

A Model for Reviewing the Operational Implementation of CDISC Standards

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ABSTRACT

Whilst progress has been made in establishing clinical data standards, their operational implementation continues to challenge many organisations at both the technical and organisational level. Using the CDISC standards vision of clinical data support from protocol to reporting, this paper presents a model that can be used to evaluate the continued gaps and challenges between published CDISC models and how they are operationally implemented to support studies. Each key requirement of standards governance e.g. versioning, mapping, validation, etc., is presented in relationship to the operational requirements needed for study implementation. A “masking” technique can then be used to review or test different aspects of the system. For example, a “MDR mask” will show where the standards repository interacts with study work; whilst staff responsibilities are highlighted using a “role mask”. Practical examples will be used to illustrate the value of the model to identify different aspects of standards governance.

INTRODUCTION

Adoption of, the requirement to use, and the investment in CDISC standards is now well established. However, there is not currently a clear implementation model that is guaranteed to deliver the hoped-for quality, efficiency and productivity gains that adopting standards should provide. Unfortunately, organisations are often faced with increased costs and workloads, with extended timelines, in order to meet regulatory submission requirements.

The management and integration of standards into operational work is complex, with no simple off-the-shelf solutions since each organisation requires a solution in sympathy with the scope and objectives of their business. This paper presents a generic standards model that can be used to identify, describe, review, and test an organisation’s CDISC standards adoption and management methods. In the early or pre-adoption stage, the model can be used to explore and test different implementation strategies, during implementation to help with operational integration, and following adoption to improve operational efficiencies.

A CDISC STANDARDS OPERATIONAL IMPLEMENTATION MODEL

MODEL FRAMEWORK

The CDISC Foundational Standards ⁽¹⁾ provide the set of end-2-end standards needed to be implemented to manage the description and interchange of clinical (and related) data. These provide the first key framework element of the operational implementation model (note: for clarity this paper will restrict itself to a discussion of the principal clinical data standards rather than all the foundational standards – e.g. ODM – or the non-clinical data standards). Fig. 1 presents an example of the key elements of the operational implementation model.

The diagram illustrates how the CDISC Foundational Standards are combined with five operational elements to form a 5x5 grid. At the intersections of the grid the specific details of each standard of interest are displayed, with relationships between the standards described by the directed lines. The details of each element are described in the following sections.

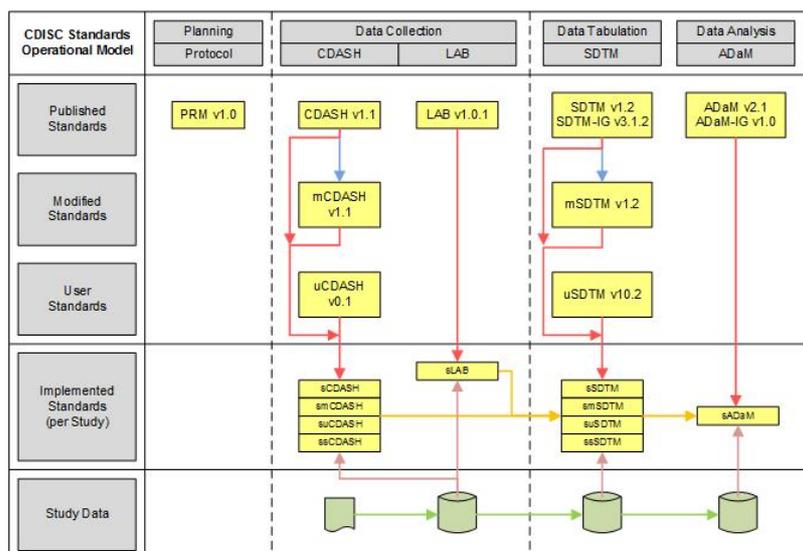


Figure 1: Key elements of the Operational Implementation Model. The CDISC Foundational Standards are represented by the columns; key operational standards concepts and the study data by the rows. Implemented standards are presented at the intersections, and relationships between each standard and operational state by the directed lines. See the text for full details.

MODEL ELEMENTS AND INTERACTIONS

CDISC Standards: The CDISC standards are represented in the model by the grid columns. Fig. 1 shows the five foundational clinical standards organised as presented by CDISC into the four standards groups: Planning, Data Collection, Data Tabulation and Data Analysis. The vertical dotted lines represent boundaries between the principal phases of a study (Planning, Execution, and Reporting). These can be extended or reduced to reflect specific situations.

