

FDA Update

CLIAC Meeting

April 10, 2018

Peter Tobin, Ph.D.

Division of Program Operations and Management

Office of In Vitro Diagnostics and Radiological Health (OIR)

Center for Devices and Radiological Health (CDRH)

Overview

- **Draft CLIA Waiver Guidances**
- CLIA Waiver Decision Summary Pilot
- Sysmex XW-100 CLIA Waiver
- Laboratory Interoperability Updates

FDA Issued Two CLIA Waiver Draft Guidances on November 29, 2017



Contains Nonbinding Recommendations

Draft – Not for Implementation

Select Updates for Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.
Document issued on November 29, 2017.

You should submit comments and suggestions regarding this draft document within 60 days of

Contains Nonbinding Recommendations

Draft – Not for Implementation

Recommendations for Dual 510(k) and CLIA Waiver by Application Studies

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on November 29, 2017.

You should submit comments and suggestions regarding this draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to <http://www.regulations.gov>. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630

- Download drafts from [Recent CDRH Draft Guidance](#)
- For more info, please see the [Webinar](#) held on January 8th, 2018
- The comment period for both was extended for 60 additional days to March 30th, 2018



FDA is Actively Engaging with Stakeholders for Feedback on the Draft Guidances

- This feedback will be incorporated so the final guidances
 - Are clearer about how to use agreement studies for CW
 - Promote increased availability of point of care tests
 - Are least burdensome

Overview

- Draft CLIA Waiver Guidances
- **CLIA Waiver Decision Summary Pilot**
- Sysmex XW-100 CLIA Waiver
- Laboratory Interoperability Updates

The CLIA Waiver Decision Summary Pilot Has Increased Transparency



Home > About FDA > FDA Organization > Office of Medical Products and Tobacco > About the Center for Devices and Radiological Health > CDRH Transparency

CDRH Transparency

Overview of CDRH Transparency

CDRH Transparency: Total

CLIA Waiver by Application Decision Summaries

[f SHARE](#)
[TWEET](#)
[LINKEDIN](#)
[PIN IT](#)
[EMAIL](#)
[PRINT](#)

Test System Name	Document Number	FDA Review Decision Summary	Effective Date (DD/MM/YYYY)
ACON Laboratories Inc., Mission Cholesterol Pro Monitoring System {Mission Cholesterol Pro Test Cartridges}	CW170010	CW170010.pdf Decision Summary	01/19/2018
Quidel Sofia 2 {Sofia Strep A+ FIA} (from throat swab only)	CW170009	CW170009.pdf Decision Summary	12/21/2017
Sysmex XW-100	CW170012	CW170012.pdf Decision Summary	11/06/2017
Alere, BinaxNOW Influenza A & B Card 2 {With Reader} (Direct Nasal and NP Swabs)	CW170003	CW170003.pdf Decision Summary	10/02/2017
Quidel Sofia 2 (Sofia RSV FIA)	CW170001	CW170001.pdf Decision Summary	06/28/2017
Quidel Sofia 2 (Sofia Influenza A+B FIA)	CW160016	CW160016.pdf Decision Summary	05/30/2017



Overview

- Draft CLIA Waiver Guidances
- CLIA Waiver Decision Summary Pilot
- **Sysmex XW-100 CLIA Waiver**
- Laboratory Interoperability Updates

FDA is Working with Device Manufacturers to Bring New Tests to Waived Settings



- Sysmex XW-100 Automated Hematology Analyzer:
 - 1st CLIA waived complete blood count (CBC) analyzer
 - Reports 12 hematology parameters including 3-part WBC differential
 - Cleared and CLIA waived through the Dual Submission pathway
 - For more info, see the [K172604](#) and [CW170012](#) Decision Summaries



http://pages.sysmex.com/XW-100_Waived_CBC_landing.html

2008/2009 Advisory Panel Concerns Were Systematically Mitigated



Selected Examples:

Panel Concern w/ HemoCue WBC System	Sysmex XW-100 Mitigation
Affected by interferences such as Nucleated Red Blood Cells (NRBCs) so that erroneous results may be produced	Comprehensive sample challenge data demonstrated the XW-100 appropriately suppressed results and the presence of potentially interfering substances did not result in the reporting of erroneous results
No external control provided	External control provided and must be run every 8 hrs and pass or lockout activated



