HL7 Study Design Structured Document Standard
Background Information

As part of its ongoing data standards research and development activities,[1] CDER is exploring the use of HL7 v3 as a future transport mechanism for standardized study content as defined by the Clinical Data Interchange Standards Consortium (CDISC) and the International Conference on Harmonisation (ICH). This 'suite' consists of four HL7 standards:

- Study Design Structured Document (for study protocol)
- Study Participation (for entities involved in a study)
- Clinical Document Architecture (CDA R2; for subject data including patient narrative)
- Individual Case Safety Report (ICSR; for expedited adverse event reporting)

The use of HL7 v3 XML is expected to provide increased semantic interoperability, leading to efficiencies in the management and analysis of study data. However, transitioning to an XML format would also require a major shift in business and data management practices for both CDER and its stakeholders.

The standards may someday replace the current exchange format (SAS Transport File (XPT)) with an HL7 v3 XML format for future electronic submissions of standardized study data. HL7 v3 can also transport additional study information that is currently exchanged using PDF (e.g the study protocol), as this information is not easily analyzed electronically or suited for XPT format.

CDER has long recognized the need to standardize study data. CDER has been accepting voluntary electronic submissions of standardized clinical study data since July 2004, and in 2011 began accepting standardized nonclinical study data submissions. Applicants wishing to provide clinical study data in standardized format are advised to follow the (CDISC) Study Data Tabulation Model (SDTM). Standardized study data submissions shall continue to increase, thereby increasing the need for a more robust exchange standard for this information.

Phase 1 testing of the HL7 study data standards, begun in 2012, focuses on testing the exchange of clinical investigator information (i.e. the information contained with the FDA Form 1572 and related information) using the HL7 Study Participation standard, and the exchange of patient narrative information using HL7 CDA Release 2.

Phase 2 focuses on testing the exchange of study protocol information using the Study Design Structured Document standard. Currently, study protocol information is exchanged as an unstructured, human-readable PDF document. This format results in a manual, labor-intensive review necessitating the reviewer to read dozens, sometimes hundreds of pages to understand the protocol and assess whether [1] adequate safety monitoring of investigative subjects is planned, and [2] the protocol is adequate by design to meet its research objectives. The HL7 v3 XML format by design is capable of exchanging all of the protocol information in a format that is both human- and machine-readable to facilitate review. This standard makes the study protocol truly 'computable' and sets the foundation for the development of new tools that can automate and facilitate the review of a protocol, enable comparisons of protocols with each other, and support automated or computer-assisted assessments of protocol compliance of study subjects.

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[1] See http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm269946.htm

To support testing, FDA uses xForms to facilitate the creation of test XML data. xForms are user friendly web-based electronic forms viewed in a browser that enable the tester to manually enter test data and automatically generate a valid HL7 v3 XML file. No prior knowledge of XML or HL7 standards is necessary. Style sheets are used to to view the contents of the XML files in human-readable format.

In addition, FDA has developed a technical infrastructure to validate v3 XML files and store the contents in a RIM database. This infrastructure is currently being used in a production environment to validate and store structured product labeling (SPL) for electronic registration and listing. This technical environment can be leveraged to validate and store study data provided in any v3 XML format, thereby reducing infrastructure/I.T. costs in adopting HL7 v3 XML for other types of regulatory information