2017 Interoperability Standards Advisory

Office of the National Coordinator for Health IT

General Notes:

Rows highlighted yellow should be removed because they are not currently accepted by the FDA.

Rows highlighted blue should be removed and put into the Base Standards section.

Rows highlighted in grey mean there are still questions about removal.

Adoption levels in red (i.e. ●●●○○) are changed from original adoption levels, as suggested by Wayne Kubick.

Section II: Content/Structure Standards and Implementation Specifications

II-S: Research

Interoperability Need: Submission of Clinical Research Data to FDA to Support Product Marketing Applications

Type	Standard/Implementation Specification	Standards Process Maturity	Implementation Maturity	Adoption Level	Federally Required	Cost	Test Tool Availability
Standard	CDISC Study Data Tabulation Model (SDTM)	Final	Production	●●●●●	Yes	Free	Yes
Standard	CDISC Analysis Dataset Model (ADaM)	Final	Production	●●●○○	Yes	Free	N/A
~~**Standard**~~	~~CDISC Operational Data Model (ODM)~~	~~Final~~	~~Production~~	●●●●●	~~No~~	~~Free~~	~~Yes~~
~~**Standard**~~	~~CDISC Dataset-XML (ODM-Based)~~	~~Final~~	~~Production~~	●○○○○	~~No~~	~~Free~~	~~N/A~~
Standard	CDISC Define-XML (ODM-Based)	Final	Production	●●●●●	Yes	Free	N/A
Standard	CDISC Standard for the Exchange of Non-clinical Data (SEND)	Final	Production	●●●○○	Yes	Free	N/A
Standard	Study Data Tabulation Model Implementation Guide for Medical Devices (SDTMIG-MD)	Final	Production	●○○○○	No	Free	N/A
~~**Standard**~~	~~Therapeutic Area Standards (to complement the aforementioned CDISC foundational standards that apply across all therapeutic areas)~~	~~Final~~	~~Production~~	●○○○○	~~No~~	~~Free~~	~~N/A~~

Limitations, Dependencies, and Preconditions for Consideration:	Applicable Security Patterns for Consideration:
• FDA published the draft guidance promoting use of EHRs in clinical research, in collaboration with ONC. (http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm501068.pdf) • FDA CDER published a FRN focusing on Source Data Capture From Electronic Health Records: Using Standardized Clinical Research Data. (https://www.federalregister.gov/documents/2015/06/26/2015-15644/source-data-capture-from-electronic-health-records-using-standardized-clinical-research-data) • FDA CDER and CBER CDER encourage the submission of study data in conformance to the data standards listed in the FDA Data Standards Catalog (DSC). Standardized study data will be required in submissions for clinical and non-clinical studies that start on or after December 17, 2016 (December 17, 2017 for INDs). See Data Standards Catalog:	• Feedback requested

Commented [RMG1]: PAGE 54: II-S: Research: Submission of Analytic Data to FDA for Research Purposes
1. WK: This information is already published by FDA in the form of the Data Standards Catalog, available at http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm.
The information in this section is not consistent with the FDA document, and since the ISA is published once a year while the FDA makes updates several times a year, it's likely to be always out of sync. To avoid confusion, we make reference to the highlighted URL below, which contains the up-to-date FDA requirements.

2. WK: The original title is not accurate – "Submission of Analytic Data to FDA for Research Purposes", since data submitted to support product marketing applications is not purely for analytic purposes (only ADaM is analytic), and it is for product approval not research in general.

Commented [LS([2]: 3. WK: Those marked as "Federally required" will only apply to new studies that begin after Dec. 17 2016, so the requirement won't apply for several more years.

Commented [RMG3]: 4. WK: The "Therapeutic Area Standards" are actually user guides for using SDTM (and, in some cases, CDASH and ADaM as well). None are required by FDA or included in the current Data Standards Catalog but a few are referred as acceptable in the FDA CDER Data Conformance Guide.

(http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm) and the Data Standards Strategy (http://www.fda.gov/downloads/drugs/developmentapprovalprocess/formssubmissionrequirements/electronicsubmissions/ucm455270.pdf). • Although CDISC standards are a requirement for CDER and CBER and not for CDRH, but FDA promotes leveraging data from EHRs and Health IT systems for clinical research and collaborates with IHE, HL7 and other SDOs.	