IFU and Software Modifications Support Waived Use

- Waived XW-100 Indications for Use includes limitations:
 - “Not for use in diagnosing or monitoring patients with primary or secondary chronic hematologic diseases/disorders, oncology patients, critically ill patients, or children under the age of 2”
- Software modifications include decreased number of reported parameters & simplified flagging
- Reports:
 - WBC, RBC, HGB, HCT, MCV, PLT, LYM%, Other WBC%, NEUT%, LYM#, Other WBC#, NEUT#
- To mitigate possibility of error, does not report:
 - MCH, MCHC, RDW-SD, RDW-CV, and MPV

The XW-100 Met the 2008 CLIA Waiver Guidance Criteria for a Simple Test



Selected Examples:

Guidance Criteria	How Addressed on the XW-100 Analyzer
Needs only basic, non-technique-dependent specimen manipulation, including any for decontamination.	On-screen prompts and pictographic representations guide the operator through the various steps of sample analysis, including collection tube verification (purple-top required), insertion of sample tube adapter, sample temperature verification (warm to the touch), sample mixing, and inserting the sample onto the analyzer.
Needs only basic, non-technique-dependent reagent manipulation, such as “mix reagent A and reagent B”.	All reagents and QC materials are stored at room temperature, are ready to use, and require no manipulation. The QC materials only require simple mixing by inversion prior to use. On-screen prompts instruct the user to mix the control by inversion.

Fail-Safe Features Mitigate Risks of Erroneous Results

For example, XW-100 system software enforces:

- Use of reagents and quality control material within expiration dating
- Use of quality control material within open container stability limits
- Quality control within range every 8 hours
- Quality control with a new lot of reagents
- Patient testing lock-out if quality control out of range
- No testing of patients less than two years of age based on DOB entry
- Weekly cleaning of the instrument with XW CELLCLEAN
- Suppression of test results when sample is compromised (lipemia, hemolysis, etc.)

Flex Studies Demonstrated Test System Robustness

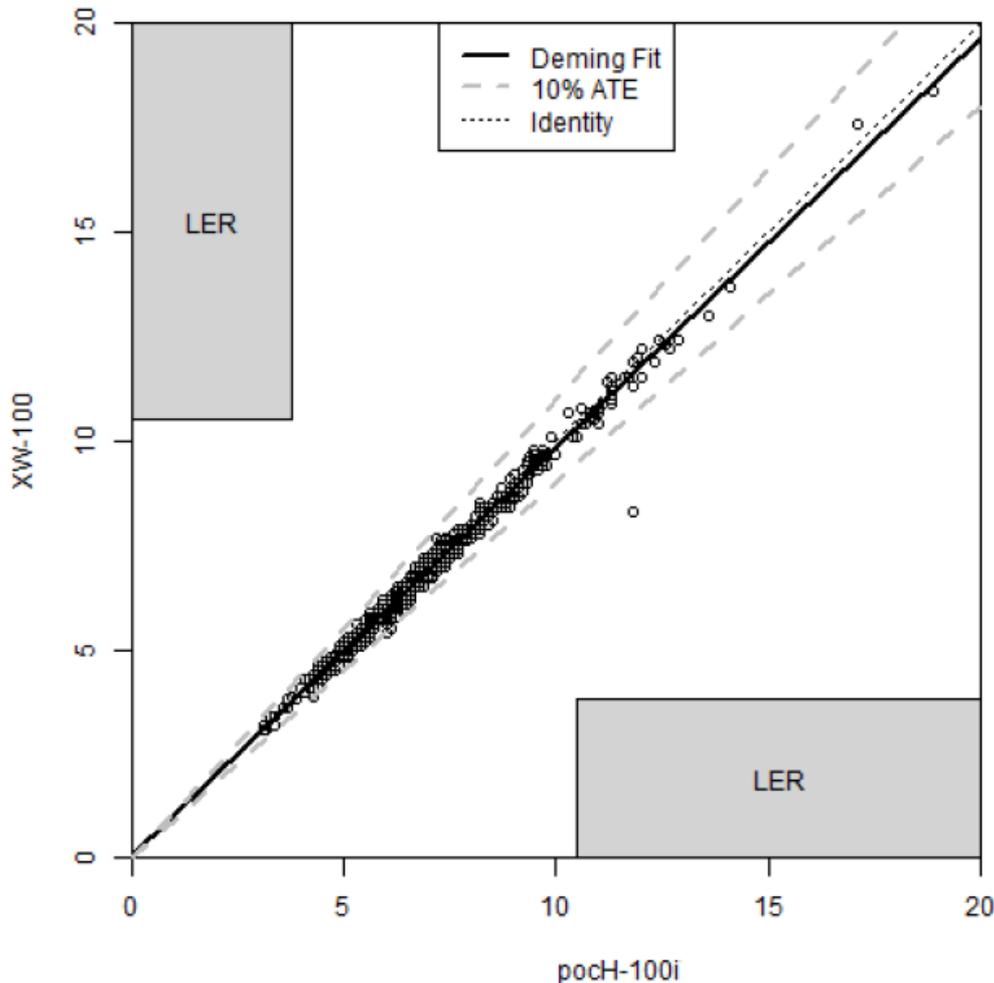
Selected Examples:

- Inappropriate Sample Storage
- Inadequate Sample Mixing
- Reagent Freeze/Thaw
- Tube Types and Sample Volumes
- Mismatching of Diluent and Waste Container Caps
- Environmental Variation (e.g., tilting, vibration, temperature)

The Clinical Study Demonstrated Accuracy at CLIA Waived Sites



WBC ($\times 10^3/\mu\text{L}$)



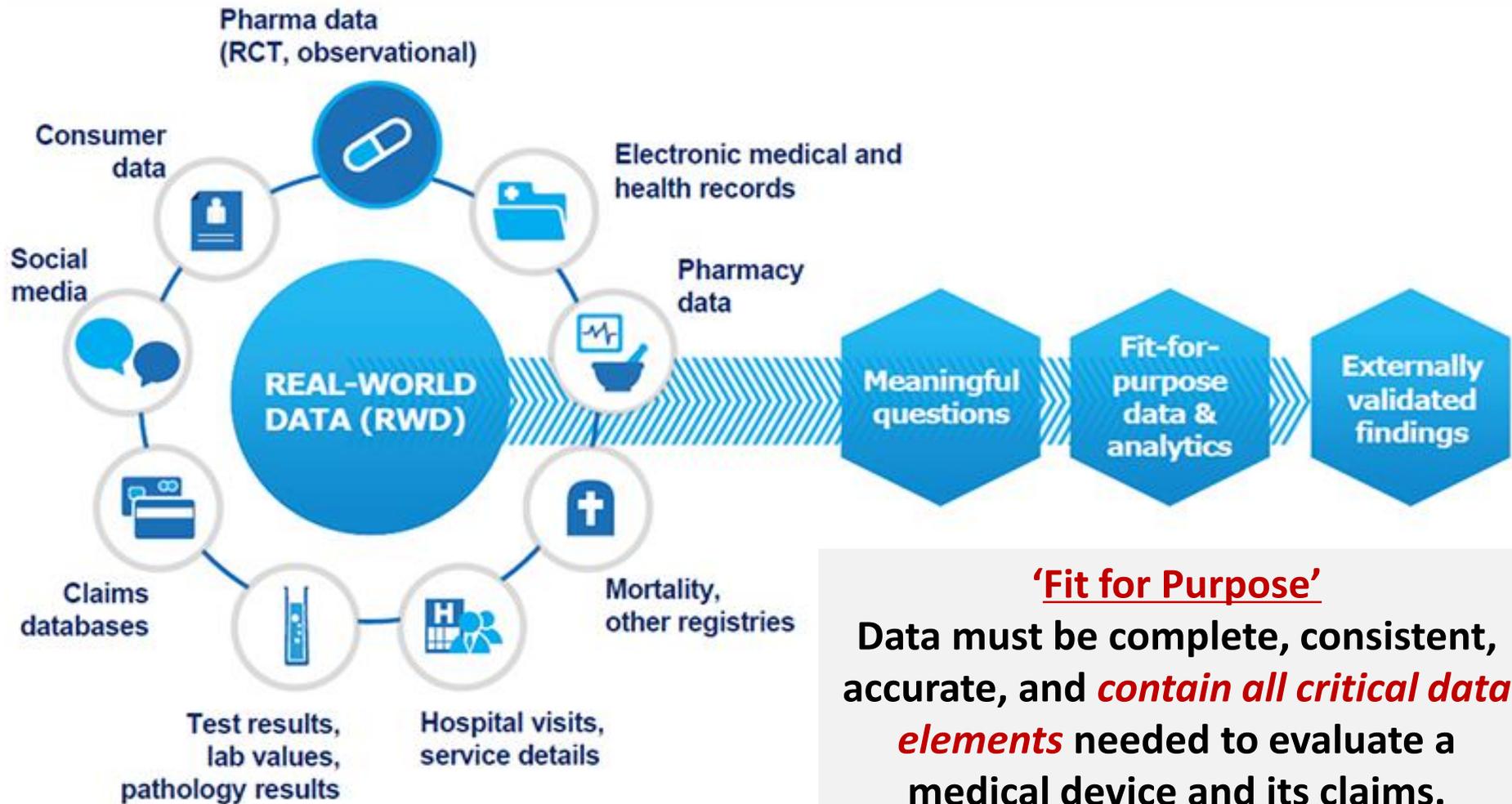
- CLIA WBC PT requirement is $\pm 15\%$
- XW-100 WBC ATE = $\pm 10\%$

