

## ***CDISC: Adoption Trends, Benefits and Addressing Barriers***

By Shannon Labout, Feng Li, William Friggle, and Rebecca Kush

### **Abstract**

Results of an online survey of CDISC stakeholders indicates that the CDISC standards continue to gain traction among clinical researchers. Among the 641 respondents who answered the demographics section, the Study Data Tabulation Model (SDTM) is the most widely used and the Clinical Data Acquisition Standards Harmonization (CDASH) standard for case report forms has the most users piloting as of the end of the survey period, March 2010. CDISC Healthcare Link Initiative was largely unknown by the respondent community. Clinical Research Organizations (CROs) are consistently adopting the standards more readily than are biopharmaceutical companies. The greatest benefits from the use of the CDISC standards were cited as: a) to improve data exchange; b) to improve study efficiency and c) to improve data quality. Perceived barriers include: a) a lack of understanding of the CDISC standards; b) cost of implementation and c) that the existing domains do not cover a sufficient amount of the data. Of the 475 respondents to a question about eSubmissions, 166 replied that their organizations have submitted at least one. When survey participants were asked how CDISC can assist in improving the adoption of the CDISC standards, the top responses were: a) to work with regulators to provide greater clarity; b) provide more case studies; and c) produce more therapeutic/efficacy standards. Significant progress has been made in terms of addressing these areas since the survey was conducted. This progress is shared in depth in the Discussion section.

### **Background**

Two different surveys were conducted by CDISC in 2010-2011. In early March of 2010, CDISC conducted the first of these surveys with the intent of reaching a broad audience to understand the trends, benefits and barriers associated with adoption of its standards. This was nothing new for CDISC as they have been collecting metrics from industry regarding standards adoption for several years. What was new in this survey was an attempt to gain specific insights regarding experience that has been gained through the use of the CDISC standards specific to eSubmissions to the Food and Drug Administration (FDA). In particular, these CDISC standards are the Study Data Tabulation Model (SDTM), Define.xml and the Analysis Data Model (ADaM) standards, as a part of a New Drug Application or supplemental New Drug Application (NDA/sNDA). In November 2010 during the North America/International CDISC Interchange and again in April 2011 for the European Interchange in Brussels, the second survey was conducted to understand the value of CDISC to its constituents, which was also a new angle for a CDISC

survey. During the 2010 International Interchange CDISC announced the new CDISC Vision Statement “Informing patient care through higher quality medical research”; Interchange presentation topics emphasized the benefits of standards to the patient and the lessons from Gartner’s CDISC business case--- that the greatest benefits accrue, as for quality, when implementation occurs at the start of a research study or program, with the CDASH and Protocol standards and the CDISC Healthcare Link Initiative. The survey was designed to better understand where CDISC constituents perceive the greatest value from CDISC, how they take advantage of CDISC offerings and how additional value could be provided. This is a summary of the initial survey; a separate manuscript describes the results of the second survey.

## Survey Organization and Methodology

The March 2010 survey was deployed on-line and consisted of 18 questions grouped into three themes: Demographics, General CDISC Standards Adoption Feedback, and Submission Standards Experience Feedback. The first six questions captured demographics about the respondents: organization type, global or single region in scope, size (based on number of employees), primary role of the respondent within the company and whether or not the organization was a CDISC member. Section two was composed of five questions which queried: 1) adoption status for the 12 CDISC standards; 2) benefits of adoption; 3) barriers to adoption; 4) ways in which CDISC can help with adoption; and, 5) the value of eleven different tools, venues or services provided by CDISC to support standards adoption. The final section of the survey focused specifically on submission experience through seven questions which probed respondents’ experience with the Study Data Tabulation Model (SDTM), Define.xml and Analysis Dataset Model (ADaM) standards including the number of submissions made, a judgment of the quality of the submission experience as well as the SDTM challenges and benefits.

There were a total of 641 persons who signed up for the survey and answered the demographic questions but the count of participants who answered questions dropped by at least 100 in section two and then again in section three. The survey and the on-line survey tool enabled support for unstructured entry of text allowing comments on most questions. The unstructured text comment areas seemed to be fairly extensively used by the respondents in section three of the survey, which may suggest that respondents are interested in the opportunity to discuss their submission experiences. Graphs presented within this report are based upon information gathered in the survey conducted March 2010. Clearly, there have been eSubmissions made since that date that are not included herein.

## Demographic Summary

The majority of the respondents (43%) categorized their organization as a Biopharmaceutical company, Contract/Clinical Research Organizations (CROs) represented the second largest respondent category (28%). However, there were 5.5% of respondents from Academic Institutions and 11.4% from Technical Service providers. Slightly over 72% (462) of the respondents identified their organization as having a “global” scope with operations in one or more regions. The majority of respondents (31%) were from larger organizations, with more than 10,000 employees; another 24% were from organizations with between 1,000 and 10,000 and 22% were from smaller companies (1-99 employees). The primary role of those who responded to the survey was either Data Management (33%) or Statistics (29%). Project Managers accounted for 4.8% and Clinical Operations 4.3% [9.1% total] while 1% were Monitors. There was a large group (18%) who identified themselves as “Other” such as Regulatory, Senior Management

and Quality Assurance. In terms of global regions represented, 56% of the respondents were from the United States, 28% were from Europe and Canada, 13% were from Asia-Pacific countries, including India, and 3% were from other regions (South Africa, New Zealand). Slightly over half of the respondents (58%) identified themselves as being from CDISC member organizations, while 26% were not from CDISC member organizations and 15% did not know whether their organizations were CDISC members or not. See the following Figures 1-5.