Operational Implementation: The operational elements are represented by the rows, and these should reflect in more or less detail as appropriate how the standards are used within the organisation. In this example, four operational standard “states” are shown:

- **Published Standards** – The ‘vanilla’ standards as published by CDISC
- **Modified Standards** – The basic standard as implemented. This might include minor additions or modifications but without significant changes from the published version (prefix: m)
- **User Standards** – Standards (or implementations) developed in compliance with the published standard for areas not currently included in those standards, principally therapeutic area domains (prefix: u)
- **Implemented Standards** – Standards that are in production use. (prefix: s)

As above, these can, and should, be extended or reduced to reflect an organisations specific circumstances.

The operational relationships between standards are represented by:

- **Light Blue:** Between-standards associations
- **Light Red:** Standards contributing to specific study implementations

Operational mapping relationships between standards are represented by:

- **Yellow:** Mapping relationships

Study Data: The final grid row in Fig. 1 represents the study data in its various forms and formats throughout the study life-cycle. The **Light Green** lines represent the data transformations required at each phase of a study to reorganise the data to meet the appropriate standard, and the **Purple** lines the points in the overall process where it is required that the data be in compliance with the standards (validation).

DEVELOPING A STANDARDS MANAGEMENT MODEL

Using these concepts, the detail in Fig 1 shows a simple standards management model reflecting a range of adopted or implemented standards, and the key operations steps in place to use them. In the example, the organisation (department, company, group...) has chosen to adopt (as Published Standards), the protocol PRM standard, CDASH and LAB for data collection, and the SDTM and ADaM standards, at the versions shown. The diagram also shows that last two standards are being used in conjunction with their associated Implementation Guides.

Operationally, the organisation permits (needs) some modification of the CDASH published standard (mCDASH) for data collection purposes, and additionally, the model implies that it has been found necessary to develop user CDASH compliant standards (uCDASH), perhaps to support the collection of particular therapeutic area clinical data. A similar standards modification and development exercise has been undertaken for the SDTM standard, probably to support the future transformation mapping requirements (mSDTM, uSDTM). It has not been found necessary to revise the LAB or ADaM standards; these meet the organisations requirements in their published form.

At the study level (Implemented Standards) a combination of these standards has been applied to support data collection. These might include some elements from the published, modified and user standards (sCDASH, smCDASH, suCDASH, sLAB), and the diagram suggests it has found it necessary to develop some study-specific variant (ssCDASH). Similarly, perhaps in preparation for the transformation of data to the SDTM model, s-, sm-, su- and ssSDTM variants have been developed. The mapping and transformation specifications and the final data transformations are to be managed by the study team (shown by the yellow directed lines at the implementation level). Finally, the purple lines indicate that it is expected that throughout the study life-cycle the resulting datasets are to be in compliance (validated) with the relevant standards.

EXTENDING A STANDARDS MANAGEMENT MODEL

The model shown in Fig.1 can easily be extended to include more standards management and/or operational implementation details. For example, the grid can be extended to incorporate a 'Define.XML' category, with appropriate references to the standards source it is to be based upon (SDTM or ADaM), or to include the SEND non-clinical data standard. Two examples of common extensions to the model are shown in Fig. 2. Fig. 2a extends the model to include versioning; Fig. 2b to include the study data sources.

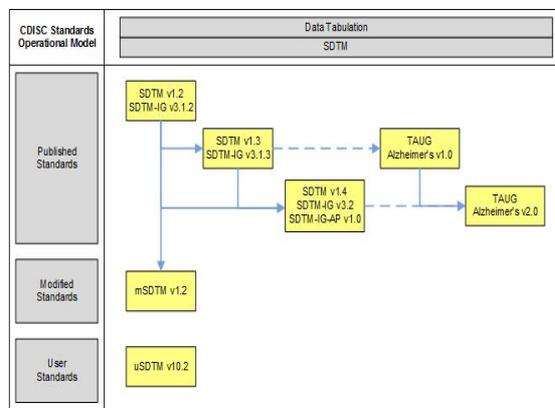


Figure 2a: A subset of the Operational Implementation Model shown in Fig.1 illustrating the extension of the model to include SDTM versioning and the adoption of a TAUIG standards implementation.

