Developing a CDISC Adoption Strategy

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Introduction

A primary objective of clinical development is to generate high-quality data as efficiently as possible; this supports the ultimate goal of clinical development—getting a safe and effective product to market as rapidly as possible. The challenge in today's environment is that generating this type of data is both expensive and time-consuming. As a result, clinical development organizations are constantly striving to find new and better ways to make the data generation process more efficient.

An example of this drive for increased efficiency is the widespread adoption of electronic data capture (EDC). The success of EDC in driving efficiency is leading more and more development organizations to implement and/or improve other time-saving technologies, such as electronic patient reported outcomes (ePRO) and clinical trial management systems (CTMS). The common element of all of these efficiency improvements is data; so it should come as no surprise that the industry is going beyond making its data-handling technology better to making the data itself better.

The driving force behind improving the data produced and used by development organizations is a group called the Clinical Data Interchange Standards Consortium (CDISC), which has established data standards that it hopes will be adopted across the industry, thereby enabling more efficient and effective use of clinical data.

The Food and Drug Administration (FDA) has shown its support for CDISC’s efforts, as industry-wide adoption of CDISC standards should enable the FDA to more rapidly review regulatory submissions. While this is just one of the many benefits of CDISC adoption, it is considered to be the most pressing reason for those in the industry to take CDISC’s efforts seriously. While CDISC compliance is not currently mandatory, it is anticipated that it will be an FDA requirement in the near future.

With the possibility of mandatory CDISC compliance on the horizon, many organizations across the industry are evaluating how and to what degree they will adopt CDISC standards. Campbell Alliance has collaborated with several development organizations in determining the approach to CDISC adoption that best fits each organization’s needs, and based on those experiences, has established a framework that can be used to tailor an approach to effectively adopting CDISC standards at any clinical organization.

Background on CDISC

In order to develop a CDISC adoption strategy, companies must first have a clear understanding of CDISC, its standards, and the degree to which regulatory authorities have embraced these standards.
CDISC is a global, open, multidisciplinary, non-profit organization that has established standards to support the acquisition, exchange, submission, and archive of clinical research data and metadata. The organization was established in June 2000 to develop and support global, platform-independent data standards that enable information system interoperability that will improve medical research and related areas of healthcare.

To achieve its goals, CDISC endeavored to create standards that are vendor-neutral, platform-independent, and freely available via the CDISC website. The following table outlines the current types of CDISC standards.

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<th>Standard Type</th>
<th>Description</th>
<th>Purpose and Status</th>
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| **Study Data Tabulation Model (SDTM)**             | Standard structure for study data tabulations that are to be submitted as part of a product application to a regulatory authority | • The SDTM standard is intended to guide the organization, structure, and format of standard clinical trial tabulation data sets submitted to a regulatory authority.  
• This model is specified in FDA guidance for implementation of the electronic common technical document (eCTD). |
| **Operational Data Model (ODM)**                  | Vendor-neutral, platform-independent format for the interchange and archiving of data collected from various sources in clinical trials | • The model represents study metadata, clinical data, and administrative data associated with a clinical trial.  
• Information that needs to be shared among different software systems during a trial, or archived after a trial, is included in the model.  
• The model complies with FDA 21CFR11 regulations. |
| **Analysis Dataset Model (ADaM)**                 | Set of guidelines and examples for analysis datasets used to generate the statistical results for submission to a regulatory authority | • These guidelines specifically address the needs of statistical reviewers. |
| **Laboratory Standards (LAB)**                    | Standard model for the acquisition and interchange of clinical trial laboratory data | • This content model can be implemented through different means, including ASCII, SAS, XML, and HL7 Version 3 RIM messaging. |
| **Standard for Exchange of Non-Clinical Data (SEND)** | Models that guide the organization, structure, and format for non-clinical data submitted to the FDA | • The focus of the SEND activities has been on data collected from animal toxicology studies.  
• SEND is intended to facilitate transfer of non-clinical data from sponsor to the FDA and subsequent loading into the FDA repository. |
| **Case Report Tabulation Data Definition Specification (CRT-DDS define.xml)** | Standard for providing case report tabulations data definitions in an XML format for submission to regulatory authorities | • The XML schema used to define the expected structure for these XML files is based on an extension to the CDISC ODM. |
| **Clinical Data Acquisition Standards Harmonization (CDASH)** | Standards intended to streamline data collection in a way that promotes improved data interoperability and enhances the interface with healthcare and electronic health records (EHRs) | • The CDASH initiative, which is led by CDISC, is currently in development. |
| **Standard Terminology**                          | Standard code lists for use in the clinical research data interchange       | • This is currently in development by the CDISC Terminology Team.  
• The team is working with representatives of government, academia, and pharmaceutical companies to identify and define these terms.  
• This work will support SDTM and other CDISC standards. |