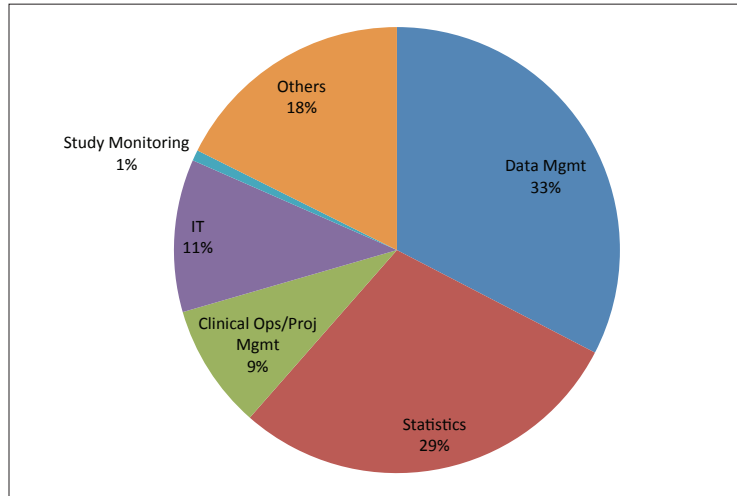
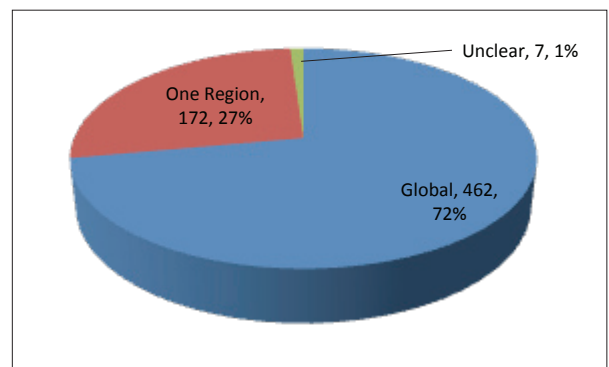
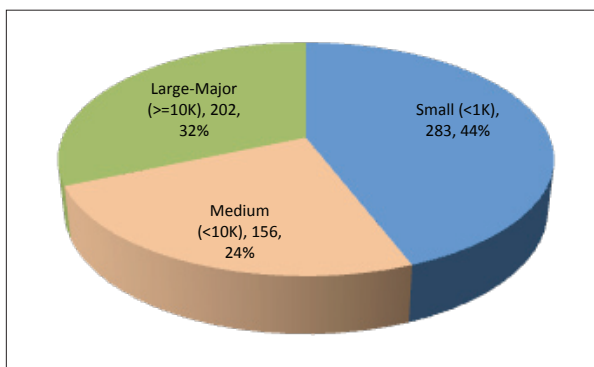
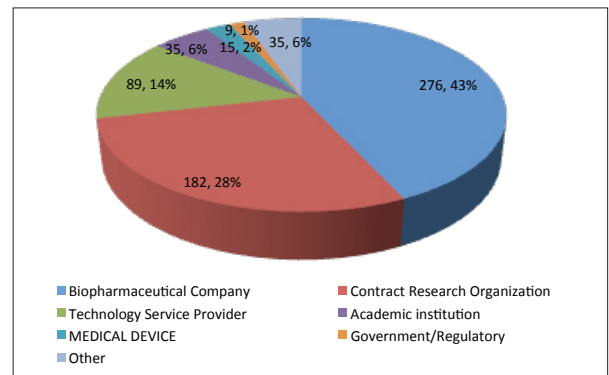
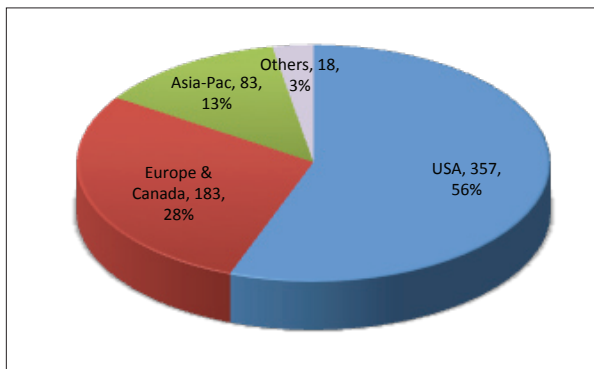


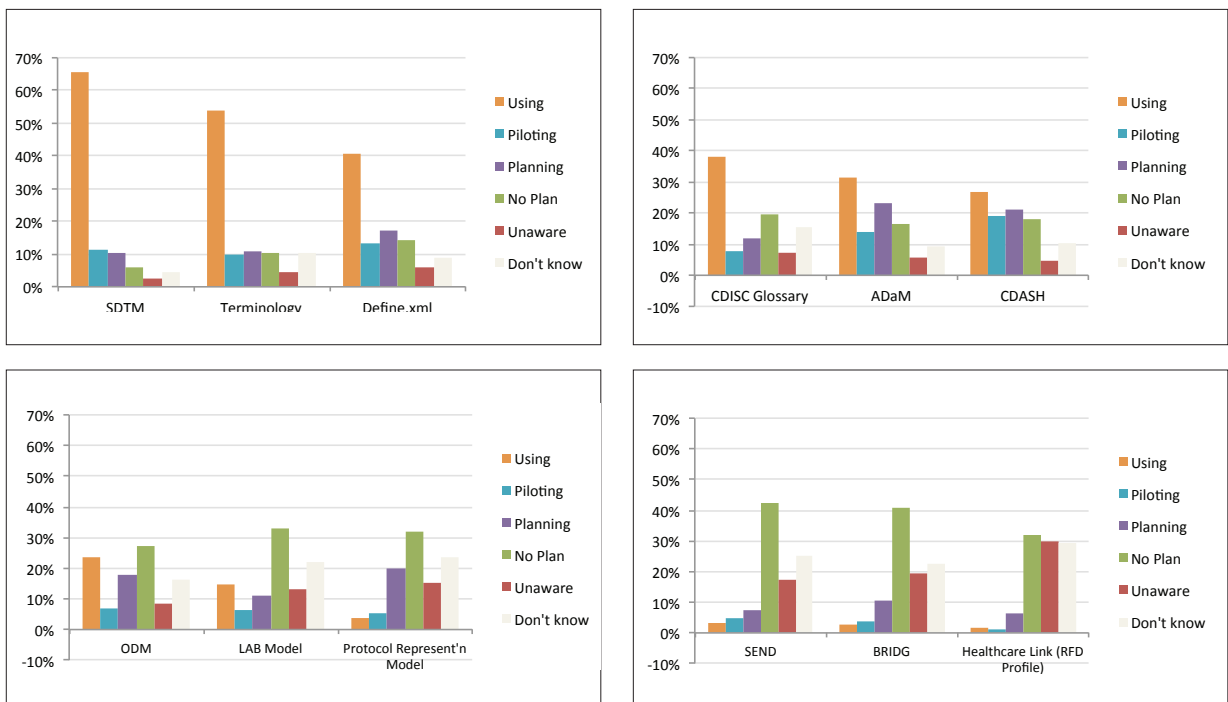
Figure 1. Respondent Roles



Figures 2-5. Respondent regions, type of organization, size of organization, one region or global organization.

## General CDISC Standards Adoption

Figures 6-9 indicates adoption rates of the various CDISC standards. As in prior surveys, the SDTM is the most widely adopted CDISC standard; this is not surprising since it was the first mature standard released and has also been cited in FDA Final Guidance for eSubmissions, and other published guidelines related to FDA data submissions. Of the 542 who responded to this question, 349 indicate they are using SDTM. Terminology, Define.xml, Glossary and ADaM followed in descending order in terms of usage. CDASH had the most respondents piloting. Respondents were largely unaware of the CDISC Healthcare Link Initiative and associated standards. See Figures 6-9 below.



Figures 6-9 indicate adoption trends for SDTM, Terminology, Define.xml, Glossary, ADaM, CDASH, ODM, LAB, Protocol Representation, SEND, BRIDG and Healthcare Link from top left to bottom right.