Interoperability Need: Pre-population of Research Forms from Electronic Health Records

Type	Standard/Implementation Specification	Standards Process Maturity	Implementation Maturity	Adoption Level	Federally Required	Cost	Test Tool Availability
Standard	CDISC Clinical Data Acquisition Standards Harmonization (CDASH)	Final	Production	●○○○○	No	Free	N/A
~~**Standard**~~	~~CDISC Shared Health And Research Electronic Library (SHARE)~~	~~Final~~	~~Production~~	●●●○○	~~No~~	~~Free~~	~~N/A~~
~~**Implementation Specification**~~	~~IHE-RFD (Retrieve Form for Data Capture)~~	~~Final~~	~~Production~~	●○○○○	~~No~~	~~Free~~	~~N/A~~
~~**Implementation Specification**~~	~~IHE Quality, Research, and Public Health Technical Framework Supplement, Structured Data Capture, Trial Implementation~~	~~Balloted Draft~~	~~Pilot~~	●○○○○	~~No~~	~~Free~~	~~No~~
~~**Implementation Specification**~~	~~IHE Quality, Research, and Public Health Technical Framework Supplement, Structured Data Capture, Trial Implementation~~	~~Balloted Draft~~	~~Pilot~~	●○○○○	~~No~~	~~Free~~	~~No~~
~~**Implementation Specification**~~	~~IHE-CRD (Clinical Research Document)~~	~~Balloted Draft~~	~~Production~~	●○○○○	~~No~~	~~Free~~	~~N/A~~
~~**Implementation Specification**~~	~~IHE-XUA (Cross-Enterprise User Assertion)~~	~~Final~~	~~Production~~	●●●○○	~~No~~	~~Free~~	~~N/A~~
~~**Implementation Specification**~~	~~IHE-ATNA (Audit Trail and Node Authentication)~~	~~Final~~	~~Production~~	●●○○○	~~No~~	~~Free~~	~~N/A~~
~~**Implementation Specification**~~	~~IHE-DEX (Data Element Exchange)~~	~~Balloted Draft~~	~~Pilot~~	●○○○○	~~No~~	~~Free~~	~~N/A~~
~~**Implementation Specification**~~	~~HL7 FHIR Implementation Guide: Structured Data Capture (SDC) Release 1~~	~~Balloted Draft~~	~~Pilot~~	●○○○○	~~No~~	~~Free~~	~~N/A~~

Commented [LS([4]: 5. WK: Adoption level for CDASH (row 1) changed from 3 to 1 because a Tufts 2015 study reported adoption at 49%, though an examination of a sample of studies showed it actually at 10%.

Commented [RMG5]: 6. WK: The Adoption level for RFD (row 3) seems rather high since I don't believe there are any documented cases where it has actually been used in production of this purpose.

CM: This is a base standard and we had previously agreed it should be pulled into a base standard section, but not be here.

Commented [c6]: 7. CM: This is a base standard not part of research per se and is mentioned in other sections and should not be repeated here

Commented [RMG7]: 8. CM: This is a base standard has not yet been widely accepted, and is mentioned already in other sections. It is not specific to research so should not be asserted here, but under the API Section.

Commented [RMG8]: 9. WK: I don't believe there have been any documented production uses of CRD (row 6).

Commented [c9]: 10. CM: These are not specific to research and should be moved to a base standard section or the sections regarding communication

Commented [LS([10]: 11. CM: As above, these are not specific to research, and should be moved to the API section.

Type	Standard/Implementation Specification	Standards Process Maturity	Implementation Maturity	Adoption Level	Federally Required	Cost	Test Tool Availability
NEW - Implementation Specification	HL7 FHIR Resources Study Registry – ResearchStudy	Balloted Draft	Pilot	●○○○○			
	HL7 FHIR Resources Study Registry – ResearchStudy						

Limitations, Dependencies, and Preconditions for Consideration:	Applicable Security Patterns for Consideration:
• See IHE projects in the Interoperability Proving Ground. •	• Feedback requested

Interoperability Need: Integrate Healthcare and Clinical Research by Leveraging EHRs and other Health IT Systems while Preserving FDA's Requirements

Type	Standard/Implementation Specification	Standards Process Maturity	Implementation Maturity	Adoption Level	Federally Required	Cost	Test Tool Availability
~~**Standard**~~	~~IHE- RFD (Retrieve Form for Data Capture)~~	~~Final~~	~~Production~~	●○○○○	~~No~~	~~Free~~	~~N/A~~
~~**Standard**~~	~~HL7 Clinical Document Architecture (CDA®), Release 2.0, Final Edition~~	~~Final~~	~~Production~~	●●○○○	~~No~~	~~Free~~	~~N/A~~
Standard	CDISC Clinical Data Acquisition Standards Harmonization (CDASH)	Final	Production	●●●○○	No	Free	N/A
Standard	CDISC Operational Data Model (ODM)	Final	Production	●●●●●	No	Free	N/A
Standard	CDISC Protocol Representation Model (PRM)	*Final*	Production	●○○○○	No	Free	Yes
Standard	CDISC Study/Trial Design Model (SDM)	*Final*	Production	●○○○○	No	Free	N/A
Implementation Specification	IHE-RPE (Retrieve Protocol for Execution)	Balloted Draft	Production	●○○○○	No	Free	N/A

