Paper DS06

Standards Library: Getting started - A Medical Device Case Study

Amy Booth, Veramed, Inverness, Scotland
Thierry Philippe, Instem, UK Office Staffordshire, UK

ABSTRACT

This paper describes a framework for implementing a Clinical Data Standards (CDS) Library which can start small and grow with you as you add more assets to the library. An in-house company standards library is one of the key foundations for achieving efficiency gains through reuse, higher quality, and reduced timelines. However, it is not without challenges - not least maintaining alignment with global standards, mappings global standards to company/franchise standards, version control and change management. This paper walks through a Medical Device case study, and describes the library structure, process flows for SDTM, ADaM and TFL submission deliverables, validation and metrics reporting, lessons learned, and future aims to support automation.

INTRODUCTION

Creation of an in-house standards library can produce a significant increase in efficiency of reporting from clinical trials. The goal of most standards libraries is to work towards the use of a Metadata Repository (MDR) to automate standards curation and allow easier tracking and use of the standards library. For most companies the path to a full MDR will take years and implementing may be costly with a large timeframe until being able to see improvements in efficiency.

To begin the journey to an MDR or full standards implementation but also see efficiency gains in the short term we have implemented a Standards library consisting of a standards framework without the technical cost and technology requirement. Starting with a framework of PDFs, excel sheets, folder structuring and tracking we can move towards the benefits of an MDR with automation being a longer-term goal.

This first step provides several benefits to your trial team; having a library of artifacts to select from at trial offset cuts build time and the time of each trial delivery phase with standard mappings from CRF through SDTM and ADaM to TFLs. Sectional libraries for smaller processes have become common place for example CRF libraries, by creating a standards framework for end-to-end usage we aim to streamline the full process while also being flexible enough to implement and track change.

When building a standards framework structure there are several considerations to be made which will be discussed in this paper: artifact creation and life cycle, taxonomy, version control and governance. While the standards framework has been created to be flexible enough for use with any therapeutic area in this case, we're applying the framework to a Medical Device case study and will reference key differences which should remain central to population of the Medical Device specific domains and Medical Device related variables in your datasets.

ARTIFACT CREATION

Collection and categorization of artifacts is an important base. For our standards library case study, we began by collecting client standard CRFs and annotating them based on CDISC standards. The CRFs and CDISC reference documents were categorized into our framework (See taxonomy section for details); the annotated CRFs (aCRF) were then available to view at the start of a trial so the study could be built from the selection of artifacts already available, with the option to add to the library based on the same CDISC reference versions. Standard SDTM mappings are then added to the library built from the aCRF forms and from then it was also possible to create standard ADaM mappings downstream from the SDTMs in the standards library. To allow standard ADaM mappings to be created we require standard TFL shells which then inform the ADaM mappings and conversion from SDTM. For full standards framework implementation these standard shells would also become part of the library.

When evaluating CRFs with Medical Device reporting in mind it was important to Evaluate the Tables Figures and Listings to allow full mapping of variables from CRF to SDTM and to make sure required variables for TFLs were mapped into ADaM. Some Key differences were noted by the team so are worth raising for evaluation with a Medical device study:

- Devices should be tracked with a set of Device Identifiers and may be reused by the same patient repeatedly or reassigned to different patients but the Device should always remain identifiable with a unique identifier SPDEVID which may be concatenation of various identifiers which when joined allow direct identification of a single device.

- SPDEVID should be defined as early as possible when collecting artifacts from the library as some domains do not require connection to a patient but connection to a unique Device e.g. DT Device Tracking does not require USUBJID variables.
- Addition of Device related variables to commonly used SDTM domains should be considered and added to your library especially if you are a sponsor with several similar devices. We added AELOC and AELAT to allow reference to adverse events experienced on localities/laterality of interest to our device usage.

