CDISC, a four-leaf clover: the SGS finder’s story

SGS Life Science Services (SGS) is one of the “early bird” Clinical Research Organizations that embraced the CDISC standards from the very beginning. SGS originally focused on submission related CDISC standards and therefore started the Submission Data Model v3.0 implementation in 2003. However, for quite some time now, SGS has been looking at the CDISC standards from a different perspective. The original idea that CDISC standards would always be pure “submission standards” has turned into the understanding that CDISC standards are there to guide users in their daily jobs. CDISC has offered the industry invaluable benefits; for SGS these benefits can be categorized in four key topics:

- **SDTM checks with a memory**
- **Hands-on solutions for SDTM and ADaM**
- **Benefits for ADaM because of end-to-end concept**
- **eSource acceptance**

In 2006, CDISC published the Electronic Source Data Interchange (eSDI) document with the goal of “Leveraging the CDISC Standards to Facilitate the use of Electronic Source Data within Clinical Trials”. Recent publications from regulatory bodies referencing this document makes the collection of data directly into electronic format (eSource) - rather than via paper – such that the subsequent clinical study data flow towards tabulations to support submissions for marketing applications. Following the acceptance of eSource data, SGS installed an automated eSource-driven system to support and enhance running of Phase I trials in their Antwerp, Belgium clinical unit equipped with 96 beds. This clinic automation system has a trial design framework that drives key operations; the framework schedule can be pushed via handheld devices directly to the clinical staff at the bedside and provide the ‘what, where, whom and when’ information they require to run the trial. The automated solution efficiently collects all data types (trial execution data, safety laboratory data and data uploaded from medical devices) directly into electronic format (eSource); this easy access of the subjects’ data helps clinical teams in making timely and likely more accurate decisions.
The use of eSource is key to achieving full efficiencies of automation at the clinical unit. Checks, time-alerts and tube barcode verification improve quality during collection; transcription is eliminated; data are available for review in real-time; and, both archiving and regulatory submissions are simplified. While CDISC has opened the gate towards eSource in 2006; it was the regulatory bodies and eSource solution providers who eliminated the last hurdles allowing sites worldwide to install eSource-driven solutions.

**SDTM checks with a memory**

The Study Data Tabulation Model (SDTM) is without any doubt one of the most adopted CDISC standards within the industry. Over time, a wide range of SDTM compliance checkers have been made available by a number of vendors making retrieval of an SDTM compliance report for any clinical trial straight-forward. Starting from the compliance report, the study team can update Extract-Transform-Load (ETL) conversion scripts and send queries to sites to resolve clinical data issues. Depending on how responsive the sites are, queries are either resolved or still pending when verifying the SDTM datasets for the same clinical trial the next time. Previously, the study team looked at the entire SDTM compliance report again, going through both new and previous issues from the preceding run which required further follow-up by the site. Looking over and over again to previously reported issues is not only time-consuming; it does not provide any added value at all. The SGS SDTM compliance checker not only creates a report with open issues detected in the SDTM datasets but also allows the clinical team to keep track of the action taken for each discrepancy. These actions can include for example "Query created in EDC", "Queried to data provided" and "Protocol Deviation created". Furthermore, the SGS SDTM compliance checker lists new and previously reported discrepancies with their assigned action status. The time-gain because of the availability of “SDTM checks with a memory” is significant and therefore allowing an earlier database lock.

Building “checks with a memory” is possible for any data structure. However, the wide implementation of SDTM within the industry makes it really worthwhile to invest in a next generation SDTM compliance checker– an investment that would not be reasonable without the availability of the CDISC SDTM standard.

**Hands-on solutions for SDTM and ADaM**

In the coming years, CDISC is aiming to release more therapeutic area standards and to continue the work of expanding the available controlled terminology making SDTM datasets more streamlined within the industry. Today, a spectrum of SDTM implementations exists because the current SDTM standard does not cover all therapeutic areas. Sponsors are independently defining proprietary custom SDTM datasets and CROs are implementing these proprietary custom SDTM datasets for different sponsors.

