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Managing Data Standards Libraries compliance (to CDISC)

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INTRODUCTION

In a world of evolving standards and applications, remaining compliant with CDISC standards can be a challenge. For companies that have already integrated their Data Standards Libraries into an application platform, the upkeep of standards compliance remains, even in the maintenance phase. By including the generic CDISC eShare Data Standards into your standards platform and implementing a set of robust Quality Control processes, organizations can reduce the data standards 'compliance burden' and deliver efficient standards management.

The presentation will give an overview of the advantages of being able to include (multiple) CDISC eShare standards, Controlled terminology versions, and existing company-specific Data Standard Libraries within an eApplications Library environment, including the ability to compare the data structures received from CROs against the sponsors' standards stored in the eApplications Library.

We will discuss the use of consistency checks for CDISC CDASH, SDTM and Controlled Terminology compliance before validating and promoting metadata to production. And finally, we will describe the benefits to an organization that improved compliance in metadata brings with the reduction of issues and increased quality from study set up through to study 'go live'.

DIFFERENT MODULES IN THE EAPPLICATION

An eApplication platform for data standards management and study conduct (CDmation®) has been developed by Business and Decision Life Sciences meeting business requirements that are specific to the needs of Data Management departments. A high-level overview of the different modules in the eApplication will be provided (Figure 1). The different modules within the platform support a managed process that enables compliance with CDISC standards, both for metadata and study data.

- Library Management (LM) module: Global metadata repository;
- Study Specification (SS) module: Selection tool to enable metadata to be pick-and-selected for a study;
- Study Metadata (SM) module: Selected study metadata repository
- Study Validation (SV) module: Validation of study metadata and dataset content
- Issue Management (IM) module: Reporting tool for issues encountered during Study Validation

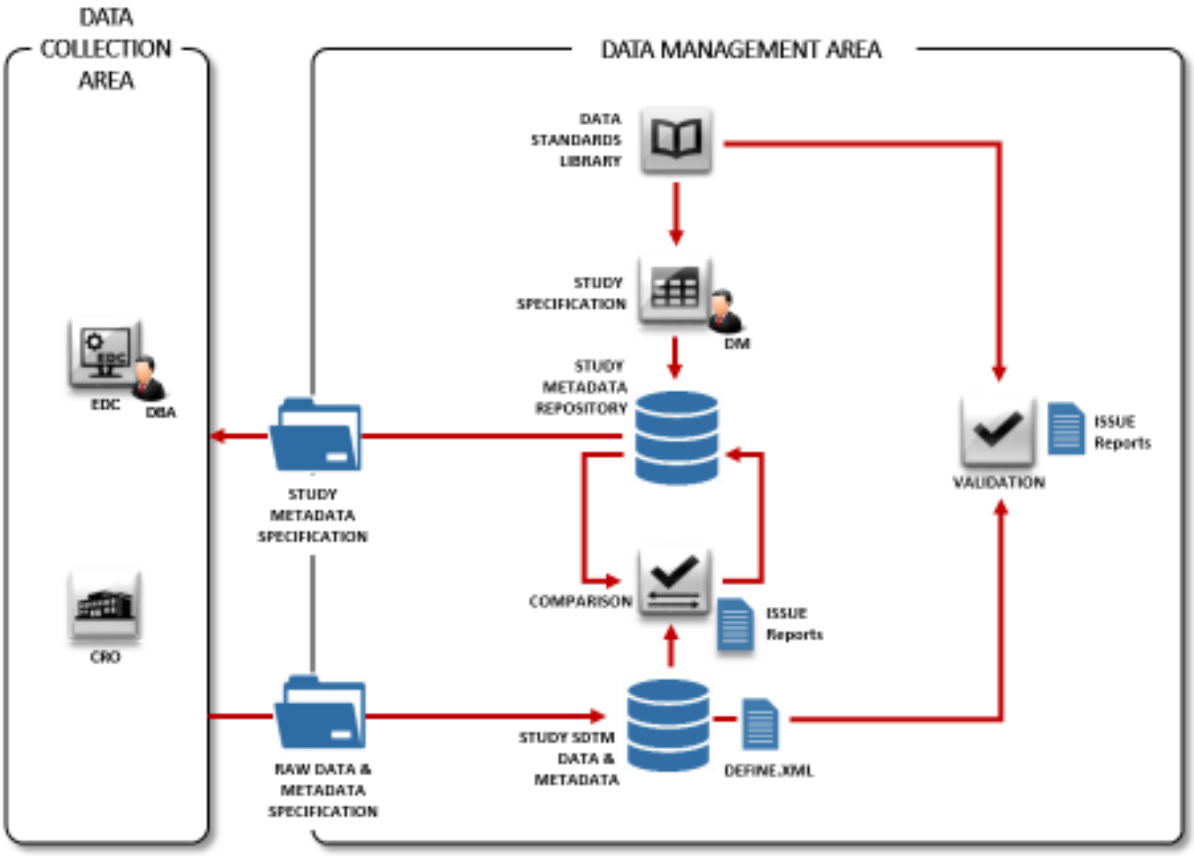

Figure 1 - Overview of the eApplication (CDmation)