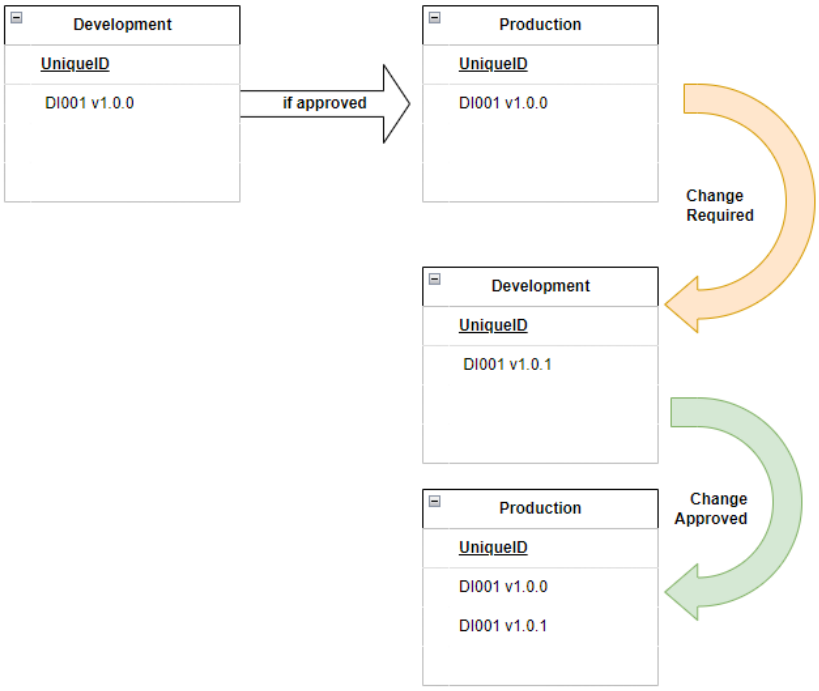
Although there are differences to be considered when using your library for a Medical Device study at the root most domains can remain similar in structure and then hierarchical classification and taxonomy allow reuse of artifacts. Being able to move away from recreating similar CRFs or SDTM mappings at every new study build has already cut time to SDTM outputs and ADaM datasets being available. For each study the more artifacts used from the library the better, but the framework also allows flexibility for artifacts to move up or down hierarchy levels when required.
When using your library artifacts with a Medical Device study care should be taken to evaluate relationships between Patients and Devices as this may differ in every protocol. SDTMIG MD v1.1 was added to the industry level of the library then referenced to create several medical device domains. Your Related Records relationships will vary based on protocol – A single use device may differ from one that is reused multiple times by the same patient or reassigned to different patients. Defining relationships and determining which combination of Identifiers should be used in SPDEVID early in the mapping process is key for identifying how Device domains are related to each other.

Now we need to consider the process of addition or retirement from the library, so an artifact Lifecycle process is developed.

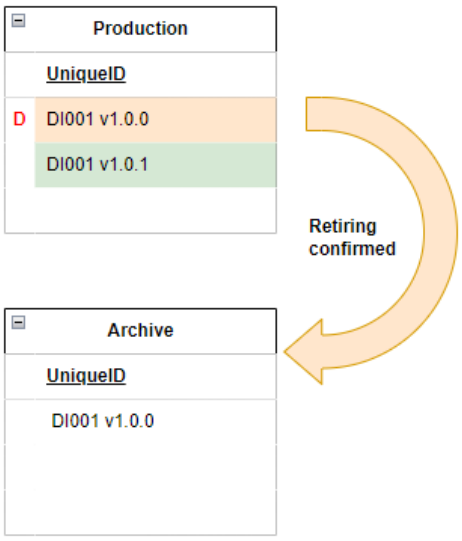
ARTIFACT LIFECYCLE

Starting with the idea of artifact life cycle we need to consider tracking of living artifacts and how to add and amend artifacts when required without overwriting the existing artifacts as they may already be in use.
All artifacts in the library will need to be grouped by status. Starting with Development and Production.

With DI001 below as an example from creation through a change cycle.

