CDISC: Implementation Strategies for SDTM

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ABSTRACT
Implementation of the Clinical Data Interchange Standards Consortium's (CDISC) Standard Data Table Model (SDTM) can be a very challenging task for an organization. When faced with such questions as the timing of implementation, impact on ongoing projects, and planning for a future where a new standard must be put in place while maintaining the efficiency of the legacy processes, it can be extremely easy to become overwhelmed. However, after the initial implications are realized and the details start emerging, solutions can be presented and applied to fully embrace the CDISC way of thinking. This paper will address the issues faced when transitioning to the SDTM standard and three specific strategies based on real practices that handle the different phases of implementation along with the challenges and achievements associated with each method.

INTRODUCTION
SDTM is the general framework for organizing clinical trials information that is to be submitted to a Regulatory Agency. It is usually described as the study source data. This data provides a standardized platform-independent mechanism for representing all of the essential information collected with intent to easily interpret, understand, and navigate. For submissions to Regulatory Authorities, this source data is often submitted along with the analysis datasets for a new drug application. Knowing the end result of SDTM data, the complexity comes in implementing different methods to obtain these standards and the various interpretation challenges that must be resolved. This paper will discuss these challenges and lessons learned from the actual implementation strategies involved.

STRATEGIES
When tackling the daunting task of implementing such a change in standards, there are four primary questions that must be addressed:

1) How to refit older studies and projects into the new SDTM standard for the purpose of generating a product standard data pool
2) Time points to consider when trying to implement this standard into studies that are currently ongoing
3) Looking ahead to do a full implementation with planned studies and have the necessary tools in place.
4) Most importantly, how to consistently adopt a standard interpretation for studies that w

Implementation solutions that have been applied to each of the above questions involve a different mapping technique:
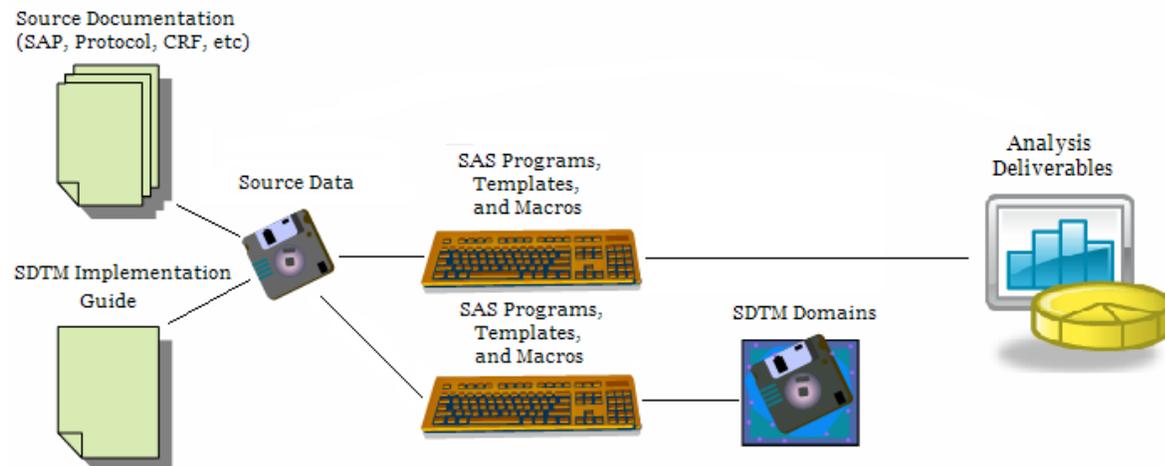
1) Retrospective
2) Parallel
3) Prospective

RETROSPECTIVE MAPPING

Retrospective mapping involves only partially remapping into the SDTM framework where reporting has already been completed or is currently ongoing past the phase of developing analysis datasets. This partial remapping typically involves the often-used safety domains. The primary purpose of the retrospective mapping is to build a product specific standard data pool. By using SDTM as the template, it would then be extremely easy to continue to build onto this data pool with new and planned studies.