Commented [LS([11]: 12. Will explain – CM: Driven by the US PCORI project, FHIR has defined two new resources that together provide a study registry- to cross the void between clinical care and research; to enable care providers to order tests or procedures on their patients and assign the action to a particular study and the assure that the results are delivered to the right place and billing is one correctly. 2 resources that just got added: http://build.fhir.org/researchstudy.html and http://build.fhir.org/researchsubject.html.

Commented [LS([12]: Page 56 II-S Research: Integrate Healthcare and Research by Leveraging EHRs and other Health IT Systems while Preserving FDA's Requirement.
13. WK: I don't understand this title, which is very broad and can extend far beyond the standards listed here. Note that both CDA (row 2) and ODM (row 4) are used in the IHE CRD profile listed in the prior section and could be included there.
14. WK: Furthermore, since any valid use under FDA's jurisdiction would have to conform to FDA requirements, I don't see why this category should be included at all. Recommend removing it and adding CDASH and CDA to the previous section

Commented [c13]: 15. CM: This is a base standard part of structured data capture. Is not unique to research (and probably not used there yet) and should be moved to its appropriate place.

Commented [LS([14]: 16. WK: Adoption of ODM for this purpose may be high since there are no documented use cases for this purpose).

Commented [LS([15]: 17. WK: The CDISC Protocol Representation Model is a reference model, but there is no published IG, and it's unclear how it meets the title listed above. It's a content model for protocols, and not directed toward integration with EHRs.

18. CM: In IHE it is described as being for research public health and quality. The last record of a discussion about this at IHE web site was 2009 suspect it is dead. And should be removed.

Commented [LS([16]: 19. WK: The Study/Trial Design Model is a way to represent the table of times and data collection events in a protocol, but there is no evidence that it's in use, nor has it been piloted.

Commented [LS([17]: 20. CM: AT the IHE web site, it is described as for research, public health and quality. The last date of a discussion was 2009. So probably dead and should be removed WK:
21. WK: I'm not aware of any production use of IHE-RPE (row 3) or CPRC (row 4). Again unsure of why these are included but if they are, should be listed as adoption level 1.

Type	Standard/Implementation Specification	Standards Process Maturity	Implementation Maturity	Adoption Level	Federally Required	Cost	Test Tool Availability
Implementation Specification	IHE-CRPC (Clinical Research Process Content)	Balloted Draft	Production	●●○○○	No	Free	N/A
	Mini Sentinel						
	OHDSI						

Limitations, Dependencies, and Preconditions for Consideration:	Applicable Security Patterns for Consideration:
• Stakeholders should review 21CFR11 for more details. • See IHE projects in the Interoperability Proving Ground.	• Feedback requested

Commented [LS([18]: 21. CM: Derived from OMOP

Interoperability Need: Submit Adverse Event Report from an Electronic Health Record to Drug Safety Regulators

Type	Standard/Implementation Specification	Standards Process Maturity	Implementation Maturity	Adoption Level	Federally Required	Cost	Test Tool Availability
~~**Implementation Specification**~~	~~IHE-RPE (Retrieve Protocol for Execution)~~	~~Final~~	~~Production~~	●○○○○	~~No~~	~~Free~~	~~N/A~~
~~**Implementation Specification**~~	~~IHE-DSC (Drug Safety Content)~~	~~Balloted Draft~~	~~Pilot~~	●○○○○	~~No~~	~~Free~~	~~N/A~~
~~**Implementation Specification**~~	~~IHE- CPRC (Clinical Research Process Content)~~	~~Balloted Draft~~	~~Production~~	●●○○○	~~No~~	~~Free~~	~~N/A~~
~~**Standard**~~	~~CDISC Protocol Representation Model (PRM)~~	~~Final~~	~~Production~~	●○○○○	~~No~~	~~Free~~	~~Yes~~
	ICH E2B r2 XML standard						

Limitations, Dependencies, and Preconditions for Consideration:	Applicable Security Patterns for Consideration:
• See IHE projects in the Interoperability Proving Ground.	• Feedback requested

Commented [RMG19]: Page 57 II-S Research: Integrating Healthcare and Research by Leveraging EHRs and other Health IT Systems while Preserving FDA's Requirement.
22. WK: Don't understand inclusion of this section, since the title is too broad and identical to previous section (which I recommend be removed). It's also unclear to me what purpose is being served by this section.