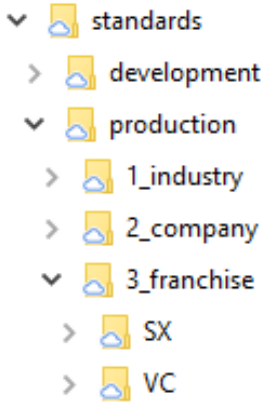


From then DI001 has multiple versions in the Production Library. If DI001 V1.0.0 is in use in an ongoing study, we want it to remain in the library but in a deprecated state (marked D below). From then all studies moving forward use DI001 v1.0.1 but traceability is ensured as the artifacts are never overwritten.



TAXONOMY

Starting to define a taxonomy for our library structure, Industry is the top level of the standards tree, where the artifacts are a direct match to CDISC standards.



From there we define groupings to allow further categorization: Company - or Global level which will hold any artifacts which should be used for all trials for the client - most common examples would be DM, DS, or IE then due to the specificity of our client we're also adding Medical Device domains that would be applicable for all their studies. DE (Device Events), DR (Device Relationships), DI (Device Identifiers) etc.

From there we move to franchise level which divides our artifacts into a more granular level if they are applicable to a therapeutic area. We start with two, SX surgical and VC vision care, but the library would become more comprehensive as other studies and therapeutic areas are added.

At the base is an area which should remain reserved for Study level items in most cases there should be very few items added to this level of the library as changes to the artifacts should be considered and triaged rare instances of questionnaires or study specific artifacts which significantly differ from existing standards should be held here.

In general creation of artifacts should begin at CRF level in this case our client had a CRF library of commonly used forms which we used as a base annotating with CDISC variable names.

The library should hold as many standard artifacts as possible and then all studies should use artifacts from the higher levels of the library before diverging from it. Diverging only when necessary - remember that each study level change will require additional work, time and testing. Study level artifacts are then moved into the library so this work can be used by other studies and then moved up levels if it is decided it should become the new standard moving forward. The emphasis being that new artifacts should only be added when necessary but also keeping in mind that Custom Domains are expected to be added at the early stages of building your standards library.

Traceability of artifacts has also been ensured with a naming structure of files as follows:
SX_SDTM_DI_MD1.1_v2.0.1 - SX is Surgical Franchise, SDTM is the mapping structure, DI (Device Identifiers) domain, MD IG version 1.1 is being used and it is version 2.0.1 of this spec.

VERSION CONTROL

Version Numbers relating to the library are held in the format 'x.x.x' (Major. Minor. Issue)

- Major Changes we classify these as changes related to a new Industry Standard, if a new version of an existing item is to be added which has several breaking changes, removal of fields or addition of several fields.
- Minor Change If an item needs to be modified to add a single field.
- Issue fix If an item needs to be modified to fix a misspelled label or incorrectly named variable.

If trials are ongoing and using artifacts which have since changed in the library the Version numbers provide useful information as to if a newer version should be picked up part way through a study. The version numbers and addition of a history tab where changes are described in the file once they are implemented also allows anyone using the library to easily decipher the changes added.

As part of an MDR it's possible that each individual variable would have further traceability added by being able to see the full detail of each variable in each spec linked to version numbers so if a variable derivation changed at V1.0.2 the previous derivation would be held against the variable and V1.0.1.

Once SDTM or ADaM programs have been created and tested relating to a specific version of specification they can then be relied upon and don't require retesting for each study as they are held under this version control process.

DATA GOVERNANCE

With a standards governance process in place, we can make sure new artifacts are only added to the library when required and keep a library that is a solid base for all trials and evolves with use. By keeping in line with CDISC standards when new guidance is released and ensuring change is only brought into the library by agreed process and after review, we can gather efficiencies for all studies moving forward. As part of the process, we also continued to give additional training to create a team who can oversee and gatekeep changes to the library allowing the library to become a resource which can be relied upon as a base when starting a new trial. This team can suggest changes or improvements, suggest the movement of artifacts, and continue to review specifications around the library artifacts. A Standards Governance Team and time allocated to specifically perform this function will provide benefits to the quality of artifacts in the library and specialized roles related to the library as an overall product rather than individual study standards will allow significant decrease in standards library implementation.

