

Implementation of CDISC standards supported by a global mapping process and a metadata library

Dimitri Kutsenko, Entimo AG, Berlin, Germany

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Introduction

In this case study, the presenter is going to open the curtain and allow a glance at a project conducted jointly by Entimo – technology and CDISC specialist – and a global CRO. The project particularly deals with the implementation of CDISC SDTM and customer specific standards in a company-wide standards library and the process of study conversion to these standards. The name of the CRO is not mentioned in this paper – the use case shall remain generic and will hopefully offer to the reader some interesting ideas to reuse at the concept level.

Gently touching some organization aspects of the process (which are certainly of interest, but not mainly in the focus of the stream Technical Solutions), this paper will concentrate on the technical side of the mapping process in the scope of this project: First we will critically look at the challenges and analyze in the next step the opportunities of working in a globalized and technology-driven world. In a series of examples, the redesigned data conversion process, involved roles as well as the innovative technology behind it will be presented. Conclusions and lessons learned will be discussed at the end.

Analysis Phase

Following the trend, big pharmaceutical companies are on the way to partly or completely outsource study conversion to SDTM, especially regarding the large stock of legacy studies available in every house. Among other factors, it was the growing workload, enormous time pressure from sponsors and increasing competition in the CRO sector what drove the CRO to step on the road of changes.

As one of the global players, the CRO has numerous locations around the globe, with front offices located in North America, Europe and Asia and supporting offices in South Africa.

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The project started with the analysis of the (at that moment) current situation. During the analysis phase, numerous improvement potentials were detected along the whole data mapping process. For example, it was found out that the approach to create specifications and programs was different from location to location promising efficiency gains from methodology standardization. Important information was collected during this phase which concerned the analysis of roles/tasks involved into the process, from specification creation up to creation of submission deliverables.

Among numerous challenges detected during the analysis phase was the fact that source extracts from databases are often delivered in different structures. In addition to the ongoing studies, numerous legacy studies need to be brought into a standardized form (SDTM) and enhanced with ADaM, define.xml/pdf and other submission components. An unpleasant specificity of many legacy studies was/is the fact of limited and missing metadata for these studies.

Standards governance is already non-trivial in the world of pharmaceutical companies. CROs face the next level of complexity: They have to manage many levels and versions of standards simultaneously for every sponsor with custom standard enhancements and specific requirements. All this happens in the front of permanently growing complexity of standards.

It was clear that a unified, company-wide mapping process needs to be developed and introduced. Such process would simplify training and would make tasks more efficient through re-use of elements and use of intelligent tools. Such a process would allow the organization to be more competitive and fast, which is especially important considering tough project timelines shortly before submissions.

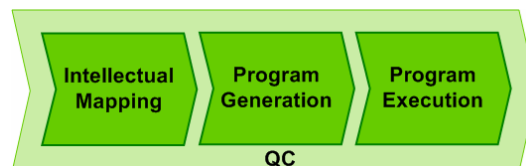
Process Re-Engineering

At the end of the analysis phase, project goals crystallized out. An ultimate goal was to define a globally distributed process and to reuse all numerous local best practices available at the CRO. The initial step was to create common use cases which can serve as a ground for a detailed process specification. The next step was to streamline the process.

Starting at the very abstract level, the data conversion process went through face lifting, where the optimized form would allow for splitting of tasks.

The following steps were identified:

- Intellectual mapping (to determine how to map the trial data into SDTM and to re-use mapping templates)
- Program generation (to automate generation of mapping programs)
- Program execution (to execute mapping programs in the controlled and traceable)
- QC (overarching activity to perform technical and functional review of trial-specific mappings at trial level)



In the next step, the process was broken down into smaller tasks. Based on the outcomes, process maps were created for all data conversion scenarios with detailed task description and exact responsibilities based on the developed role model. Access set-up for blinded vs. unblinded programmers or technical programming code review are examples of such process maps.

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Same process look and feel promised easier training of new colleagues. In addition, tasks can be shared between team members located remotely all over the world and global teams can be dynamically created to support necessary skill matrix.

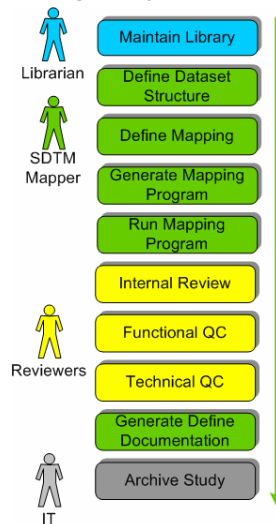
To use advantages of a global player working in a global and technology-driven world, several requirements were detected and assessed as essential:

- All components shall be available in a central location to easier implement best practices
- Standard elements shall be consistently reused
- Global teams shall follow the streamlined process

The following roles were defined in the redesigned process:

- Administrator
- Clinical Programmer
- Reviewer
- Librarian

The following figure illustrates the redesigned process at the top level:



Due to the importance of standards, the metadata library and the librarian play a key role in the new process and will be addressed more detailed in the next chapter.

