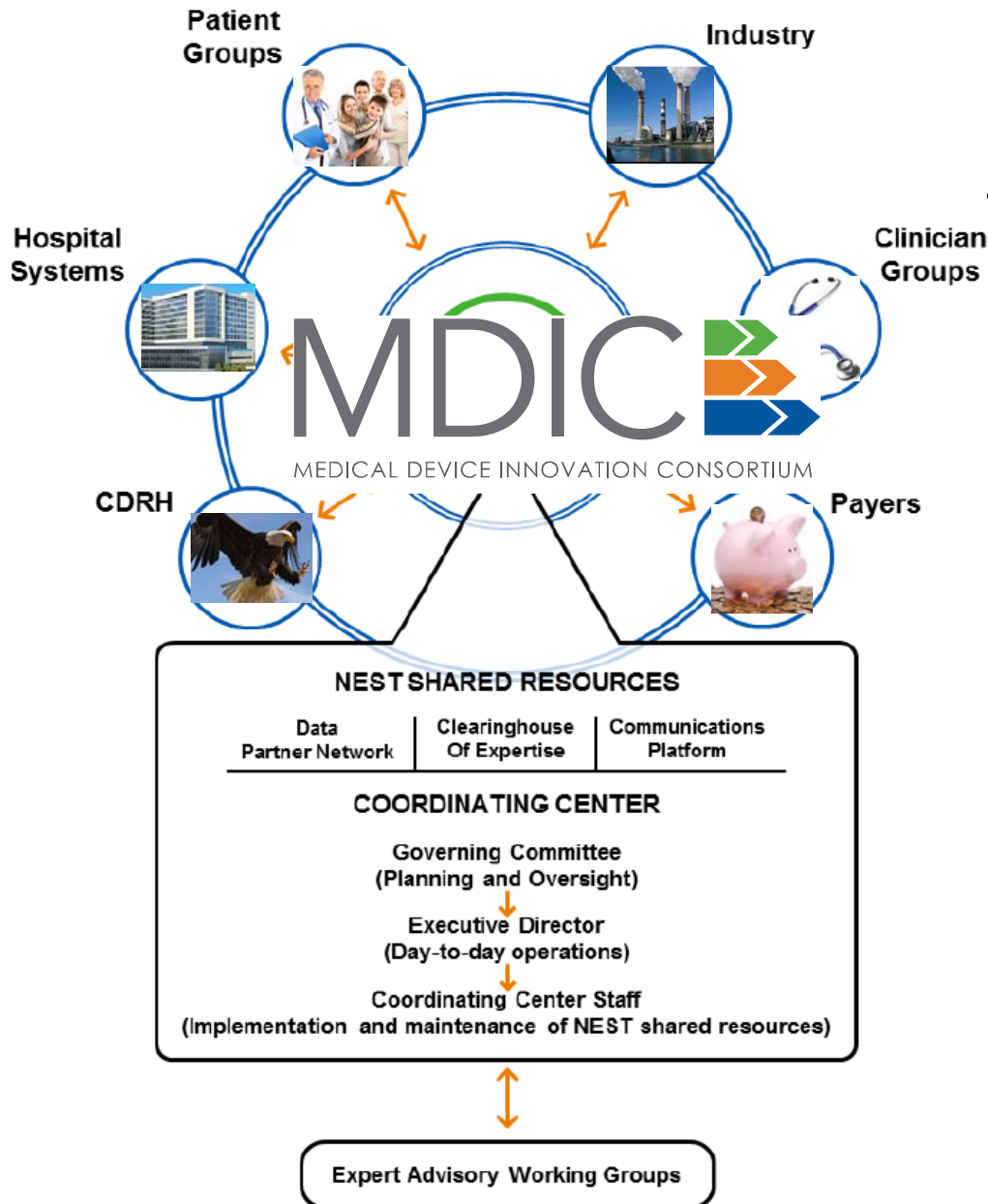*http://mdic.org/cc/landscape/

NEST: Concept to Reality

CDRH Priorities to Support NEST*

1. "Award grants … to support NEST development and implementation."

2. "Issue draft guidance to clarify how RWE may be used to support… regulatory decisions"

3. "Increase access to and use of real-world evidence to support regulatory decisions"

4. "Work with the medical device ecosystem, e.g., federal partners, health care system, manufacturers, payers and patients to build NEST."