PROJECT GOVERNANCE

Implementation of a Clinical standards library requires first a solid project governance to transition to your future state. It means for the pharma organization: people. Roles and responsibilities of those who will have the exciting, yet challenging tasks to plan, execute and monitor the different milestones.

That is especially critical if you are engaged with vendor(s) who also provide their workforce and expertise, who is accountable for what? Who is responsible for what? Who validates the milestones? Who controls the activities? Etc. So, a project governance team is required to be defined before the project, actively present during the project and keeps to some extent overseeing the stability and the efficiency of the standards post project. If not existing already a governance committee is a cornerstone to the stabilization and the extension of the newly implemented standards. You create a chain of command, as well as establishing process of decision making, which allows the operational teams to cope with deviations, new standards, or new elements at franchise or company level, and to get engaged in any future development.

CHANGE MANAGEMENT

As a subset of Project Management, change management is a key aspect of the transition, that responds a single question, "how are we going to make that CDS library a success and a buy-in for the end-users?" There are several components of change management, but we will focus on two of them, training, and communication. Each of them must have a plan. It describes the purpose, the means and the different steps which lead to success.

Training is about ensuring timely and customized training sessions are provided throughout the implementation so that the end users gain the necessary knowledge, also consider regular evaluation or monitoring. It is also to integrate regular training updates for the seasoned staff, or early training for new staff in your training matrix.

As for communication, that starts with an assessment about whom needs to know about the standard library, in other words who are the stakeholders, ranging from being informed in detail to general information, that goes both for operational and leadership level. A thorough plan of communication management will formalize the stakeholders identified and apply appropriate communication strategy.

FUTURE IMPROVEMENTS

As the library grows and starts to evolve metadata generated from the library will be a valuable resource. The review of this metadata can lead to implementing change and toward improvement. For example, being able to view a spec changing many times within a year - what was the reasoning for this change? If a spec is not being used due to the franchise no longer being required for new studies, should it remain in the library indefinitely? The full study artifacts can also be reviewed for standardization at end of study informing how much of the library was used or if high deviation from library artifacts is discovered are significant changes required? Information such as this can inform change and can then feed change back into the library. Reporting and visualization of how conformant study artifacts are in relation to the library can also inform how much expected effort from teams will be required to create and test new specifications, programs, and review of artifacts.

Moving forward the library can continue to evolve with the addition of automated outputs and at least basic versions of study design specifications for implementation with study builds, SDTM and ADaM specifications, programs, and reviewer guides.

The benefit of not having a full MDR in place here is that data collected can change as studies are using the library and full schema can evolve more readily than needing to have set schema in place at implementation.
With the efficiency gained and standard reporting structure it will also be possible to easily group data from related studies or follow on study types. Reporting outputs will also be available much earlier in the study. When you are ready to implement an MDR you will already have a process and much of the required schema in place so the burden for implementation will be significantly decreased.

CONCLUSION

The creation of a standards library doesn't have to be a process which replaces your current process immediately and can be built as an incremental process. By building your standards library starting with a simple file structure rather than an expensive MDR solution you can gain the benefits of more efficient analysis with all stages of trial data mapping. The standards library framework also allows you to amend file structure or metadata collected with minimal cost and time for changes. The framework process outlined in this paper makes use of the implementation of artifact creation, lifecycle, taxonomy, version control and a governance process for you to take the first steps towards an MDR but gaining efficiency benefits and knowledge while building. Moving forward an automated library and metadata from library usage will feedback to inform future changes.

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Michael Beers

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:
Author Name: Amy Booth
Company: Veramed

Email: amy.booth@veramed.co.uk
Website: https://www.veramed.co.uk

Your comments and questions are valued and encouraged. Contact the author at:
Co-Author Name: Thierry Philippe
Company: Instem LSS
Email: Thierry.philippe@instem.com
Website: https://www.instem.com/solutions/

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