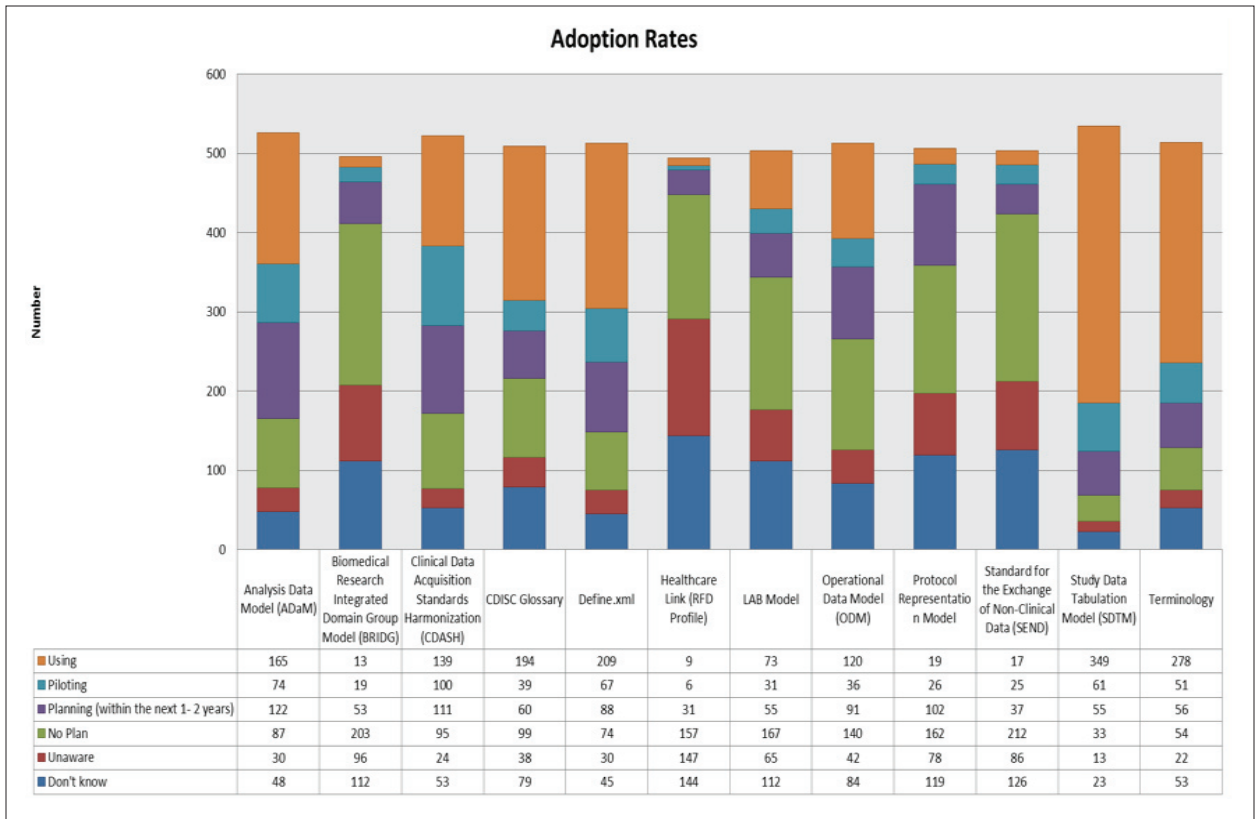
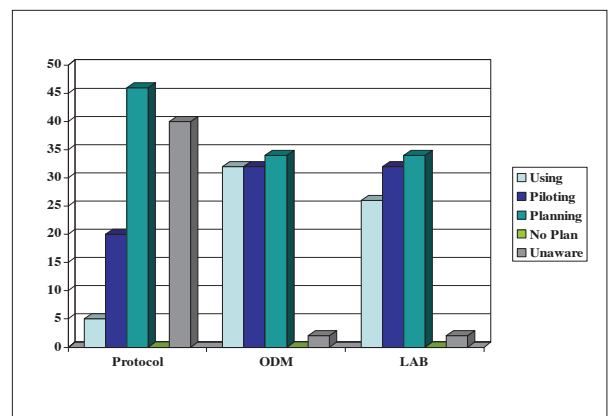
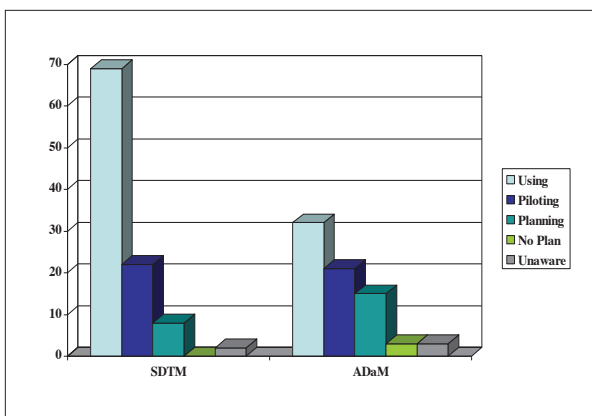


Figure 10. The adoption rates are shown in this figure by number of respondents per CDISC standard.

By comparison, the CDISC Survey conducted with Tufts in 2007 indicated the following adoption rates, again with SDTM in the lead. Glossary and Terminology were not included in this survey and CDASH was released in 2008. See Figures 11- 12.



Figures 11 and 12. The 2007 Tufts Survey on the adoption of CDISC standards indicated the highest usage rates for SDTM, ADaM and ODM followed by LAB and Protocol Representation.

The March 2010 Survey presented a consistent trend; CROs are adopting the CDISC standards more readily than other organizations.

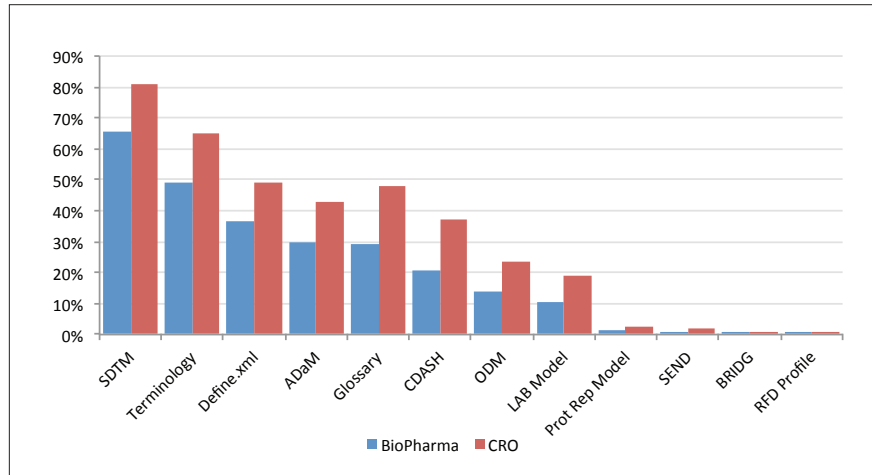


Figure 13. Adoption rates for CDISC standards – Biopharma vs. CROs.

Benefits of the CDISC standards, as indicated by all survey respondents who answered this question, were as follows:

1. to improve data exchange (52%);
2. to improve study efficiency (46%);
3. to improve data quality (41%);
4. to reduce the burden of regulatory submissions (38%);
5. to improve speed of approval (32%);
6. to reduce the time spent mapping legacy data (31%), and
7. to reduce the cost of data transfer (18%).

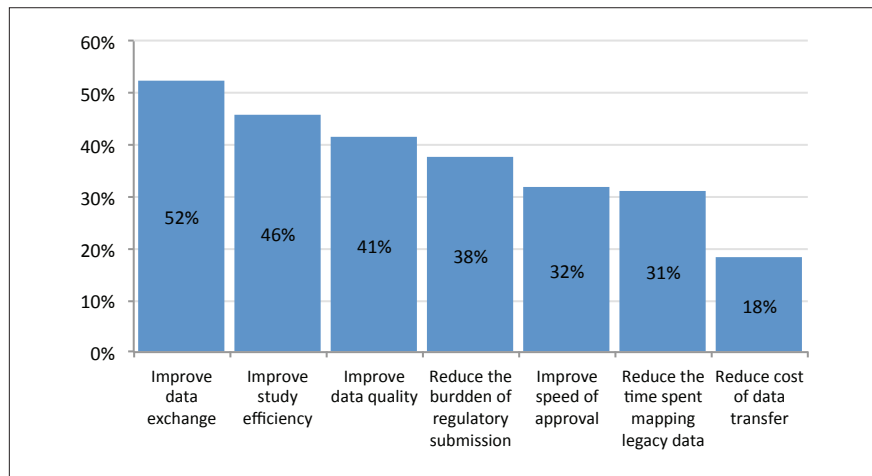


Figure 14. Benefits of CDISC standards (all respondents), i.e. n= 508 individuals, each allowed to identify up to 3 CDISC benefits.

