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Achieving End-to-End Traceability Using Trace-XML

Jan 12, 2017 By Samuel Hume

Traceability is an essential element of data quality and a regulatory requirement for studies submitted to the US Food and Drug Administration (FDA) and the Japanese Pharmaceuticals and Medical Devices Agency (PMDA). Because a study's strength hinges on the integrity of source data as well as the quality and reproducibility of the processes used to generate the results, traceability plays a crucial role in reinforcing clinical research analysis results. In regulatory submissions, sponsors must demonstrate that the content of a submission database can explicitly trace back to the original source data in an unbroken chain, including any transformations or derivations that may have altered the data.

The Clinical Data Interchange Standards Consortium (CDISC) has developed the models, Operational Data Model (ODM-XML) and Define-XML, to represent metadata for data artifacts, such as case report forms (CRFs) and datasets created for use in clinical research. Define-XML is required as part of

a standards-compliant, regulatory submission to the FDA and PMDA and plays a key role in establishing traceability for submission datasets. Define-XML 2.0 provides most of the metadata needed to enable software traceability. Specifically, it provides descriptive metadata that displays the previous step in the clinical research data lifecycle. However, it does not provide the explicit references to source variables that would enable computable end-to-end traceability. Without these source variable references, automated end-to-end validation and traceability queries are not possible.

Trace-XML is a new extension to Define-XML v2.0, which delivers end-to-end, clinical data lifecycle traceability from data collection through final analysis. The Trace-XML extension enables standardized clinical study metadata to be represented as a graph, displaying the complete history of each data element to facilitate assessing audit trail completeness and correctness. The metadata supplied by Define-XML v2.0 and ODM-XML v1.3.2 includes the variables, datasets, sub-forms, forms, and computational methods that become the nodes in the graph representation of the study metadata.

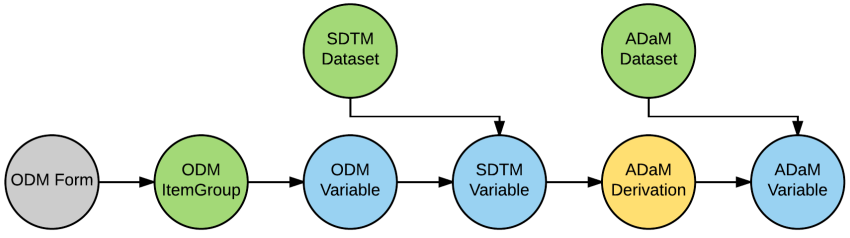

Figure 1. Conceptual example showing the type of Trace-XML content created for a variable trace.

Trace-XML adds the metadata needed to connect a variable, represented as

(API), or from SHARE exports. Source variables and connecting edges generated by the Trace-XML software are derived directly from CDISC standards, enabling it to graphically illustrate how these standards are interconnected based on variables used across different standards and in different versions of those standards. Once the graph representation of the study metadata has been created, an analysis variable can be traced back to its source providing traceability across a full study. For reviewers, Trace-XML

allows end-to-end querying, validation, and visualization of metadata across the data lifecycle. Traces generated by Trace-XML can be referenced in Define-XML to package full lifecycle traceability in a regulatory submission. Moreover, Trace-XML can broaden the concept of end-to-end by beginning with eSource data (electronic healthcare records) and flowing through to analysis results.

The Trace-XML end-to-end traceability improvements complement the existing ODM-XML audit trail and Define-XML traceability features to provide an enhanced CDISC provenance capability. CDISC will make Trace-XML (the software and Define-XML extension) freely available on our web site in early 2017.

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