Commented [LS([20]: 23. CM: Adoption level is exaggerated. Not supported by the major EMR venders. It is suggested for one application in MU. But more importantly, this is not specific to research and is mentioned elsewhere so should be put in its right pace.

Commented [LS([21]: 24. WK: I don't believe IHE-DSC has been updated since it was piloted 5 years ago, and question whether it's still current. Same with CPRC. (Rows 2-3).

Commented [RMG22]: 25. WK: The CDISC Protocol Representation Model is a reference model, but there is no published IG, and it's unclear how it meets the title listed above. It's a content model for protocols, and not directed toward integration with EHRs.

Commented [RMG23]: 26. WK: I don't see the relevance of the CDISC PRM (row 4) to submitting adverse event reports. I'm not aware of any PRM content on this topic. Recommend it be removed.

Commented [LS([24]: 27. WK: Currently the primary standard in use for drugs is the ICH E2B r2 XML standard, which should be included.

There are several other standards used by other federal agencies that are not included here, so these should be added before publication.

Interoperability Need: Complete Disease Registry Forms and Submit to Reporting Authority (ACC)

Type	Standard/Implementation Specification	Standards Process Maturity	Implementation Maturity	Adoption Level	Federally Required	Cost	Test Tool Availability
~~Standard~~	~~CDISC Clinical Data Acquisition Standards Harmonization (CDASH)~~	~~Final~~	~~Production~~	●●●○○	~~No~~	~~Free~~	~~N/A~~
~~Implementation Specification~~	~~IHE-RFD (Retrieve Form for Data Capture)~~	~~Final~~	~~Production~~	●●●●○	~~No~~	~~Free~~	~~N/A~~
~~Standard~~	~~HL7 Clinical Document Architecture (CDA®), Release 2.0, Final Edition~~	~~Final~~	~~Production~~	●●●●○	~~No~~	~~Free~~	~~N/A~~

Limitations, Dependencies, and Preconditions for Consideration:	Applicable Security Patterns for Consideration:
• See IHE projects in the Interoperability Proving Ground.	• Feedback requested

Interoperability Need: Registering a Clinical Trial

Type	Standard/Implementation Specification	Standards Process Maturity	Implementation Maturity	Adoption Level	Federally Required	Cost	Test Tool Availability
~~Standard~~	~~CDISC Clinical Trial Registry (CTR-XML)~~	~~Balloted Draft~~	~~Pilot~~	●○○○○	~~No~~	~~Free~~	~~N/A~~
~~Standard~~	~~CDISC Operational Data Model (ODM)~~	~~Final~~	~~Pilot~~	●●●●●	~~No~~	~~Free~~	~~N/A~~
Standard	ClinicalTrials.gov	Final	Pilot	●●●●●	No	Free	N/A

Limitations, Dependencies, and Preconditions for Consideration:	Applicable Security Patterns for Consideration:
• The CDISC Clinical Trial Registry (CTR-XML) is used internationally, but in the US, the primary area for registering Clinical Trials is via ClinicalTrials.gov.	• Feedback requested

Commented [RMG25]: Page 50-51 Complete Disease Registry Forms and Submit to Reporting Authority (ACC)
28. WK: I don't understand this category description. Why is ACC listed? How does it differ from collecting research data from EHRs (SDC or pre-population)? Recommend dropping this category since it's already addressed on pg 48.

Commented [RMG26]: 29. WK: I'm not aware of any CDASH implementations in registries. Since CDASH describes CRFs for clinical studies, not sure it's relevant (but may be mistaken in this case).

Commented [RMG27]: 30. WK: This is all part of the IHE structured data capture, It is not specific to Research, and is not adopted by any major EMR. And I know of no usage in research yet. Should be included somewhere in the specification but not in the research section.

31. CM: A base standard used in lots of places should be in base standard section.

Commented [RMG28]: PAGE 58: II-S Research: Registering a Clinical Trial
32. WK: Not sure why this is included with Interoperability standards, since it doesn't seem like an interoperability use case. Recommend removing it.
33. WK: If it's retained should specify the XML standard format required by clinicaltrials.gov.

Commented [RMG29]: 34. WK: CTR-XML is under development but I don't believe it has been piloted yet. I believe most work on this has been in Europe, and I'm not aware of any plans for NIH or clinicaltrials.gov to adopt it, so including it in the US ISA may be confusing.

Commented [RMG30]: 35. WK: ODM (row 2) is not used for registry purposes. Though CTR-XML is based on the ODM spec, it is an entirely different standard. Recommend this be removed. - ODM is mentioned in another section