Note that, when only those who had actually produced a submission were counted, the perceived benefits were higher for (4) reducing the burden, (5) improving the speed and (6) reducing the time to map data. See Figure 15.

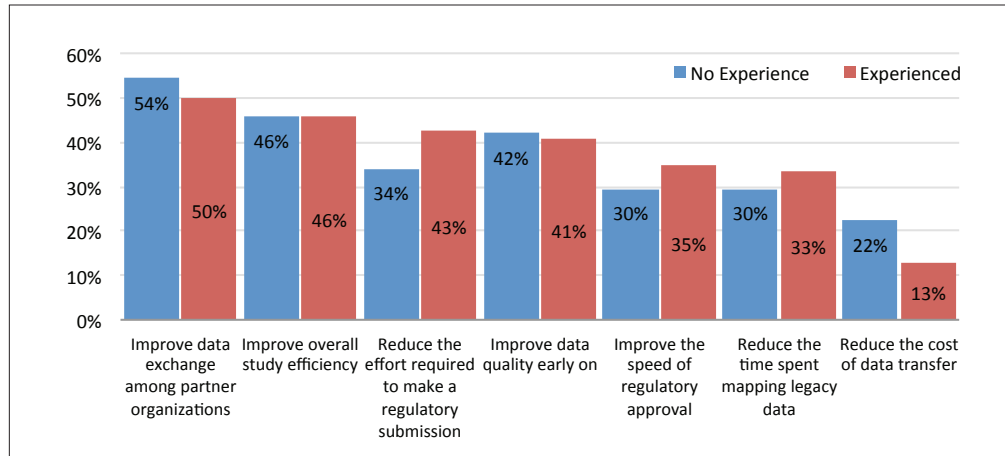


Figure 15. Benefits of CDISC standards for those having experience with eSubmissions vs. those without (n = 236 with submission experience).

Perceived barriers to the adoption of CDISC standards are shown in Figure 16. These were listed as:

1. lack of understanding of the CDISC standards (46%);
2. cost of implementing the standards (37%);
3. the existing domains do not cover a sufficient amount of the data (32%);
4. lack of FDA or other regulatory authority regulation (28%);
5. lack of available applications to support the standards (24%);
6. standards keep changing (24%);
7. concern about SDTM being replaced by an HL7 format (18%);
8. management resistance to change (16%);
9. concern about the longevity of the CDISC standards (15%), and
10. that they are only useful in the USA (9%). (Note: This last option was added as a “trick question” to test perceptions and comprehension of CDISC standards, since CDISC standards are being used around the world to improve clinical research processes, regardless of whether the data are eventually included in an FDA eSubmission.)

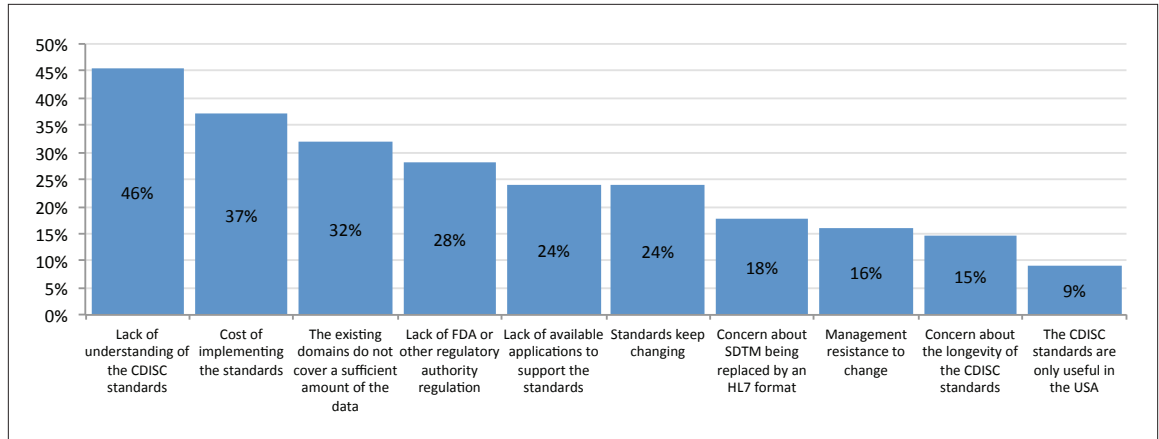


Figure 16. Perceptions of barriers of CDISC standards adoption by all respondents.

The perception of barriers tracked quite well when viewed in terms of whether the respondent had experience with an eSubmission or not, with lack of understanding of the standards still being the leading barrier (47% with no experience and 43% experienced in eSubmissions).

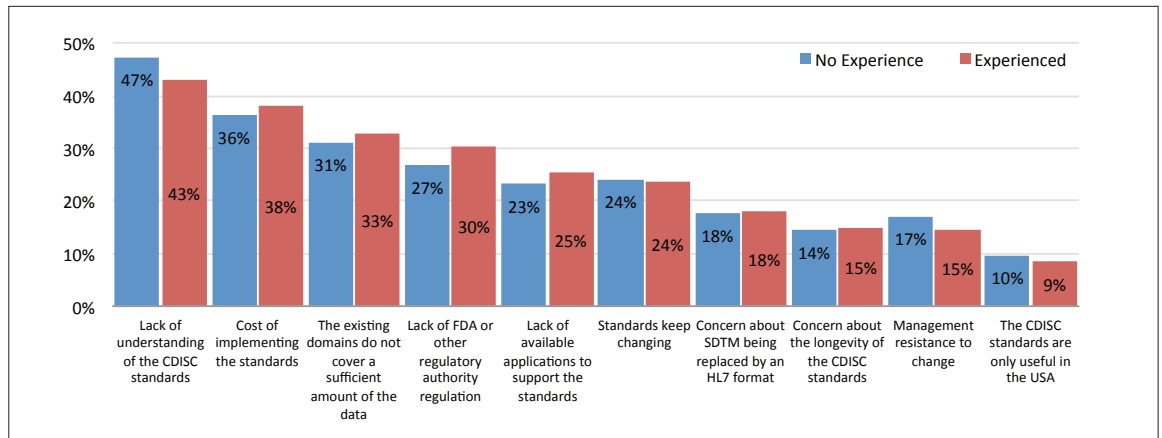


Figure 17. Perceptions of barriers to CDISC standards adoption by those with eSubmission experience vs. those without eSubmission experience.

When asked how CDISC could help assist in improving the adoption of the CDISC standards, the responses were (as shown in Figure 18):

1. work with the regulators to provide greater clarity;
2. provide more case studies;
3. produce more therapeutic area/efficacy standards;
4. demonstrate the value of the standards more clearly;
5. improve the current standards;
6. provide more educational courses.