OVERVIEW OF DATA STANDARDS LIBRARY MANAGEMENT MODULE

The Data Standards (DS) Library concept is based on a five-level metadata cluster approach (domain metadata, variable metadata, value level metadata, controlled terminology, computational algorithms) which ultimately provides a 'pick' and select solution for building submission ready study specifications as from study start.

The DS Library is designed to contain all sponsor-specific standard CRFs annotated in CDASH and SDTM (Figure 2). Each unique CRF is linked to a cluster of metadata specifications containing all standard domain structures, variables, code lists, value level metadata and computational algorithm(s), in order to facilitate the build of the study specifications.

To enable rapid/bulk development of CRFs and metadata specifications, these can be imported into the DS Library in a single batch using an Import file template - or can be entered and updated manually through the Library Management (LM) User Interface (UI).

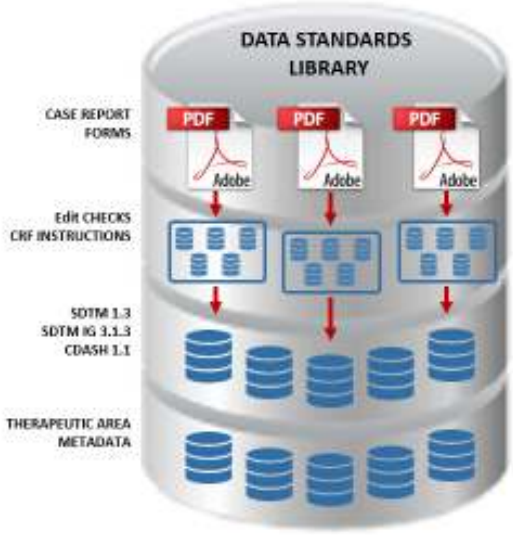

Figure 2 - Data Standards Library

OVERVIEW OF STUDY SPECIFICATIONS MODULE & STUDY METADATA MODULE

The Study Specifications module is used to generate study metadata by "picking & selecting" CRFs from the DS Library. The Study Metadata module then stores the selected metadata in the study metadata repository.

As part of the process, the study metadata is used to automatically transform the study specifications into a Define.xml file. The Define.xml file can be provided to external service providers who will collect your data and convert it to SDTM as specified. As this type of file is part of any standard submission to the FDA, the external provider will generate and provide a Define.xml that can be compared to the original file provided. Hence, it can be used to measure the consistency of metadata via comparisons across study metadata versions, projects and compounds.

OVERVIEW OF STUDY VALIDATION MODULE

Validation of SDTM datasets will be done through the Study Validation module where checks can be managed and selected to check structure and content of datasets according to CDISC standards and business rules, and according to the study metadata repository. It provides a set of checks to meet FDA CDER requirements and the ability to manage and apply checks specific to different therapeutic areas.

These checks have been developed by BDLS originally within BDLS DMCC tool (Data Model Compliance Checker) and included in the eApplication. The eApplication hereby contains an expanded & enhanced list of checks based on 227 OpenCDISC checks. Checks for SDTM are maintained and enhanced through the update of the CDISC standards and sponsor customized checks can also be added.

OVERVIEW OF ISSUE MANAGEMENT MODULE

Checks write issues in the Issue Management database that can then be assigned and tracked for resolution.
An Issue Tracker module enables the automatic tracking of exceptions throughout the study life-cycle. It can provide detailed metrics report on the average issue resolution time and the performance of external and internal partners (volume, quality and cycle times).

CURRENT CHALLENGES AND SOLUTIONS FOR BEING CDISC-COMPLIANT

A key objective of the Data Standards platform is the creation of standardized CRFs and associated metadata that are CDISC-compliant and at the same time fit the sponsor's needs. Whilst the platform provides a robust framework in which to define and manage standards, both at a global and study level, there still remain challenges that need to be overcome to ensure long-term CDISC-compliance. In implementing the platform, we encountered challenges in three main areas:

- Creation of the metadata specifications;
- Loading of the metadata specifications into the platform;
- Performing manual updates into the platform;

As there are inter-dependencies between modules, the development of solutions to these issues required a holistic approach; a solution upstream in the process had to work for downstream activities and vice versa.

