The Case Report form (CRF) is a tool used to record data in a clinical study. Data in a CRF should be collected in a specific format in harmony with the protocol and in agreement with regulatory requirements. The importance of standardized CRFs is revealed in facilitating the exchange of data across drug compounds, disease indications as well as across companies. Standardized CRFs which are harmonized with the CDISC CDASH model require minimal mapping (if at all) in order to exchange the data. If a well-designed CRF is adopted, it will provide improved productivity in processing and analyzing clinical data from start-up throughout all downstream processes. Saving time and money in collecting and analyzing clinical trial data is the main outcome of using well-designed CRFs where data could be reused effectively.

Biogen Idec Experience with the CDISC Standards

The Biogen Idec experience with CDISC started in 2003 when the company made the decision to utilize CDISC SDTM Standard to build their standard Case Report Form libraries. As Idec and Biogen merged to become one company, Data Management and Biometrics team members recognized that having two distinctive “company specific” CRF libraries would result in inefficiencies in their processes, time and resources! A cross-functional team (called the Data Standards Team) was formed including data managers, clinical operations, statisticians and statistical programmers who worked together -under the principle of organization and collaboration- to build a new CRF library that could be used for all studies (regardless of disease indication) moving forward based on CDISC SDTM standard. The CDISC standards could then be easily used as part of all the downstream activities including mapping to their SAS datasets and analysis of data in their programming world, these standards facilitate the creation of analysis datasets, the clinical trial results, and their submission.

Biogen Idec adopted the CDISC standards in the early stages of their clinical trials (Phase 1 through Phase 3 trials) and built tools and applications to help them utilize these standards throughout clinical processes; they are currently in the process of maturing their internal therapeutic area standards. After building the standard CDISC SDTM based CRF library in 2005, Biogen Idec team members developed more than 50 standard CRFs and associated documentation for Neurology (Multiple Sclerosis) and Immunology (Rheumatoid Arthritis) indications.

CDISC standards have proven to be very beneficial for them where more than 90% of their drug programs, including their current studies, comply with the CDISC SDTM 3.1.1 or 3.1.2. CDISC standards helped them be more efficient and more “submission ready” by speaking the same language with their
data management colleagues and their vendors. They educated their senior management and MDs about the usefulness of standards, shedding a light on their significant role in the submission process.

The figure below, presented by Lynn Difinizio, a CDISC Advisory Board member, at the CDISC International Interchange 2010, highlights how Biogen Idec applied the CDISC standards, the tools that they utilize, and how they are trying to grow the CRF library further.

The top of the figure represents the key clinical milestones during a clinical study, from the development of the protocol and CRF, through data collection from input to a database based on CDISC SDTM standards (“System Live”), through patient treatment/collection of data and then through the finalization of a CDISC SDTM based database at Database Lock. At database lock, data from the CDISC SDTM database feeds into the ADaM (analysis dataset) model and then to analysis tables, listings, graphs (Standard Safety “SMART” tables and study specific efficacy table results). Little to no mapping is required post-hoc to prepare the data for electronic submission.

The figure also shows how Biogen Idec creates and utilizes standards across all of the processes for a study. Underneath the Protocol, we observe the DST (Data Standards Team) that created the standard CRF library. We also notice the Therapeutic Area standards that were developed with their MDs while engaging them at the CRF level. In 2011, Biogen Idec’s senior MD represented their company on the NINDS (National Institute of Neurological Disorders and Stroke) Common Data Elements Committee with other MS specialists and provided Biogen Idec’s current Multiple Sclerosis Standard CRFs for consideration. The NINDS common data elements for MS are currently out for final review through NINDS and CDISC; these elements will be the required data elements for NIH funded trials. During the
committee meeting, light was shed on CDISC being the lead in this domain as CDISC is working on creating several Therapeutic Area Standards. Biogen Idec is really excited to be part of the whole mission as CDISC is partnering to develop further standards.

