In the CDISC Standards, analysis datasets using the standards (ADaM) hold a unique place in the end to end process and must be created with both a prospective and retrospective view of the entire clinical trial process. Analysis datasets must support the statistical analysis plan (SAP) by providing accurate efficacy and safety analyses. Companies must be pragmatic in deciding which processes can be automated by tools. Industry has tools to effectively transform data to the SDTM structure. These tools should be able to build a large portion of the appropriate ADaM datasets with maximum efficiency. The burning question: Can ADaM datasets be built with a mapping tool just like SDTM?

ABSTRACT

In order to automate, must decide on standard structure within set of Analysis Plan. ADaM is therefore the missing link using an MDR to provide mappings the various CDISC documents, the collected data with machine readable metadata, are used CRO Raw collection to SDTM is handled by many Organizations (CROs) that then update to SDTM. Often they hire Clinical Research Organizers to create derived fields. The MDR stores metadata that contribute to the process. In order for the process described to work we need to produce machine consumable metadata. This part requires the end in mind from the end goal. The biostatistician has input at the beginning as to what is collected as described in the protocol. The focus then goes into the SAP, where the tables are mocked up and final hypotheses will be tested.

INTRODUCTION

The theme of this poster is to describe how standards can be used in the process of automating analysis datasets, to give programmers and biostatisticians more time to focus on the science and unique analyses for new indications and treatments. Automated processes require the proper governance by sponsors internally, and through collaboration between Clinical Research Organizations and the Sponsors. The standards made interpreting the standards need to be assimilated and documented using a Metadata Repository (MDR) so that rigorous and consistent implementation can be assured. The MDR provides consistent input to the processing of the data from collection to Tables, figures and listings (TFLs) which are then used by medical writers to create the Clinical Study Report (CSR).

Although the CDISC standards have evolved greatly, there is still a lot of room for improvement by users of these standards. (see below)

### Retrospective Process

First and foremost, the analysis datasets must support the statistical analysis plan (SAP) by providing accurate efficacy and safety analyses. The Biostatistician creates the SAP for the study and this becomes a detailed roadmap for the clinical programmer to create any derived fields. Part of the SAP is a set of mock tables. These can be annotated just like an eCRF with ADaM-compliant variable names so that these can be derived or mapped from the SDTM data. This process is also being standardized by work groups in various organizations such as PhUSE in developing standard analysis scripts by therapeutic area. These scripts intend to provide guidance on recommended tables, figures and listings (TFLs) that are part of standard clinical submissions.

The retrospective process is described by the picture below. Traditionally, the ADaM datasets have been considered to be derived from the SDTM domains without influence from the analysis. The newer method is to think from the biostatistician’s viewpoint and look backwards from the end goal. The biostatistician has input at the beginning as to what is collected as described in the protocol. Then the focus goes into the SAP, where the tables are mocked up and final hypotheses will be tested.

### Proactive Process

CDISC standards are the first component in the metadata build. There are available machine readable form and read into the CRO/Sponsor Global Metadata Repository (SMDR). Any interpretations for individual custom forms, domains, and ADaM datasets are added to the Study/Sponsor Metadata Repository (SMR). Since CDA standards offer some flexibility, the Sponsor must have their interpretations clearly described in the metadata that is stored in the SMDR.

Data in the above model can be accessed at all levels of processing, whether it is at the collection point, the data reviewed by data management teams, or by programs that process and push the data to the next data store.

Machine consumable metadata in the form of detailed specifications, control terminology and required forms by the basis of automation. Further automation is possible through ODM XML. In the future through ODM XML, we should be able to automatically push additional metadata from CDASH to SDTM to ADaM. See example below. (here we collect time, although not usually collected unless a pediatrics study)

### How We Should Be Approaching the Standards

Building the MDR required for this approach involves the involvement of all the stakeholders along the process. Having the end in mind requires an integrated team approach from the following groups:

- Electronic Data Capture team (EDC)
- Data management (DM)
- Clinical Programming (CP)
- Biostatistics (Stats)

One of the ADaM premises, to be one ‘proc’ or step away from creating the tables and listings plays on this theme. Only by working backwards and literally ‘annotating’ the table with the required fields can we be sure to collect what is needed up front.

Conclusively, the ADaM process requires that the end in mind from the beginning with an integrated team approach will better integrate systems earlier during data collection and SDTM conversion. Strict adherence to CDASH and SDTM interpretations must be maintained to support ADaM automation. Proactively for the process to be automated we need to produce machine consumable data in the form of an MDR and other tools that are able to push metadata form one standard to the other in a linear process. The use of ODM XML does have features that allow for better information system interoperability so that hardware devices and software routines work harmoniously together. Organizations must be pragmatic in not taking on too much at one time. For success, clear commitment and sponsorship from the leadership in the company is essential with funding for tool implementation and governance.