CREATION OF THE METADATA SPECIFICATIONS

Challenge: During the initial development of the process for creation of metadata specifications, the alignment of vision of the different functions and roles involved was often difficult. Different team players (librarians, data managers, clinical team) had divergent viewpoints on the requirements, priorities and understanding of standards, as well as the implementation processes for development of standard CRFs, including the need to support different platforms.

Solution: To achieve the creation of standardized CRFs and associated metadata, at the start of each data standardization project, it was decided to make it mandatory to set and maintain a clear, streamlined vision throughout the project. With agreed development principles and framework used by all, everyone focussed on the end goal of creating a DS Library that was CDISC-compliant, not only at the point of creation, but capable of supporting expansion of the data standards library.

Additionally, as part of the DS Library design principles, it was agreed that the solution would be platform independent (i.e. not tied to any particular EDC system) and should follow CDASH standards. Where development issues arose due to conflicts between EDC system design principles and the DS Library design principles, regular

reviews were held to reinforce compliance with development principles and support the team with quickly reaching agreement on the best way forward (Figure 3). To allow the solution to be implemented across different EDC systems, an additional EDC auto-conversion layer was proposed that allowed the CDASH-compliant library specifications to be consumed by the EDC system.

Figure 3 - Data Standards Development Cycle

LOADING OF THE METADATA SPECIFICATIONS INTO THE PLATFORM

Challenge: When metadata is being loaded into the platform, it will first pass a series of BDLS-defined validation rules (principally, metadata attributes checks) before being promoted from a development workspace into the repository in the LM module. Although the validation rules check for consistency with platform requirements at the point of promotion, CDISC metadata validation rules to confirm the conformance of the metadata content against the CDISC standards were not included in the scope of the DS Library development phase. The consequence of this was the potential risk that the DS Library whilst compliant with the system specifications, may not be compliant with CDISC standards.

Solution: In order to eliminate the risk of loading non-CDISC compliant metadata into the repository, we created a set of external QC tools to check for compliance between the metadata created and CDISC CDASH UG, SDTM IG and Controlled Terminology. These external QC Tools allow to use and check against different available versions of the CDISC industry standards.

PERFORMING MANUAL UPDATES INTO THE PLATFORM

Challenge: Whilst external QC Tools resolved the risk at data load into the platform, the absence of CDISC validation rules meant there remained a further potential risk that even if a CDISC-compliant DS Library was created, there was still a chance that non-CDISC-compliant library objects could be created when working with the LM User Interface directly.

For example, if a Librarian updates an existing metadata object in the Library, there is always a chance of human error, such as a typographical error. Since there are no CDISC validation rules available at the LM module level, the error would go undetected in the repository, and be available for consumption in the study metadata repository after creating study specifications.

Solution: To establish a compliance baseline, we performed an exercise to check CDISC-compliance of the loaded DS Library by creating an export file of the Library, and running our external QC tools over the file. The exercise showed that the DS Library was CDISC-compliant, but identification of the applicable standards' version identifiers for a Library Object was not captured. Whilst this should have little impact on daily use of the Library, it could be problematic in trying to differentiate between versions of a standard within the Library at any given time point.

CDISC ESHARE: THE FUTURE SOLUTION

Although the solutions put in place allow the creation and validation of CDISC-compliant Library Objects, our longer-term solution is to extend the Data Standards Platform and to integrate it with CDISC eSHARE via an API, and develop a more sustainable, robust, long-term solution.
For our solution, the creation of CDISC-compliant DS Libraries consists of two parts (Figure 4). The first part of the solution is to load the CDISC eSHARE pharmacy standards into a separate CDISC eSHARE DS Library in the LM module. This Library will contain all versions of CDISC standards.

The second part of the solution includes implementation of a reporting tool which will contain a set of CDISC validation rules in the LM module. These validation rules will allow the comparison of a sponsor-specific DS Library against the CDISC eSHARE DS Library.

By implementing CDISC eSHARE DS Library this ensures that only CDISC-compliant metadata will be loaded into the platform. Furthermore, when performing manual updates in the LM User Interface, the presence of CDISC validation rules eliminates the risk of promoting non-CDISC-compliant objects into the Library.

An additional benefit of including CDISC validation rules in the LM module will be the assurance that the generated study specifications delivered to external service providers will be CDISC-compliant. Following on from this, when receiving clinical study data from external providers, it will be possible to compare study data to sponsor-specific DS Library or to any of the data standard versions contained within the CDISC eSHARE DS Library.