These responses were given in the same order whether the respondent was experienced with eSubmissions or not.

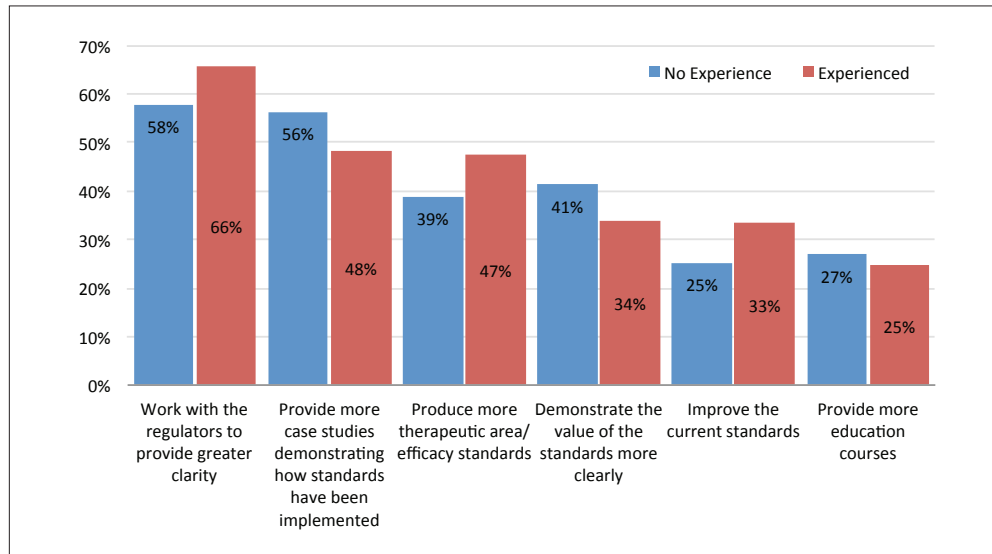


Figure 18. Responses indicate what CDISC can do to assist with adoption of the standards

In addition to what CDISC can do to assist in adoption, there was a question on what tools are provided today to provide benefit in the use of the CDISC standards. By far the most useful tool was recognized as the documentation that goes with the standards, with the CDISC website being the next most useful. CDISC Interchanges and Educational Courses were cited as the third and fourth places in term of useful tools followed by User Networks, Webinars, the CDISC eNewsletter and the CDISC book Introducing the CDISC Standards. The blog, vLearning and the CDISC Advisory Board were cited in descending order. The order was consistent whether or not the respondents had experience with eSubmissions, however, the frequency was slightly higher for those who were experienced and substantially higher for those who are CDISC members. CDISC member organizations clearly see more benefit from what CDISC can provide when compared with organizations that are not CDISC members. See Figures 19-21.

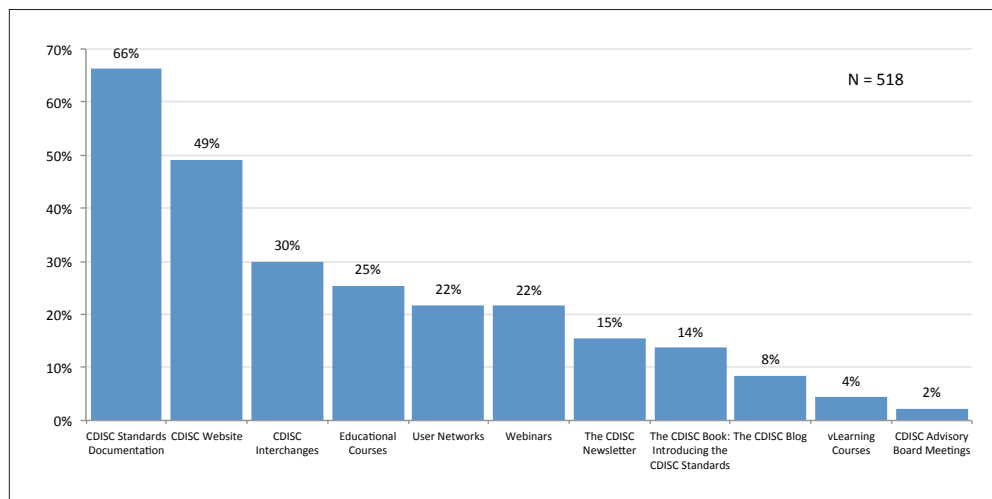


Figure 19. Usefulness/benefits of "Tools" that CDISC provides to assist with CDISC standards adoption and implementation.

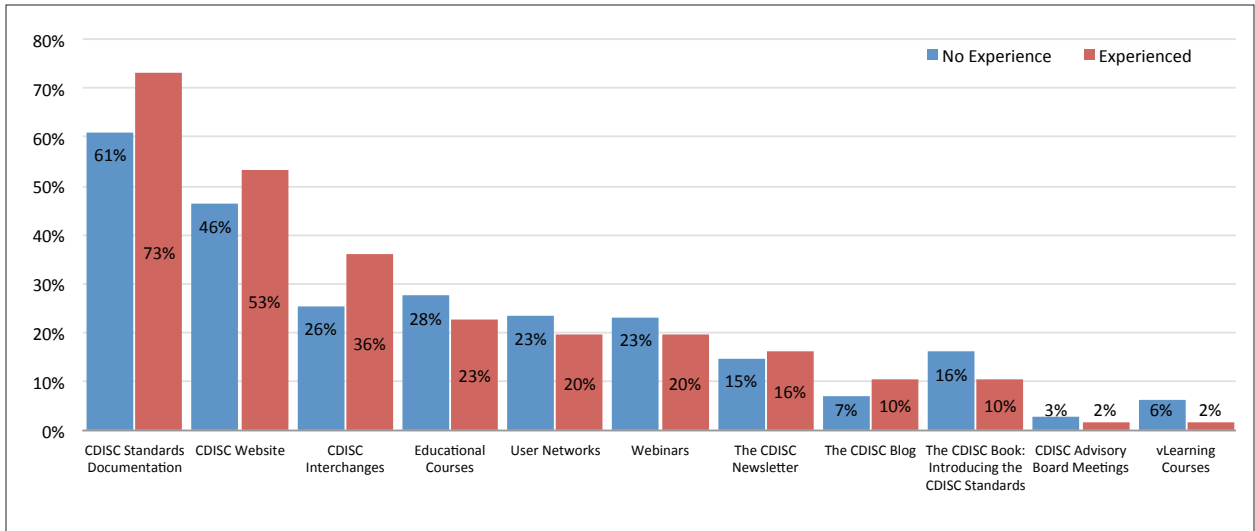


Figure 20. Usefulness/benefits of Tools that CDISC provides to assist with CDISC standards adoption and implementation (for respondents with eSubmission experience vs. no experience with eSubmissions).