Having a spectrum of SDTM implementations might sound dramatic. However do not despair, storage of complete and accurate metadata in a repository helps in overcoming most disadvantages and controlling all deliverables. At study start, (e)CRF forms are pulled out of the metadata repository library and added to the study design. During the trial, the metadata repository is used to generate SDTM datasets and to verify the trial’s metadata with what has been specified in the repository. Subsequently, the biostatistics team consults the trial’s metadata allowing them to be fully aware of all study design specifics which significantly helps in creating ADaM datasets. CDISC published the define.xml metadata standard in 2005. Originally, a define.xml file was only used to ‘report’ metadata; later on, people started to actually ‘use’ metadata in their business processes as a building, verification and communication tool: a major step forward!
Benefits for ADaM because of end-to-end concept

The launch of the CDISC Analysis Data Model (ADaM) guidelines on how to structure analysis datasets made a world with different analysis dataset concepts history. Before CDISC ADaM it was general practice at a CRO to handle a different approach per sponsor. Because of confidentiality and intellectual property, the CRO could not harmonize different analysis dataset structures from one sponsor to another. By implementing CDISC standards from the beginning, standardization benefits ripple through from SDTM to ADaM lowering the level of complexity when creating analysis datasets. The combination of a robust CDISC SDTM model for data tabulation, together with validation software ensuring consistency of the CDISC SDTM variable attributes between studies, increases the comfort level at the biostatistics department. The algorithms used for derivation of variables and records needed for the statistical analysis are stored in a repository for sponsor independent re-use across trials so that sponsors no longer have to provide extensive guidance for the creation of analysis datasets.

Today, thanks to the different CDISC models available, an author of a statistical analysis with thorough CDISC standards knowledge can work in a more autonomous way. Also, by using data standards, knowledge sharing at the CRO across dedicated sponsor teams becomes more transparent and efficient because the same language is spoken.

Although CDISC ADaM needs further development to support more therapeutic areas and integrated safety and/or efficacy summary, already strong benefits of this model are palpable in the daily work of our statistical department.

Summary

The benefits that CDISC standards have added to the clinical trial development process within the past decade are innumerable. The CDISC vision of the end-to-end concept has proven to be a strategic masterstroke. Standard CDASH CRFs are easier to complete and therefore generate fewer data queries. As a next step, standard CDASH CRFs can be transformed to standard SDTM datasets using standard extract transform load (ETL) code. Furthermore, statistical analysis can be performed at a much faster rate on a locked SDTM compliant database. The end-to-end concept has turned into reality today: standardization benefits really ripple through from the start to submission!

CDISC & SGS Life Science Services

SGS Life Science Services (SGS) is both a Platinum member and a CDISC Advisory Board member. Additionally, SGS is a CDISC Registered Solution Provider for SDTM, ADaM and define.xml; and provides an authorized CDISC ADaM trainer.

SGS also supports the CDISC standards by “spreading the word” and sharing CDISC implementation experiences at numerous occasions such as the CDISC Interchanges. SGS staff are pleased to be involved in a variety of CDISC teams.

SGS Life Science Services is a leading contract service organization providing clinical research, analytical development, biologics characterization, biosafety, and quality control testing. Delivering solutions for bio-pharmaceutical companies, SGS provides clinical trial management (Phase I to IV) services encompassing clinical project management and monitoring, data management, biostatistics, and regulatory consultancy. For a qualitative and faster patient recruitment across the Americas and Europe, SGS has a large data base of investigators and key opinion leaders with therapeutic expertise in Infectious Disease & HIV/HCV, Vaccines, Oncology and Respiratory.

www.sgs.com/lifescience
References

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2) CDISC Europe Interchange – April 2012: “Introducing an eSource system in a Phase I unit and processing eSource data downstream”

3) CDISC French Speaking User Group - February 2012: “SDTM and ADaM: Hands-on solutions”


5) CDISC Europe Interchange – April 2011: “ADaM 2.1 Implementation: A Challenging Next Step in the Process”

6) CDISC Europe Interchange – April 2010: “Getting the Most out of CDASH, Metadata and Terminology”

7) RAPS conference – October 2012: “eCRF: From Start to Submission”