*https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cdrh/cdrhreports/ucm301912.htm

12

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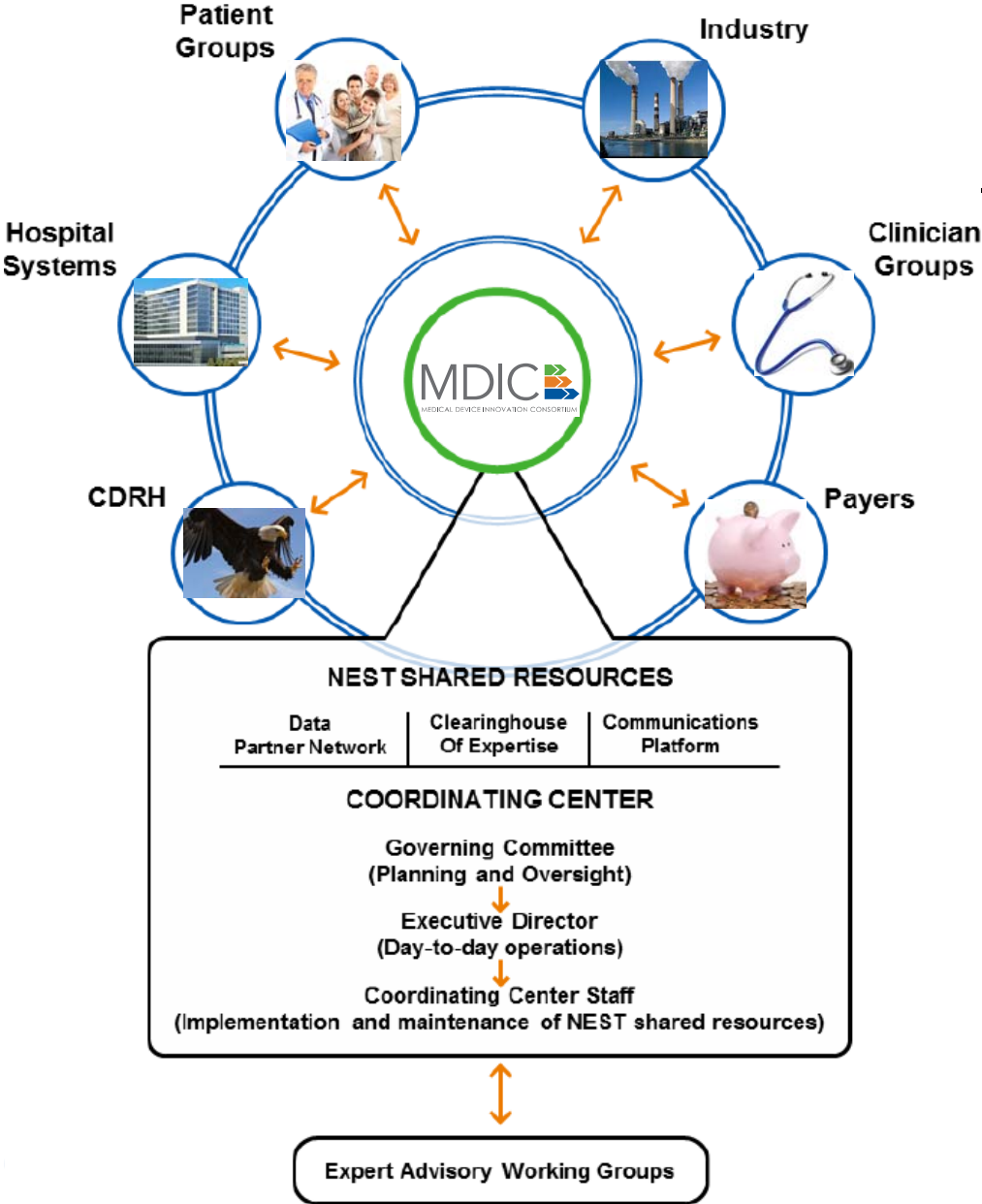