All of the standard CRF libraries that Biogen Idec has built with the CDISC SDTM Standard are used by their tools to collect the data for electronic data capture; they have several macros and tools that perform minor transposition mapping into the SAS world. Biogen Idec invested a lot of time initially in the CDISC SDTM standard, creating their CRF library, processes and tools; now, over the past couple of years, they have started adopting the CDISC ADaM standard more broadly in order to have ADSL/Safety ADaM datasets for new studies, and adopt ADaM for efficacy datasets as well. They are currently investigating how to move forward with a broader adoption of the CDISC ADaM model for the early phase trials as well.

The Benefits of the CDISC Standards According to Biogen Idec:

Having a stable set of standards that people can refer to (“speak the same language, get the right result”), in addition to educating all team members on CDISC Standards; automating from the beginning of the study to the end; and having a very transparent and traceable flow are some of the benefits of the CDISC Standards. The CDISC standards help them to be more “submission ready” with their drug compounds, saving them the burden of remapping everything at the end.

Biogen Idec perceives the CDISC standards as an opportunity to bring more data together easily, not just from one drug compound but across multiple compounds if applicable. The standards help provide more information from the data in a manner that could facilitate the reuse of data and to follow how it was created. After the trials are completed, the legacy is the data – and its ability to provide information years hence – furthering and impacting future drug development.

Biogen Idec still has some legacy data for some of their studies associated with their new partnerships; however, adopting CDISC standards has resulted in significantly less work, enabling them to focus their resources on the unique and non-standard while counting on standards throughout their work processes.

Streamlining the Clinical Trial Process

Standards Governance Processes are still a challenge for the company as it is not easy to achieve worldwide adoption of data standards. The health industry needs additional formal processes and education for our senior folks explaining to them that adopting standards is a must and not an optional process/requirement. Various teams beyond data management and programming still need education on the benefits of standards. MDs are not necessarily programmers or database designers, therefore standards might be a complicated concept for them. Lynn stated that their role is to explain the importance of these data standards to all team members involved in the process of collecting, analyzing and submitting clinical trial data to Regulatory authorities.
Effective and continuous communication around the advantages of standards should be focused on our patients in the real world; we should be able to prove to them how these standards play a significant role in shortening the time to new treatments. Lynn DiFinizio, CDISC CAB member stated, “we have a principle in our group that we do important meaningful work which makes a difference to patients. Whether we are writing a piece of SAS code or mapping a dataset, at the end of the day it is making that data represent what is happening with the patient”. MDs and regulatory should recognize the necessity of talking about this with FDA and reviewers, therefore, attending the CDISC Interchanges would be a good start where the real benefits of standards are discussed pointing out their substantial effect on our patients.

Biogen Idec is trying to partner with people who can speak the same language of MDs and have in-depth knowledge about working with CDISC, FDA and external groups like the NINDS for the purpose of defining and clarifying the analysis of data and subsequently obtaining meaningful results. CDISC plays a very significant role in this area as standardization is needed between those groups of people.

Lynn DiFinizio stated: “If we link this case to all the People, Processes and Tools involved in developing drugs, we can deliver great results. So let’s all ponder how do we do that!”

Biogen Idec continues to be involved as a CDISC Platinum member where they are represented in the CDISC Advisory Board. The CDISC mission is accomplished through our volunteers who work for different member organizations and dedicate their time and resources to help define the right means to accomplish the CDISC mission and vision. Adding work to their extremely busy schedules highlights the importance of the CDISC mission and reflects the value of partnership between CDISC and its member organizations.

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NOTE: One of the various benefits that CDISC offers to its Platinum members is the Global Approach To Accelerating Medical Research course. This course was developed for managers and MDs to explain CDISC at a high level along with its relevance and importance to improving medical research. It is available at no charge for all Platinum Members and can be delivered in-house at their request providing that the only expense for their company will be the instructor’s travel expenses.