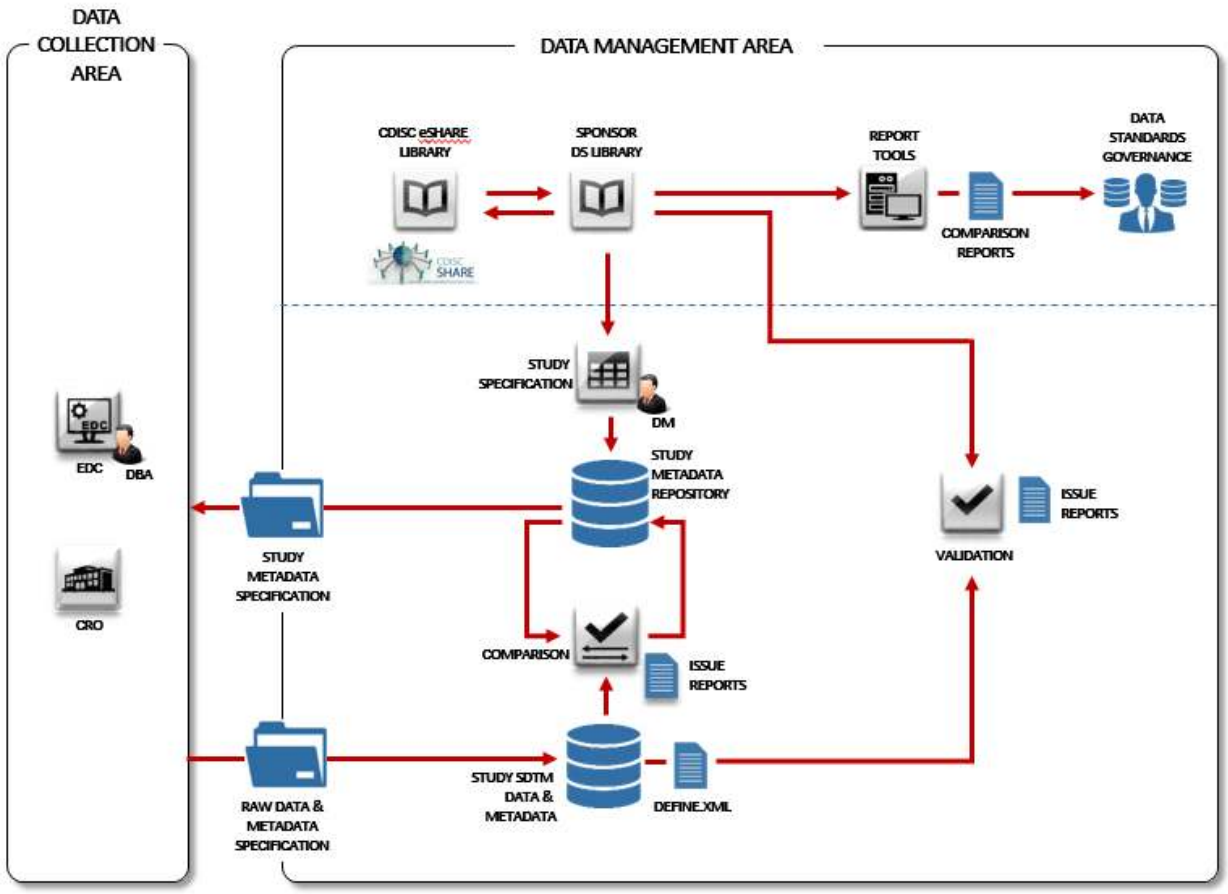

Figure 4 - Overview of CDmation (Extended Solution)

CONCLUSION

When developing a Data Standards management platform, there are a number of factors that need to be considered. In the initial stages, it is important to align the vision of the team, to define objectives and processes, and to agree/enforce Data Standards Library design principles.

As standards are developed and updated for the DS Library, it is important that Data Standards Governance mechanisms are in place for safeguarding compliance with CDISC industry standards throughout the life cycle of a standard. Implementation of CDISC validation rules and sponsor-specific business rules ensure standards remain compliant within the DS Library, at study specification and in the study metadata repository.

With the development of CDISC eSHARE DS Library, it will be possible to develop a more sustainable long-term solution that provides a more robust enforcement of compliance, both for the DS Library and for study metadata repository. The implementation of both a CDISC eSHARE DS Library and CDISC validation rules will ensure only CDISC-compliant metadata will be promoted to the repository, and that the study specifications generated from the DS Library will be CDISC-compliant as well. Standardizing metadata in libraries together with the ability to automatically verify conformance of clinical study with the defined standards will ultimately save time, improve the overall data quality, and consistency of study data across studies.

CONTACT INFORMATION

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