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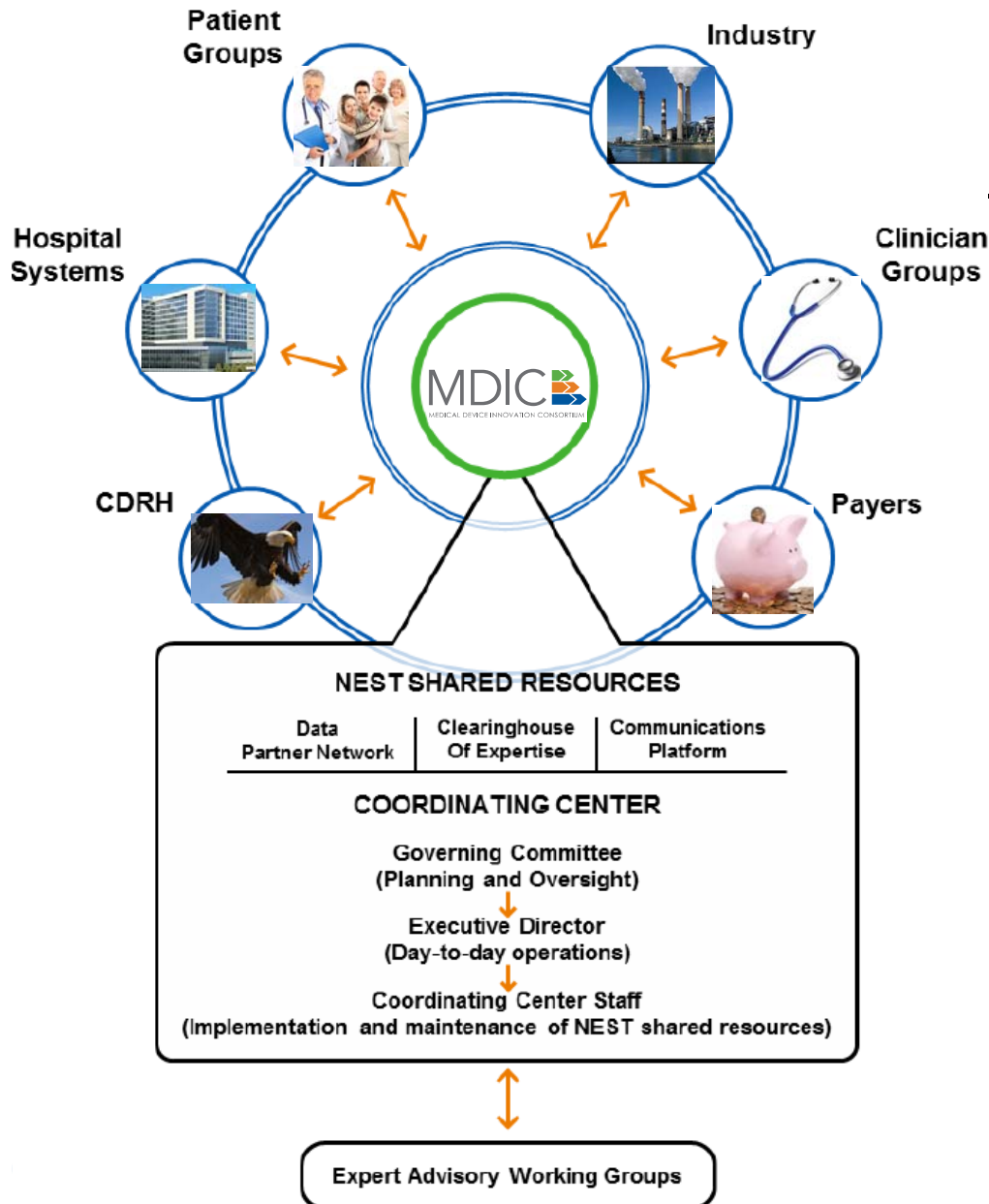
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Outline

