

Building upon CDISC Industry Standards for Trial Specification, Production and Execution

Formedix has over two years experience in integrating CDISC standards into software products and providing CDISC consultancy for the pharmaceutical industry. This technology primer explains the company's use of CDISC standards and the software technologies that Formedix has built around the standards.

BACKGROUND

Over the past decade many information-led industry sectors have adopted vendor neutral platform independent data standards, to solve interchange problems, promote global harmonisation and lower operational costs. For example, consider the evolution of the Internet and the World Wide Web (WWW), predicated upon a whole set of global standards that have led to worldwide conformance and massive adoption of technologies. In the pharmaceutical industry the specification and handling of clinical data from disparate sources is a critical area that has long been problematic, time consuming and expensive. These factors affect drug companies, contract research organisations (CROs), laboratories, and regulatory agencies alike. The pharmaceutical industry is the latest to see major benefits from global standardisation through the work of the Clinical Data Interchange Standards Consortium (CDISC). CDISC is developing industry standards to support the electronic acquisition, exchange, submission and archiving of clinical trial data and metadata for medical and biopharmaceutical product development. The CDISC Operational Data Model (ODM) refers to the standard data interchange models that are being developed to support the data acquisition, interchange and archiving of operational data. The Submission Data Model (SDM) refers to the standard metadata models being developed to support the data flow from the operational database to regulatory submission.

THE CASE FOR A DEDICATED METADATA AUTHORING TOOL

Standards become truly useful when tools and services appear to implement them and make them accessible to the community. In the particular case of the ODM, the specification defines an XML-based format. XML is a platform independent, human readable, open-standard data description format. The ODM can represent both study metadata and collected clinical data. Therefore, for any study to make use of the ODM the starting point is a correctly defined ODM specification authored in XML.

If we return to the earlier example of the Internet and the WWW then it is obvious that there has been massive development effort to allow large and sophisticated web sites to be built, in short time scales. The most fundamental core language used by web sites is the Hypertext Markup Language (HTML), allowing the content and presentation of web pages to be defined. It is obvious that (for many web developers) if all sites were written just in HTML, without the use of specialist tools, then there would be very low productivity, higher cost and significant difficulty in completing the work within a realistic time scale. Web developers now use sophisticated software environments that deliver dedicated visual interfaces and tools to eliminate (mostly) the need to use HTML directly. Industrial-strength versions of these environments can allow concurrent access by many authors to allow different parts of the same website to be developed at the same time. Many extra productivity tools are also delivered to the authors. This is just one example where fundamental Computer Science principles are applied to create abstract, productive human interfaces and toolkits that protect the users from the underlying lower-level structures.

CDISC ODM development has many parallels with this last example. Although an ODM specification can be built by hand using an XML editor, it is time consuming, more frustrating and error-prone and requires specialist XML knowledge. Finding and reviewing content can become a protracted process. No facilities are available to support parallel working practices within the community responsible for clinical study origination. Creating and reviewing content in this way ignores the lessons learnt from the past. What is actually required is a tool that is dedicated to allowing a team to work together productively, at a powerful level of abstraction, with integrated tools, libraries (promoting reuse) and validation facilities. Our first trial specification tool, Formedix Origin Study Modeller, is designed to do just that. It facilitates the rapid creation of CDISC ODM-based specifications for your clinical databases - shortening study set-up time, increasing quality, and improving your business processes by enabling internal teams and your external suppliers to work together more effectively.

The Origin Study Modeller delivers interfaces that make it simple to originate, edit and review all parts of an ODM project, without the user requiring XML skills or ODM knowledge. Any component of an ODM project

can be rapidly created and edited, using intuitive human interfaces and specially designed wizards. The complete ODM structure can be navigated quickly and easily. Users can concentrate on study functionality, while Origin Study Modeller creates the underlying XML ODM representation.

A critical part of ODM authoring is the creation of valid files that are fully conformant to the standard. The Origin Study Modeller ensures that all files created are automatically validated and that any ODM file, from any source, can be read and validated against the standard. Throughout ODM creation, automatic validation is carried out and a compliance report is generated on screen. Users know instantly about problems with definitions, references, naming conventions, etc.

A pharmaceutical company can build libraries of reusable study elements (such as field groups, forms and code lists) within Origin Study Modeller. Once these are verified against in-house standards, they become reusable elements for subsequent studies. The savings in study database definition time and validation cost cannot be understated.

The Origin Study Modeller forms a unique collaborative workspace for study authors and reviewers. Multiple concurrent users can connect to take part in the study definition and review process.

USING ODM SPECIFICATIONS TO RAPIDLY GENERATE CLINICAL STUDY DATABASES AND eCRFs

Electronic data capture (EDC) systems have evolved significantly over the last decade to a point where there is more acceptance of EDC as an enabling force to shorten the trial lifecycle. The availability of reliable and high performance computing together with secure global communications has delivered a solid foundation on which to build upon. However, in many cases there is still a system build time of six to eight weeks for EDC vendors, for each new trial. This may be unacceptable, especially if EDC is being considered for Phase I trials with short lead times. Making use of our CDISC ODM skills and expertise coupled with Formedix Transform automated trial production technologies, we have taken the lead by introducing high speed translators and program-generative techniques which deliver higher quality EDC systems faster. Elimination of costly, error prone manual coding gives us the capability and capacity to deliver on time, every time. Formedix Transform technologies use CDISC ODM and other XML-based specifications to automatically generate Formedix Express databases. All user interfaces, navigation, eCRFs, business logic and back-end database definitions are automatically generated from pre-validated software libraries. The result is high quality and timely rollout of validated EDC systems with a rich feature set.

A RAPID BUILD EDC SYSTEM CENTRED ON CDISC STANDARDS

Formedix Express is an EDC solution, which can operate in a connected or disconnected mode and has a number of unique features such as Autoguiding, real time concurrent data capture and support for biometric signatures. The content and structure (metadata) of our EDC database is based on the ODM, and contains a robust version control and release system that makes mid-study protocol changes simple and auditable.

Every data value in Express can be exported to a populated ODM file. Selecting Express as your EDC system means that clinical data is portable and can be read and moved anywhere, now or in the future. Consequently, your clinical data and metadata will no longer be tied to the particular version of the proprietary EDC or clinical data management software you are using today or the upgraded version you may be using tomorrow.

WORKING TOWARDS STANDARDISED SUBMISSIONS

The pharmaceutical world is manifesting significant interest in the continuing development of the CDISC Submission Data Model (SDM). Formedix is actively working on technology that will allow customers to model their clinical domains in SDS 3.0, the version that has been developed specifically to meet FDA requirements and looks likely to be referenced soon in FDA guidance documentation.

FORMEDIX - WORKING WITH YOU

We want to work with you... Our consultancy practice provides comprehensive education, implementation and software development services as well as advice and guidance on business re-engineering and return on investment projections for clients who are considering migrating to CDISC data standards



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