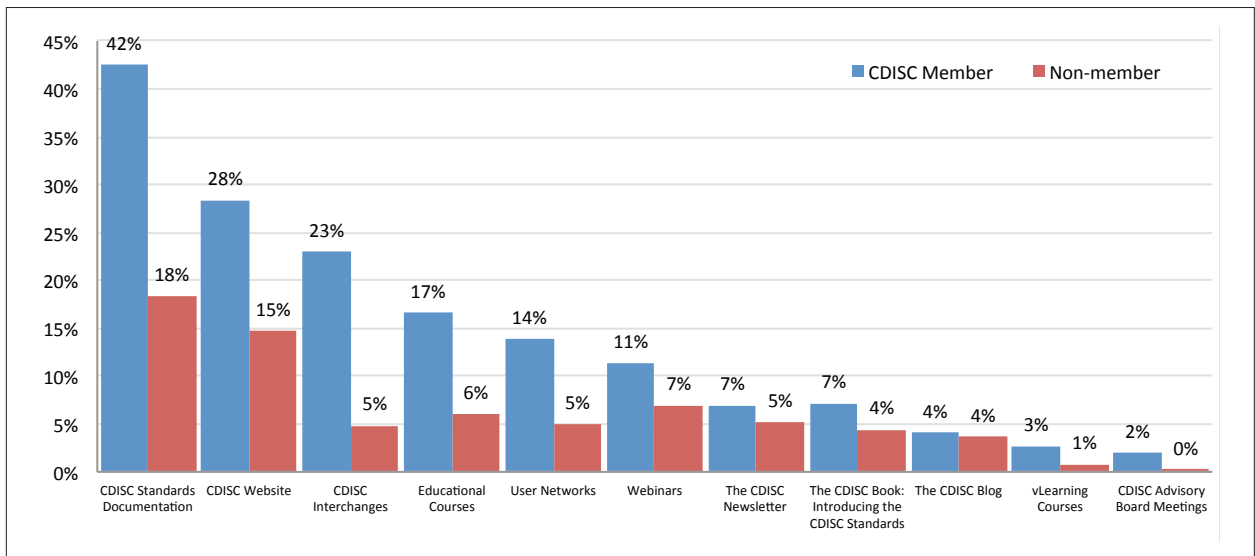


Figure 21. Usefulness/benefits of Tools that CDISC provides to assist with CDISC standards adoption and implementation for respondents from CDISC Member organizations vs. those from organizations that are not CDISC members.

### Submission Standards Experience

Of the 641 individuals who responded to the survey, 475 responded to the question of whether their organization had made a submission to the Food and Drug Administration using CDISC standards. There were 166 respondents who indicated that their organization had produced 1, 2, 3 or 4 or more submissions using CDISC standards, although over 100 respondents were unsure of how many their organizations had submitted. Those who used the SDTM v 3.1.1 numbered 169 while those who used

SDTM v 3.1.2 numbered 67. 158 of the respondents had employed Define.xml and 103 had used ADaM. Once again, many were unsure of which version their organization had used or whether or not ADaM or Define.xml were deployed. See Figures 22-25.

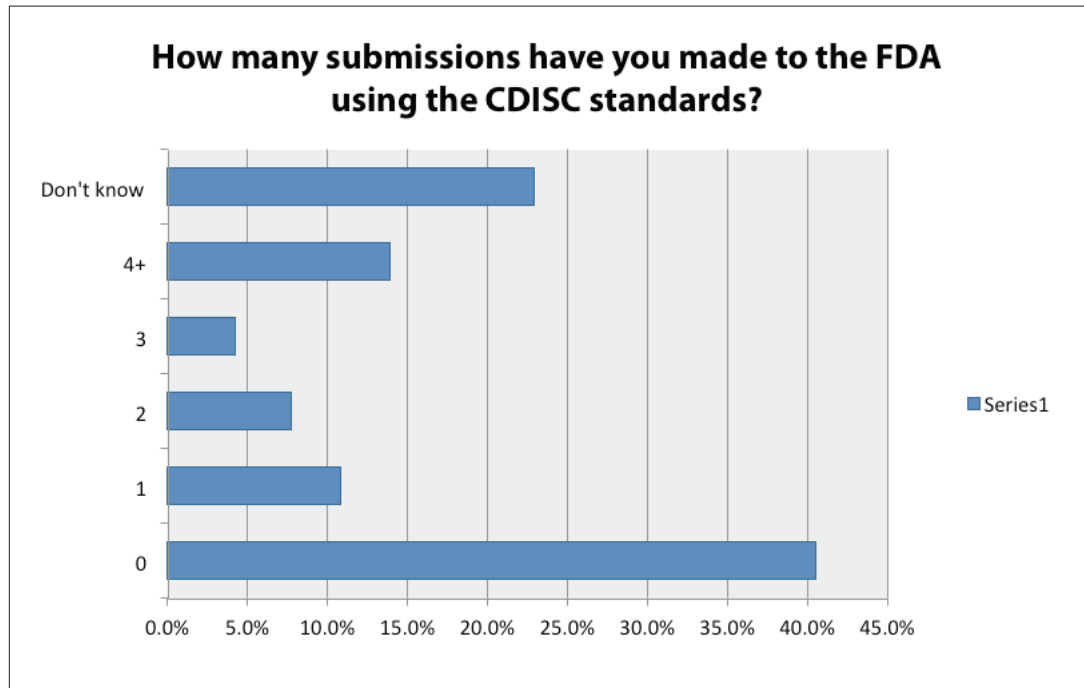


Figure 22. Number of eSubmission made to FDA using CDISC standards.

How many submissions have you made to the FDA using the CDISC standards?		
Answer Options	Response Percent	Response Count
0	40.5%	184
1	10.8%	49
2	7.7%	35
3	4.2%	19
4+	13.9%	63
Don't Know	22.9%	104
Additional Comments		43
Answered Question		454
Skipped Question		187

Figure 23. Actual counts for the numbers of eSubmissions made to FDA using CDISC standards.

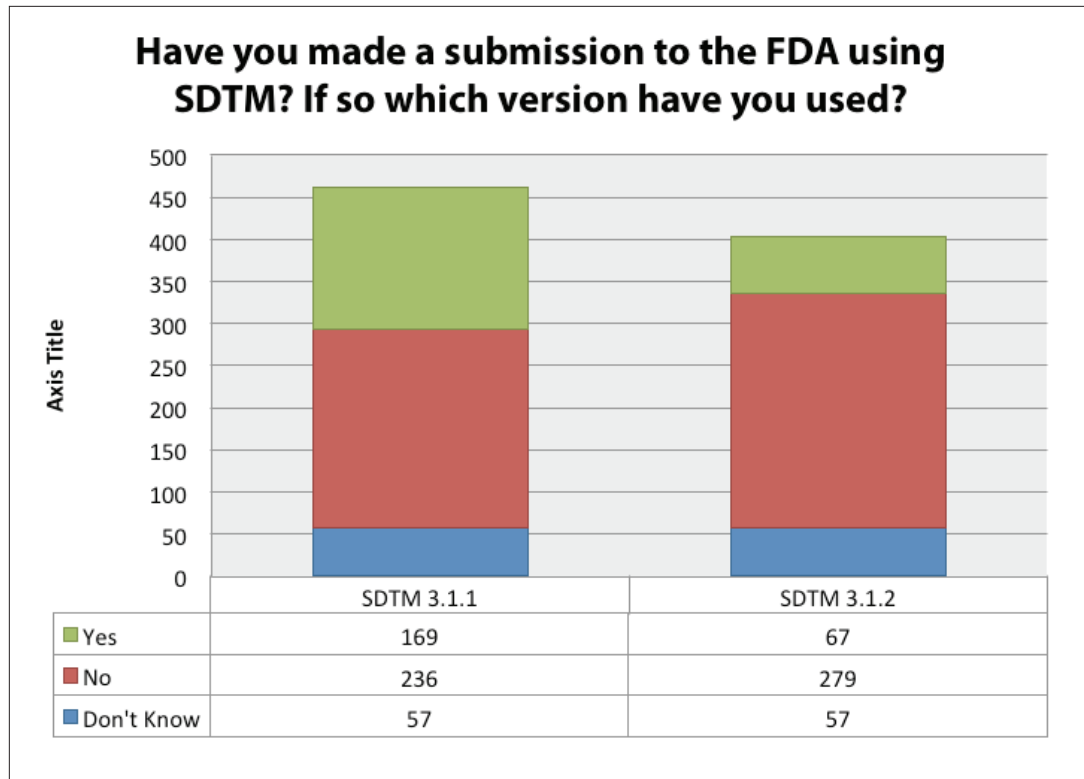


Figure 24. Version of CDISC SDTM used in Submissions to FDA.