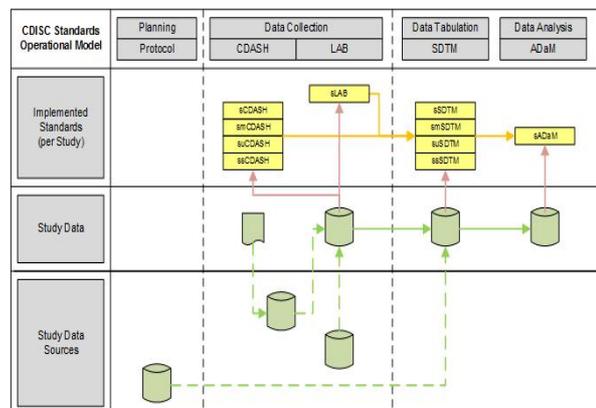


Figure 2b: A subset of the Operational Implementation Model shown in Fig.1 extended to include the study data sources. The dataset in 'planning' represents the source of the Trial Design Datasets.

USING A STANDARDS MANAGEMENT MODEL

The value of presenting the range of an organisation's CDISC standards and usage using this model comes from the immediate insights they offer in understanding precisely where and how the standards are being used (or being considered to be used). Once developed, the model can assist in the evaluation and analysis of how the standards are implemented and used from different perspectives, including, for example, where technical solutions are used, where standards details need to be communicated, to optimise process or governance, and so on.

There are a number of general review methods that are helpful:

- Inclusion or exclusion of specific elements in the grid – include only adopted standards, exclusion of specific operational categories (e.g. no study specific standards permitted)
- Recognising, confirming or establishing specific relationships between elements – between standards or versions of standards, or between different standards (e.g. mapping rules)
- Masking – to understand roles and responsibilities - highlighting departmental/inter-departmental tasks
- Specification - to document the specific standards to be used for a study or studies, and where they may need future re-working
- Analysis – as a tool to systematically explore, compare and contrast the implications of different standards implementations

OPERATIONAL IMPLEMENTATION EXAMPLES

Q1: WHY IMPLEMENT THE CDISC STANDARDS?

To maximise the value of the model it is initially helpful to establish clear terms of reference for why the CDISC standards are being adopted and implemented. It is suggested that there are three principal over-arching reasons why CDISC standards are adopted:

- To support the **Creation of Accurate and High Quality (Clinical) Data Products**
- To ensure **Compliance with Regulatory Authority (Data Submission) Requirements**
- To support **Operational Efficiencies**

Establishing clearly these terms of reference for any specific case, and also considering their priority and importance, then forms the basis for testing the specific details in any particular model. The questions: “Does this model ...support creating high quality data products? ...ensure compliance with requirements? ...support operational efficiencies? ...within my organisation” provides a firm framework for subsequent observations the models reveal.

Figure 4 shows four examples of how the model can be used to understand and review the implications of different aspects of implementing the CDISC standards.