With the retrospective strategy, the "best data" is considered. Usually this will be the source data; however, if that data is neither available nor feasible then the analysis data will be used in its place. It must be stressed, that using the analysis data is not without its own serious issues. If the data pool needs to be updated at a regular interval which will often be the case, then the analysis datasets will need to also be updated since they are considered the SDTM source in this example. This adds a level of complexity that can be avoided if the original source data is used instead.

Another major issue for retrospective mapping is the general interpretation from original source to SDTM data fields. Often times, there is no SDTM annotated CRF or ample documentation beyond a study protocol or statistical analysis plan. Thus, there remains a large field of interpretation assumptions that may be incorrect. To ensure that these inconsistencies are kept at a minimum, extra time must be considered in the creation of the SDTM domains using this method. Adding to the extra time involved, one also needs to make sure that any and all of the interpretations are carried out in a consistent fashion and applied to all other retrospective mapping activities within a project.

This strategy is the easily hardest of the three since there are times where based on the age and where the trial was conducted the documentation is lacking. In addition to using the SDTM Implementation Guide supplied from the CDISC Submission Data Standards (SDS) Metadata Team, any documentation is an asset. This can be in the form of a Case Report Form (CRF), study protocols, or a SAP. Illustrated below is a simple graphical representation of the retrospective method:

The advantages to retrospective mapping are:
1) it can be done at the end of the study so it will have minimum, if any, impact on project timelines
2) it will have a reduced impact of upstream standards versions
3) it supports early adoption

The disadvantages are:
1) back engineering
2) much more programming and validation involved
3) analysis datasets that may be submitted have the strong possibility of not matching the SDTM data
4) documentation is indirect and sometimes lacking; therefore more time is spent investigating the translating into SDTM.
5) Cannot be submitted to Regulatory Authorities without the original source data.

PARALLEL MAPPING

Parallel mapping differs from retrospective in that it involves the complete remapping of the CRF into SDTM standards. This strategy is used for studies that have just begun or in the planning stages. However, due to the short duration of the recruitment period and reporting timeline of a particular study, analysis reporting will still be based on the original source data and not the SDTM data.

This method is a much easier approach than retrospective however. In most cases, an SDTM annotated CRF of the study can be supplied in addition to the SDTM Implementation Guide making the mapping much more efficient and less prone to interpretation errors:
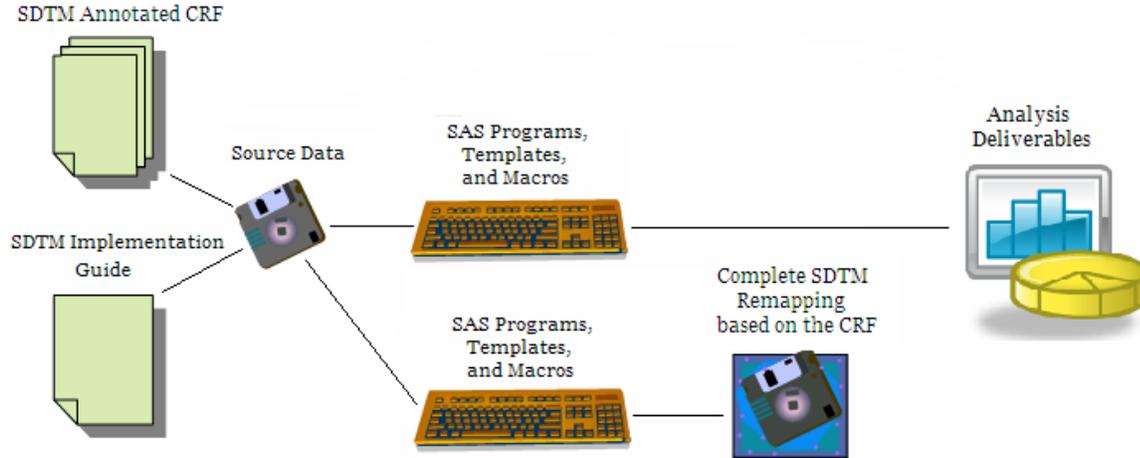
The advantages to parallel mapping are:
1) it can be done at almost any point of the study so it will have minimum, if any, impact on timelines
2) the process can be somewhat streamlined through the use of standard programs, macros, and templates
3) better documentation is available (SDTM annotated CRF)
4) can remap the entire CRF

The disadvantages are:
1) still cannot submit the SDTM data to the regulatory agencies without the source data since the analysis data is not based from the remapped SDTM domains
2) downstream impact of standards versions
3) need to plan out entire project timeline as to stay with the same SDTM version
4) Still cannot submit SDTM data to the Regulatory Authorities without the source data

PROSPECTIVE MAPPING

The ideal way of implementation when facing a new standard as SDTM is naturally prospective mapping. Prospective mapping are for those studies that are planned but have not yet started or have not at least started analyses, and timelines have been adjusted to account for the new standard to be applied.