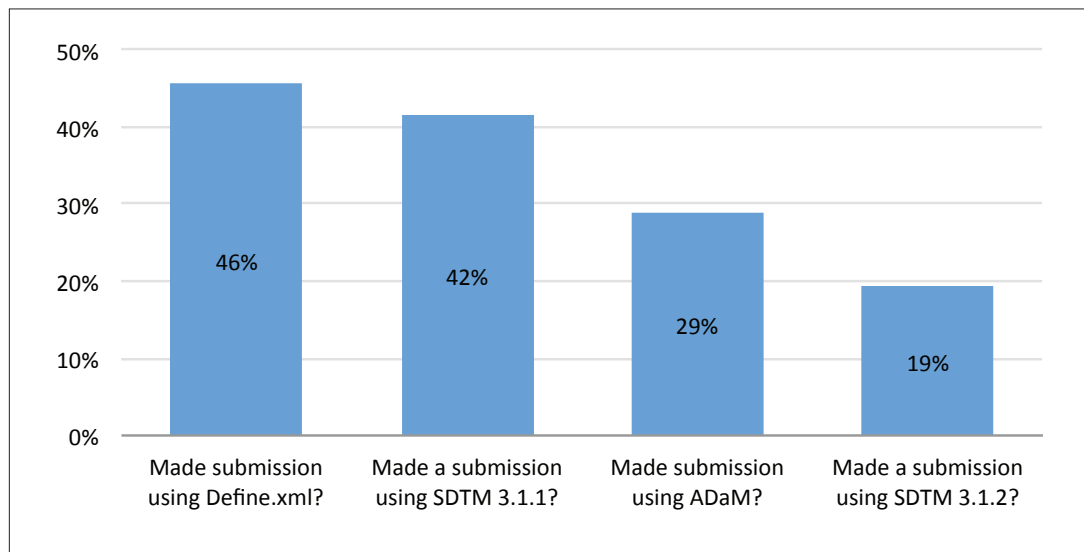


Figure 25. Use of Define.xml, ADaM, SDTM v3.1.1, SDTM v 3.2.1 in submissions to FDA.

## Discussion

It is clear from this survey data that adoption of the CDISC standards continues to increase and that the CDISC standards have provided increasing value to the research community over the years as they have matured. The trends in outsourcing and the adoption rate of CDISC standards by CROs would also indicate that an even more rapid adoption is likely in the next few years. The survey revealed that, even though adoption is increasing, there remain barriers to adoption and areas where CDISC can assist in this regard. This places an imperative on the CDISC organization to work even harder to facilitate this adoption, to communicate what is already being done to improve understanding and uptake of CDISC standards and to help reduce or remove the remaining barriers.

So, what is CDISC doing to assist in order to improve adoption of the standards? The response to that question can be organized according to the categories that were identified in the survey, beginning with “work(ing) with regulators to provide greater clarity”.

CDISC and FDA have been able to re-establish an active and ongoing collaborative relationship over the past few years. This involves working directly with representatives from the review divisions and their leadership to develop or augment the standards, improve communications, and clarify the expectations for data submissions. Clarifying the FDA expectations for electronic data submissions and their interpretations of the CDISC implementation guides has been addressed through several means. Following an FDA session during one of the popular CDISC International Interchanges in Baltimore, with the FDA Deputy Commissioner as a keynote, was the publication of an FDA CDER Data Standards Plan, which also received support from FDA CBER and CDRH. This resulted in an upsurge in FDA-initiated activities related to the CDISC standards, including the initiation of a CDER Data Standards Council and a regular teleconference among representatives of FDA, NCI and CDISC.

The recent development of a CDER Common Data Standards Issues Document, which was tied to the development of Amendment 1 for SDTM, has been a significant step forward in providing greater clarity around what the FDA wishes to see in terms of data included in eSubmissions. The purpose of this document was to clearly communicate where FDA (CDER) is experiencing issues in the varied interpretation by sponsors on how to implement the CDISC standards in an eSubmission. This document is now posted on the FDA website, at <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM254113.pdf> In addition, FDA (CBER) has been posting their issues directly via the web, rather than in a document, at <http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/ucm209137.htm>.

A webinar was held for users to ask representatives of FDA CBER and CDER their specific questions on this document and other submission issues, and the questions and responses are being shared openly. The ‘Common Issues’ document refers to the SDTM documentation, but also goes further and states specific preferences from CDER that are intended reduce the variability in the representation of similar data from multiple submitting organizations. These preferences have also been incorporated into CDISC-authorized training on SDTM to help communicate them to the wider community. The Center for Biologics Evaluation and Research (CBER) has published a web page with a well-defined process for submitting standard SDTM data.

Another means of working directly with FDA representatives to provide greater clarity in terms of CDISC implementations and also to address the third item in the survey to “produce more therapeutic area/efficacy standards” is a series of FDA Colloquia meetings. The first set of these Colloquia was organized by FDA and CDISC in March 2011 and another set is planned around the 2011 October CDISC Interchange. These Colloquia are attended by representatives from FDA, CDISC members and new participants who can provide clinical expertise in certain therapeutic areas (e.g. research physicians and clinicians and even patients). These meetings started as open forum at which specific data issues were discussed and methods for further standard development took place (e.g. development of the standards for efficacy data in certain disease areas or new areas such as the trial summary/protocol information needed in a submission). They have proceeded in a number of therapeutic areas where additional domains/standards are needed.

CDISC standards development teams also invite and actively encourage ongoing participation from FDA representatives on standards development teams and sub-teams. FDA representatives actively participate on several existing teams, including those developing standards for representing coded medication data (WHO-DD), immunogenicity data, non-subject data, device standards, and standard validation checks for SDTM submissions.

CDISC has also been actively involved in training FDA reviewers and other staff. Since 2008 CDISC has trained more than 250 FDA participants from CDER, CBER and CDRH through various training venues. These training sessions for reviewers help them to become familiar with SDTM and ADaM data formats in advance of receiving a submission. Recent courses specifically targeted to reviewer needs have been very well-received.

The CDISC International Interchange is routinely held in close proximity to FDA so it is easier for FDA representatives to attend. A session in which FDA representatives can present the current thinking from their different areas within the Agency and to respond to audience questions is always reserved and well-attended at the Interchange.