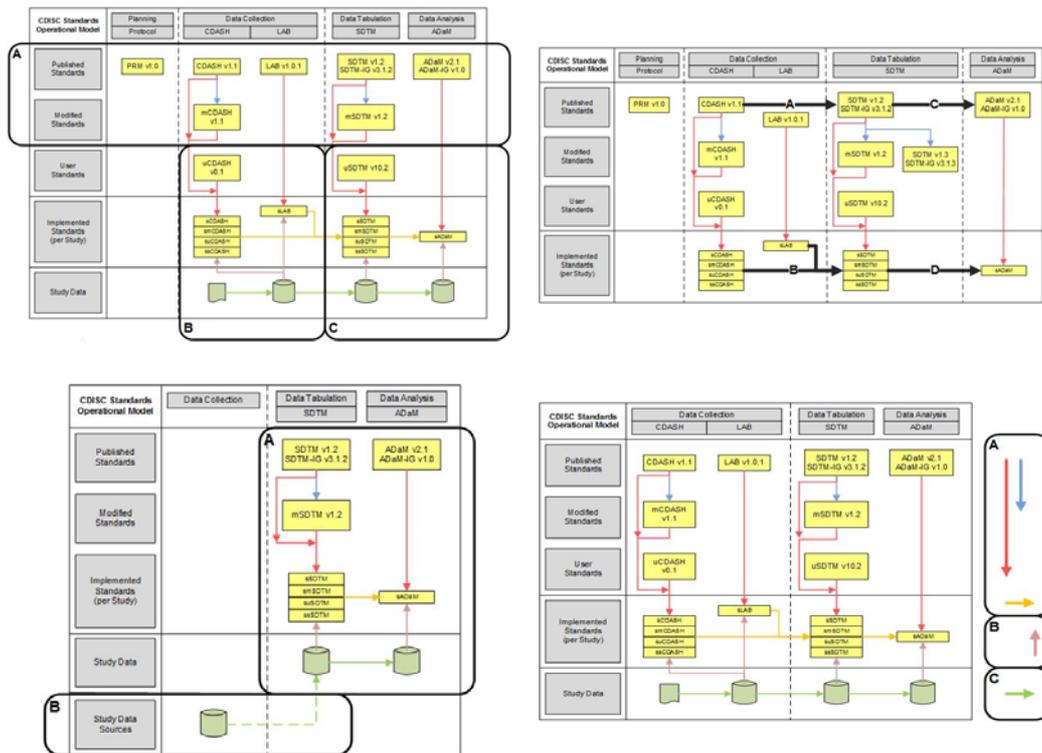


Figure 4: Four examples of the model to describe and assess different aspects of various possible CDISC standard operational implementations. See text for more details.

Upper Left: Departmental roles and responsibility masks.

Upper Right: Mapping specification review.

Lower Left: External service provider interface.

Lower Right: Utilities and tools functionality description.

EXAMPLE 1: DEPARTMENTAL ROLES AND RESPONSIBILITIES (Fig 4: Upper Left)

This model shows a not untypical example of how standards responsibilities might be distributed across different functional areas. The responsibility for published and modified standards is with a single group (**A** in the model) and would represent a central “CDISC Standards Group”. The group represented by (**B**) is clearly concerned solely with the use of the standards for data collection, and (**C**) for their implementation in support of reporting. (**B**) is likely to be the data management group and (**C**) a statistics department.

A number of interesting observations can be immediately identified. For example, the model implies that the data management group and statistics departments are developing user extensions to some standards for study use (User Standards), possibly independently. Is this operationally efficient? Perhaps, Yes (there is no standard). Does it aid the creation of high quality products? Possibly not (there may be no development coordination between the different groups). It also highlights that all the CDISC standards expert knowledge is efficiently concentrated within (**A**), but will also be needed at some level by staff in (**B**) and (**C**). Are training courses available?

EXAMPLE 2: MAPPING SPECIFICATION REVIEW (Fig 4: Upper Right)

This example illustrates another common dilemma for CDISC standards implementation; are the mapping specifications (**A**) and (**C**) required to move data between the various standards part of a metadata repository (MDR), or are they developed and used as part of each study implementation (**B**) and (**D**)? And why, in this model, are there no mapping relationships between the Modified and User Standards? As shown these variations or new standards will be mapped only at the study level. Will the resulting data remain consistent and compliant as it is transformed?

EXAMPLE 3: EXTERNAL SERVICE PROVIDER INTERFACE (Fig 4: Lower Left)

External service providers are regularly commissioned to undertake clinical operations work including the delivery of data in CDISC format. This example illustrates a classic contract case where the sponsor requires delivery of the study data compliant with their standards. This model implies the sponsor has no direct interest in any of the data collection CDISC standards, only requiring the delivered data to meet their implemented study standards. This highlights the commonly met dilemma when using third parties for data management, that is: which sponsor standards are to be used, and when and how should they be to be communicated to the third party? The model illustrates clearly that the only point of “real” standards management interaction between vendor and sponsor is at the point data is delivered, where it is required to pass the sponsors validation and compliance checks. Does this guarantee the immediately availability of high quality data products?

EXAMPLE 4: UTILITIES AND TOOLS FUNCTIONALITY (Fig 4: Lower Right)

Fig. 4-LR illustrates how the model can assist with a high-level review of which applications, software, utilities, and other tools are supporting a CDISC standards implementation. The example shows an MDR (**A**) that is managing (a) standards versioning (light blue), (b) operational study communication of standards (red) and (c) inter-standard mapping specifications (yellow). A different application (OpenCDISC perhaps) is supporting compliance and validation checking (**B**), whilst data transformation is undertaken by yet another system (**C**), quite likely to be SAS.

The model here highlights two important technical standards management points. Firstly, it shows where the definitive version of any standard, and data resides (and therefore where copies are needed). Secondly, it illustrates where a high level of interoperability is desirable. If this second point cannot be achieved, then it focuses attention to where manual (procedural) steps might be needed to compensate. This can help optimise meeting the need to create high quality products (better managed technically?) with the need for operational efficiency (processes are too onerous).