The most important difference of prospective mapping versus retrospective and parallel mapping is that the analysis data and reporting will be **_solely based from the SDTM mapped data!_** As with parallel mapping, an SDTM annotated CRF should be available in the aid of the remapping. Again, this will greatly reduce the errors in data interpretation. As you can see in the below illustration, a simple logical linear progression occurs with prospective mapping, as one would expect:
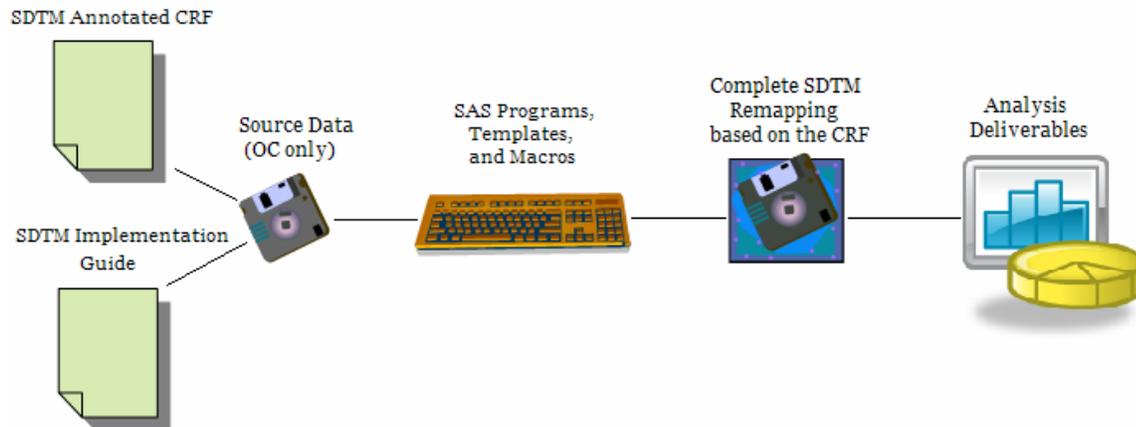
The advantages to prospective mapping are:
1) it is done upfront with timelines that take this into account
2) the process can be somewhat streamlined through the use of standard programs, macros, and templates
3) logical flow and better documentation is available (SDTM annotated CRF)
4) through personal experiences, fewer analysis datasets are needed
5) truly acts as a first step to sustain a complete standard process: SDTM -> ADaM -> Standard reporting of tables, listings, figures
6) Can submit the data to the Regulatory Authorities as the source data since the analysis is based from the SDTM

The disadvantages are
1) extra component in overall process in terms of development and validation
2) downstream impact of standards versions
3) need to plan out entire project timeline as to stay with the same SDTM version

CONCLUSION

Through three specific implementation strategies, a straightforward approach can be applied when adopting the new CDISC standard of SDTM to clinical trials. Retrospective mapping should primarily be used only in older studies where there is interest to create a standard data pool with intend to build upon that with current and planned studies. It is the most complex method that can lead to most of the data fields' interpretation issues. This method also takes the most time to complete. The parallel strategy is better in that you should have better documentation to correctly map the original source data to SDTM. However, with this method, once must still submit the original source data to the regulatory authorities since the analysis datasets were not based from the SDTM domains. Finally, the prospective mapping is the ideal process in creating a logical linear flow. Most importantly, when one adopts this method, there will be no need to submit the original source data! As demonstrated, the work involves a time consuming first effort and is far from easy; however, as procedures and processes evolve through experience in the methods mentioned above, confidence as well as efficiency thrives as a new standard is solidified in the industry.

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