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1. Using Real-World Data/Evidence (RWD/RWE) to support regulatory decision making for *in vitro* Diagnostic (IVD) devices

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FDA Perspective on LOINC for IVDs*

1. **Any similar coding system for characterizing IVDs (e.g., LOINC) is voluntary and will <u>not be required or reviewed</u> 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*)**

Digital Format for LOINC to IVD (LIVD)
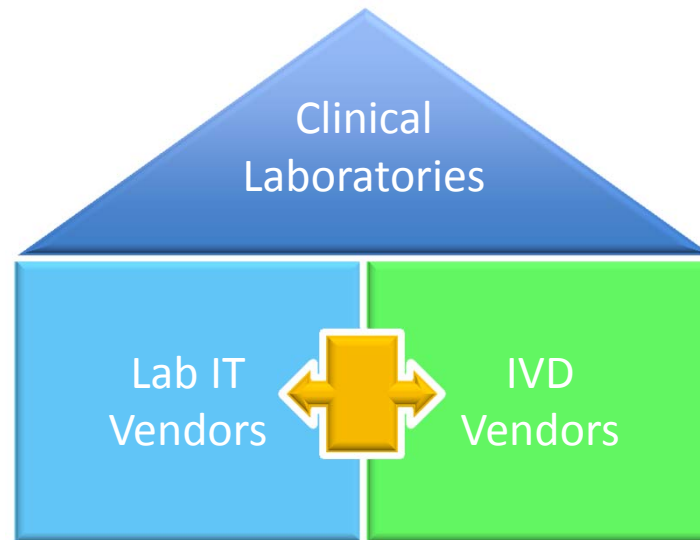
IVD Industry Connectivity Consortium (IICC) Mission:

- 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

FDA

IICC

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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
Regenstrief Center for Biomedical Informatics
Roche Diagnostics International, Ltd
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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Participating

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http://ivdconnectivity.org/livd/

Abbott Laboratories ... m (IICC)
Advanced Medical Technology Association (AdvaMed)   Medical Device Innovation Consortium (MDIC)
Association of Public Health Laboratories (APHL)   National Laboratory of Medicine
BD Life Sciences   Orchard Software
bioMerieux   Phast
Cerner Corporation   Regenstrief Center for Biomedical Informatics
Epic   Roche Diagnostics International, Ltd
Geisinger Health Systems   Swiss Laboratory Interoperability Interest Group (Joint
HL7 Orders and Observations   U.S. Centers for Disease Control and Prevention (CDC)
IHE Pathology and Laborator   U.S. Food and Drug Administration (FDA)
Technical Committee
Intelligent Medical Objects, Inc   Vernetzt, LLC

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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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

LOINC Codes for Laboratories

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Top 10 Lab Domain Overview

Microbiology	10,700
Chemistry	9,700
Drug/Toxicology	7,500
Allergy	3,800
Chemistry - Challenge	3,700
Serology	2,400
Hematology	2,100
Antibiotic Susceptibilities	1,700
Cell Markers	1,300
Molecular Pathology	1,700

Harmonization for Microbiology LOINC Codes

Microbiology Code Harmonization Challenges/Needs:

- Microbiology codes (>10,700)
- Antimicrobial Susceptibility Test codes (>1,700)
- Multiple panels
- Open-ended tests (e.g., culture)
- Coding for molecular assays
- New technology

Proposal: IVD Infectious Diseases LOINC Mapping Manual

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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 (Labs, Industry, EHR vendors, CDC, ONC, CMS, etc.).
- Post manual feedback, revision, implementation, support

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Unlocking Meaningful RWE in Electronic Healthcare Records (EHRs)

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CDRH has a strategic priority to **"increase <u>access</u> to and use of real-world evidence to <u>support regulatory decisions</u>."**

<u>First Steps:</u>

- Harmonize the application of semantic interoperability coding standards.

- Identify data elements needed to leverage in a regulatory decision.

- Populate a structured data format with needed content.

- Ensure that results are directly tied to the performance of a specific device (e.g., through a Unique Device Identifier system)

Conclusions/Requests

FDA

- There is an unused wealth of RWE siloed in data repositories which may be leveraged in regulatory decisions which can only be unlocked if the data is harmonized.

- OIR is engaging in cross-center and multi-stakeholder efforts to assist in the adoption of semantic interoperability standards and structured data formats, beginning with LIONC.

- Stakeholder input is critical to realizing the benefits of these efforts; please contact us via *pre-submission* or *directly* to let us know how we can help you.

Questions/Comments?

Contact: Michael.Waters@FDA.hhs.gov

FDA U.S. FOOD & DRUG
ADMINISTRATION