The second area is “provide more case studies”. Those CDISC organizations joining at a level to have a member on the CDISC Advisory Board (CAB) have been appreciating presentations on a regular basis from their peer organizations. These are included in the CAB agendas for teleconferences and face-to-face meetings and are focused on their experiences in implementing CDISC standards in their organizations or on tools they have used or implemented. There is also a CAB committee reviewing tools that are said to validate use of CDISC SDTM. Other means of communicating case studies of CDISC users include a CD of articles that have been collected over the past two years on specific topics that CDISC members have chosen to share; these are also posted on the CDISC website. The Annual CDISC Interchanges in the U.S., Europe, Japan and now China have also been venues where CDISC case studies have been shared.

The third and fifth areas in which CDISC can help with the adoption of standards are to ‘produce more therapeutic area/efficacy standards’ and to “improve the existing standards”. CDISC faces unique challenges as an organization that is powered primarily by “volunteer energy”. The nature of “open, consensus-based” development requires that the process of standards development be transparent and

that it include the input of the public; this consensus-based process results in more robust standards, but it also takes time. To accelerate that process without diminishing the quality of the end product requires the development and implementation of a new way of doing business for CDISC.

A CDISC initiative was launched in 2009 to help accelerate the development of both existing and new standards, in addition to improving access to these standards. This initiative is called the Shared Health and Research Electronic library (SHARE). SHARE will be a global, accessible, electronic library, containing the existing CDISC standards, such as CDASH and SDTM, as harmonized, machine-readable elements/concepts. SHARE will also be designed to facilitate the further development of the standards in a collaborative online environment. SHARE is BRIDG-based (BRIDG being the model that ensures harmonization across all of the CDISC clinical research standards); it is the future of CDISC.

CDISC is now also accelerating the development of standards through key collaborations with other organizations, such as the Critical Path Institute (C-Path), the National Cancer Institute (NCI) Enterprise Vocabulary Services (EVS), the American College of Cardiologists (ACC), Duke University, Tufts University, the University of Rochester, AdvaMed and many other partners working in specific areas of research. Through these partnerships, the CDISC teams have been able to produce several new therapeutic area-specific implementation guides (IG) that either have been out for public review or will be out for review in the near future. These include IGs for Oncology, Alzheimer's Disease/Mild Cognitive Impairment, Polycystic Kidney Disease, Cardiovascular Disease, medical devices, imaging and non-subject data.

Recently, the FDA shared with CDISC their priorities in terms of therapeutic area standards and awarded a small grant to CDISC, through the National Institutes of Health, to encourage innovation in terms of a newly designed process for building upon the core CDISC standards to cover the efficacy data. CDISC is in the process of redesigning this process along with a strong governance mechanism.

The fourth area identified in the survey in which CDISC can encourage the adoption of standards is to “demonstrate the value of the standards more clearly”. Communicating and demonstrating the value of standards is one of the core activities in which CDISC engages. The message of “value” is communicated through all of our educational offerings, including training, conferences, webinars and other presentations. There are also specific activities that are designed to demonstrate the value of standards in specific use cases, such as the Healthcare Link Initiative. The CDISC Healthcare Link Initiative embodies the Business Case for CDISC standards, specifically that the most value comes when implementing standards from the beginning of a research study (thus eliminating costly back-end mapping and legacy data conversion). The primary goals of this initiative are: a) to make it easier for clinicians to do clinical research, integrated into their busy workflow of patient care; b) to enter data once for multiple purposes; c) to improve data quality and patient safety. This work is based upon the CDISC eSource Data Interchange (eSDI) initiative (a collaborative project with FDA) and integration profiles developed through collaborations between CDISC and Integrating the Healthcare Enterprise (IHE). Interoperability showcases have demonstrated this opportunity to use EHRs for research and safety reporting to contribute to a learning healthcare system where research data can more efficiently inform clinical care. Several articles on this work have been written by CDISC Healthcare Liaison, Landen Bain, and CDISC President and Founder, Rebecca Kush, since this was one of the founding

principles of CDISC. EMA has incorporated the eSDI requirements into its Guidance for eSource, and representatives from the FDA Office of Scientific Investigation have expressed interest in this initiative (see the CDISC Blogs about the Interoperability Showcase at DIA 2011). It is important for clinical researchers to be 'at the table' as electronic health records (EHRs) roll out throughout the globe in order to ensure that they will support research without added burden on the part of the clinicians.

Another CDISC activity that focuses on communicating the value of standards is our workshop entitled "CDISC: Global Approach to Accelerating Medical Research". This includes an overview of the CDISC standards within the context of the data life cycle, and discusses specific ways in which standards enable process improvements, collaborations, and reusability within the research process from protocol through analysis and reporting (regardless of whether the data eventually end up in an eSubmission or not). This workshop emphasizes the value of CDISC standards for all medical research, including academic research or investigator-initiated research, particularly when implemented up front in the process (per the CDISC-Gartner Business Case). This three hour presentation is offered at various public training venues throughout the year, and is also offered as a complimentary session Platinum level member organizations, delivered for them at their venue.

The survey also revealed that CDISC can promote the use of standards by "provid(ing) more educational courses". CDISC training is going on somewhere in the world almost every week in the year. CDISC Education has increased the number of public training offerings over the past few years, with the goal of having at least one public training session per year in Asia, two in Europe and four in the United States. As of this writing, CDISC Education has issued more than 780 training certificates in 2011 (January through September). CDISC Education is working to make it easier for people who need authoritative training to access it. We have added information and functionality to our website that makes it easier for organizations and individuals to find course descriptions, register for public training, and to request private training. Planned and in-process enhancements to our courses include ongoing updates to all existing training materials, the development of new training courses to keep pace with the development of new CDISC standards, and the launch of online training in the near future. The goal of the CDISC Education is to ensure authoritative training is available and accessible to global users.

CDISC has made a concerted effort recently to increase Communication activities through the CDISC Blog, Website, eNewsletter, Press Releases and even Linked In and Twitter. Additional Communications activities and strategies are planned for 2012. The efforts of FDA representatives in making this a 'two way street' to encourage synergistic activities has been very much appreciated by CDISC stakeholders.

CDISC believes in 'strength through collaboration' and has devoted much effort to collaboration with other key organizations around the globe, in addition to the aforementioned partners in developing therapeutic area standards and maintaining controlled terminology. Collaborations with other standards organization include leading the Joint Initiative Council (CDISC, ISO, CEN, HL7, IHTSDO, GS1) for global harmonization of standards, i.e. research standards with healthcare standards; Innovative Medicines Initiative, which is encouraging the use of CDISC standards in their consortia and for their Knowledge Management needs; TRI for the translation and adoption of CDISC standards in Japan; Absolute Clinical Data for the translation of CDISC standards in China. CDISC sincerely appreciates the efforts of the J3C, C3C, CCAC and E3C in leading active CDISC groups and communicating with users and regulatory authorities and academics in their regions.

CDISC is all about 'productive collaboration' and relies on its members, supporters, 'commenters', team participants and other volunteers around the world to be successful and remain viable. It is through surveys such as this one that CDISC can understand their needs better. CDISC wishes to express our appreciation to all who participated in this survey and the Value Survey, the results of which are reported in a companion document.

---

© Copyright CDISC October 2011 [cdisc.org](http://cdisc.org)