The model might also be used to compare and contrast how a particular software vendor solutions can or cannot support the required elements of an overall CDISC standards implementation.

COMMON MODEL FEATURES

Presenting the overall scope and relationships of the CDISC standards implementation problem using the approach outlined here reveals a number of common themes. It shows unambiguously the basic dilemma of

adopting an end-to-end CDISC standards strategy where the need to balance the “downward” availability and control of standards (governance) challenges the study-by-study day-to-day data mappings and transformations required to put them into practice. The problem of versioning and adopting new standards or agreed implementation methods (the Implementation Guides) can be reviewed by extending the models to show where and how these changes will impact current or future study or submission data.

By establishing clearly where and how the CDISC standards are to be used – at the study, the programme, the submission levels, for example – the model then offers a way to test or guide where and what processes, applications, organisation and so on, might support that implementation most efficiently. Where changes to existing methods are being considered the model can support “compare and contrast” reviews of different approaches to give a solid basis for starting more detailed work in areas such as determining the consequential costs of each model.

Figure 5 shows a variation of the general approach to illustrate more realistically the scope of the overall CDISC standards implementation challenges. It shows the CDISC standards management together with nine study implementations, representing perhaps, the set of studies required for a submission. Even without introducing any additional issues such as new versions of standards, combining data for integrated safety summaries or the use of different software applications, the model shows there already at least 17 data transformations required, two mapping specifications to validate, and up to possible 29 variations how to represent specific data. And the data must be remain at all times accurate and fully auditable. Annotating this diagram with more details could now assist in confirming precisely what is required to achieve overall consistency, and help with planning and scheduling the necessary work.

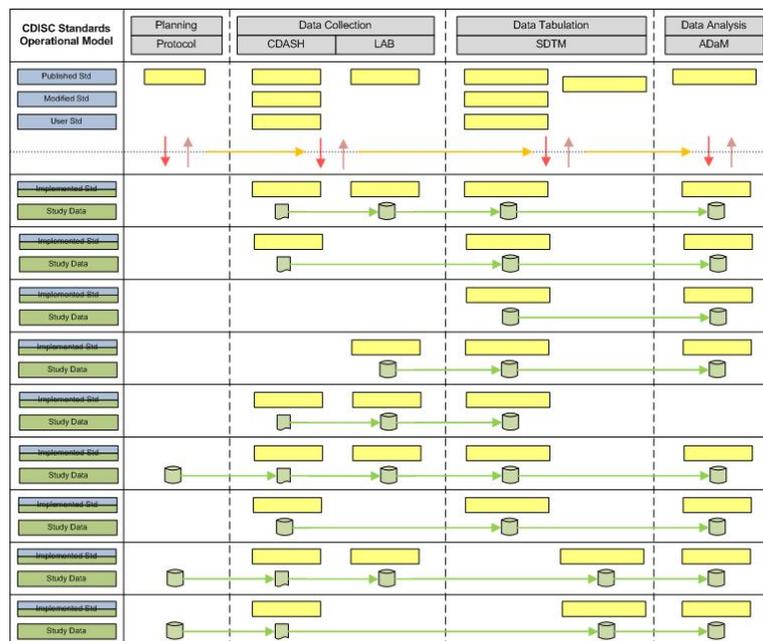


Figure 5: An example of the model extended to include 9 studies that may, for example, be required as part of a future submission. The grid is the same as in Fig.1 but with all the direct associations summarised for clarity (arrows). Blocks: Light blue: CDISC Standards and variants. Light Blue/Light Green: study implemented standards. Light Green: Study data. Each row represents a different study. The differences and similarities in the standards in use by each study is clear (columns), as are the differences in the requirements to use a standard (rows, e.g. no laboratory data is collected).

CONCLUSION

By presenting the overall and specific details necessary for adopting and implementing the CDISC standards into everyday operations using this model offers a simple but clear method to understand and review the range and depth of the issues involved. It can be adapted to support many different aspects of standards adoption, including: determining the current state of an organisations standards management, planning clinical programming work, identifying areas for improvement - changed practices, revised roles – or understanding where particular software applications are supporting standards adoption.

It is not suggested that this approach should replace any of the more detailed or specific methods to develop and understand system requirements, review business processes or assess technical capabilities. Rather, as an

alternative presentation method it provides a solid framework, particularly at higher levels, to focus and guide the often complex decisions needed for a successful CDISC standards implementation.

REFERENCES

1. CDISC Foundational Standards, <http://www.cdisc.org/foundation-standards>

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