ATE = $\pm 10\%$
Percent of samples inside of ATE
99.8%
(552/553)
95% CI: (99.0%; 100.0%)

Overview

- Draft CLIA Waiver Guidances
- CLIA Waiver Decision Summary Pilot
- Sysmex XW-100 CLIA Waiver
- **Laboratory Interoperability Updates**

Unlocking Electronic Health Data



KEY: Coordination/Harmonization (Interoperability)



Systemic Harmonization and Interoperability Enhancement for Lab Data

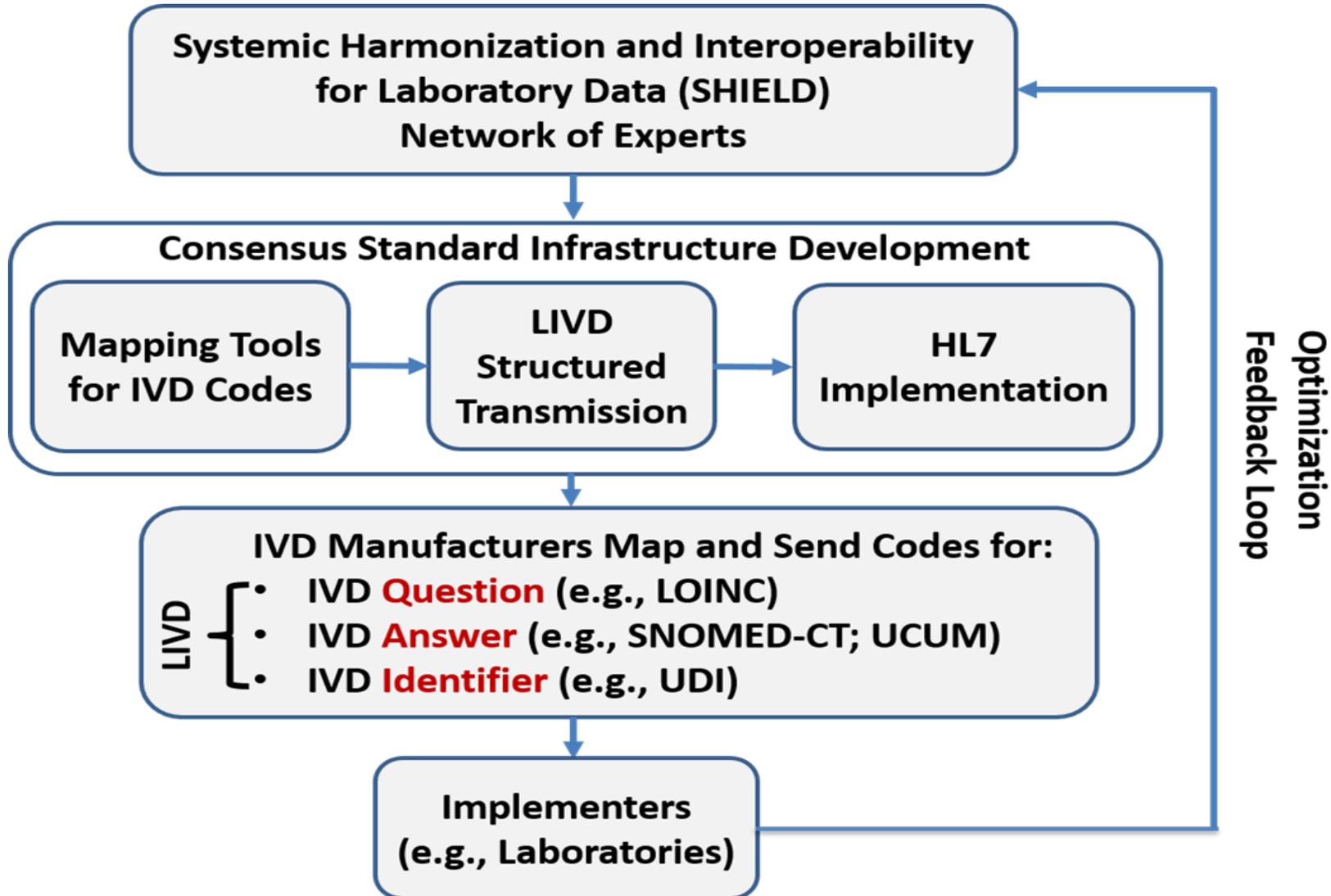
SHIELD supports efforts to harmonize and harness *in vitro* diagnostic (IVD) data sources to:

- 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

Systemic Harmonization and Interoperability Enhancement for Lab Data



SHIELD MEETING**FDA, White Oak – May 30-31, 2018**

Objective: Address practical limitations of IVD implementation, focusing on adoption of answer lists for qualitative/semi-quantitative tests & discrete units for quantitative test values.

Representatives: Industry, Labs, EHS/LIS Vendors, CDC, FDA, NIH, ONC, CMS, Standards

Day 1

- 8:30 – 8:45 **Presentation:** Overview of challenges in implementing SHIELD framework (*FDA*)
- 8:45 – 9:05 **Presentation:** Value set examples and issues (*NIH*)