Metadata Library

The metadata library is the key element of the process. A strong requirement was related to the fact that the metadata handling must be flexible to allow not only to support common company and standardized metadata (e.g. CDISC-compliant), but also to allow the integration of sponsor specific metadata and be extensible to cope with future changes (e.g. new CDISC versions). In addition, parallel versions of standards shall be managed due to longitude of clinical projects. We see the library in the project in a broad sense: It is not limited, for example, to such elements as domain definitions, terminology, codelists, format catalogs only. Huge potential is related to the reuse of standard algorithms, standard macros and standard mappings. To make the process even more efficient, the library is used to store specifications, guidelines. Moreover, due to the enabling technology, even such elements as study folder structures were made available as templates to rapidly create studies with pre-configured roles and other properties.

Tracing the usage of SDTM structures on the target side, we can see that they are used in several outcomes of the process, for example, in the mapping specification, mapping programs and define.xml. Consequently, the management of target domain definitions reveals a great deal of potential for reusability. Due to this fact, the process was designed to begin with the

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definition/usage of metadata templates for target structures. The templates contain all core information such as domain and attribute level metadata as well as links to controlled terminology and/or dictionaries which is already pre-configured. This approach reduces the work in a mapping project to adjustments, smaller in comparison with setting up the structures from the scratch. Certainly it means more work initially, but allows users to benefit later from reusable domain definitions.

The librarian was entrusted with the following tasks:

- Maintain information model and related logical data models
- Develop mapping templates and standard algorithms
- Develop standard codelists, macros
- Maintain consistency of variables (content, process)
- Prepare recommendations for standards governance

To continuously improve the library, a change management process was developed. Also in this case, the technology plays a key role: the process was introduced based on electronic change requests for creation or update of standards. Concerned objects can be attached or linked to the electronic forms allowing reviewers and the librarian easy navigation even in complex hierarchies. Change requests are enriched with workflows and automatic notifications to dedicated roles.

Continuous Quality Control

The QC function plays a critical role in the whole mapping process. During the analysis phase, QC steps were identified, described and installed in the process.

Due to their importance, the domain definitions were the first candidate for comprehensive quality control. This sounds obvious, but has wide-reaching consequences, especially given the number of mapping-related work results where the target domain definitions are used.

For this reason, the concept of "metametadata" was introduced. They can be grasped as configuration rules for metadata structures with additional metadata checks. Based on the defined rule set, for example, if the user tries to enter a sequence number violating the rule "integer, unique and starts with 1" the environment refuses to store changes.

This helps control quality already in the metadata definition phase.

The workflow includes several QC points, such as internal review, functional and technical QC.

Standards used in the project help significantly reduce validation effort. The process includes standard SDTM checks enhanced, where necessary, with sponsor-defined checks integrated into the workflow. Such comprehensive quality control guarantees that the formal aspects and defined requirements are validated, leading to improved data quality at the end.

Conclusions

The described project has been evolving meanwhile for several years and is constantly progressing by refining the process and environment configuration. The growing metadata library with reusable standards saves time, increases quality and efficiency in the data conversion process.

One of the system introduction aspects, which is repeatedly stressed in the management literature and was confirmed in this project, is the importance of continuous and intensive training in the process and enabling technology until users gain confidence in the live system. The concept "train the trainer concept" was successfully used in this project to increase internal user acceptance and buffer the switch to the new process and new technology and to overcome the human resistance factor.

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Besides the process definition broken down into task descriptions with clear responsibilities, requirements to the enabling technology belong to key success factors. Summarizing top-level technical requirements in this project, which are especially relevant for a CRO, the following can be mentioned:

- Flexibility to deal with different types of standards and metadata at different levels (company, sponsor, trial, study)
- Flexibility to support different data models and workflows
- Reusability of work results within the library and at study level
- Global accessibility of the process and the library across trials
- Easy user access right management based on roles (librarian, clinical programmer etc.)
- Validation and regulatory compliance (21 CFR Part 11)
- Scalability to handle growing amount of work
- Extensibility and openness for future changes and advancements

Summarizing: The approach to start quality control activities very early in the mapping process combined with the integration of reusable metadata definitions and metadata-based tools shortens the process duration, supports more efficient data QC, secures the quality of deliverables and consequently contributes to overall business success.

Contact Information

Your comments and questions are valued and encouraged. Contact the authors at:

Dimitri Kutsenko
Entimo AG
Stralauer Platz 33-34
Berlin / 10243
Germany
Work Phone: +49 30 520 024 100
Fax: +49 30 520 024 101
Web: www.entimo.com

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