- 9:05 – 9:25 **Presentation:** Review available ordinal coded value sets for qualitative IVD tests (*IMHC*)
- 9:25 – 9:40 **Presentation:** Current laboratory implementation approaches (*APHL*)
- 9:50 – 11:45 **Discussion:** Value set standard(s) for implementation across IVD tests (*Epic*)
- 12:30 – 2:00 **Discussion:** Technical considerations for facilitating harmonization for ordinal values for semi-quantitative, coded tests for laboratories, including messaging
- 2:00 – 2:20 **Presentation:** Review LIVD structured framework, expansion to incorporate value sets, and associated challenges (*Abbott*)
- 2:30 – 4:15 **Discussion:** Discuss challenges and approaches for assay value set transmission from IVD vendors to laboratories
- 4:15 – 5:00 **Panel Discussion:** Discuss technical considerations for facilitating harmonization value sets for quantitative tests for laboratories, including messaging.

Day 2

- 8:15 – 10:15 **Discussion:** Discuss potential solutions for interoperable infrastructure implementation across the breadth of labs
- 10:30 – 12:00 **Discussion:** Next steps for development/implementation

Get involved. Contact: Michael.Waters@fda.hhs.gov

Thank you

CLIA@fda.hhs.gov

Peter.Tobin@fda.hhs.gov



U.S. FOOD & DRUG
ADMINISTRATION