While development of most of the standards described above is complete, each is at a different level of adoption by the industry and, more importantly, the FDA. The FDA is playing an active role in CDISC’s initiatives and is already supporting regulatory submissions in SDTM format, as
evidenced in the final guidance it issued on electronic submissions (i.e., electronic common technical documents [eCTDs]) that references the CDISC SDTM as a study data specification for electronic submissions to the FDA\(^3\). Building on that guidance, an FDA regulation is being proposed that will require all data submissions in electronic format and the use of CDISC SDTM for those submissions\(^4\). While there will be an appropriate period of time allowed for compliance with this regulation\(^4\), the potential for this change has many development organizations hustling to become CDISC compliant in advance of the requirement.

The potential requirement of SDTM-compliant submissions is certainly the most pressing of the CDISC standards in terms of adoption, but it is not the only standard with which the FDA is involved. The FDA is also working with CDISC and Health Level 7 (HL7) on transport technologies that may ultimately replace the current SAS file method used for submissions today\(^5\).

**Benefits of CDISC Adoption**

While FDA support for CDISC standards may be the most compelling force driving CDISC adoption, compliance with current FDA preferences and likely future FDA requirements is only one of the benefits of adopting CDISC standards.

Beyond the regulatory submission process, implementing these data standards should drive efficiency in any clinical organization. When data outputs from different data collection tools (e.g., EDC, CTMS, ePRO) are the same, then data can more easily be shared both within Development and across functional areas. Furthermore, organizations can more easily share data with industry partners and vendors if everyone is using the same standard format for all data.

In addition to the data handling and sharing benefits associated with CDISC adoption, there are many benefits related to data analysis. For example, it will be easier for those who do analysis on clinical data to do their work if all of the data they receive is in the same format, and easier analysis should translate to faster analysis. Also, adoption of CDISC standards lays a foundation for implementation of data archives capable of cross-study analysis.

Ultimately, all of the above-mentioned benefits enabled by CDISC adoption support a development organization’s highest priority—rapid and successful submission of high-quality data to the FDA—as a simplified data submission process may lead to quicker approval.

**Framework for CDISC Adoption**

Given all of the benefits of CDISC adoption, it is no surprise that many development organizations are deciding to take the plunge; however, while deciding that CDISC adoption is a worthwhile endeavor may be simple, the process of implementing CDISC adoption is significantly more complex.

Based on Campbell Alliance’s experience in supporting several CDISC adoptions, organizations must take a careful and staged approach to adoption in order to truly benefit from implementing CDISC standards. Below is a high-level illustration of Campbell Alliance’s CDISC Adoption Framework.
Like any change initiative, CDISC adoption must start with the identification of clear goals. Organizations’ goals for CDISC adoption vary based on an organization’s size and structure. For example, an organization that outsources the majority of its development activities to contract research organizations (CROs) may consider identification of CROs that are CDISC compliant to be one of its highest-priority goals. In contrast, an organization with a large in-house development group may put the most emphasis on training its staff on creation of SDTM and ADaM datasets with CRT-DDS (define.xml) and SDTM annotated CRFs for FDA review.

Whatever the selected goals, they are the driving force behind selecting the desired degree of CDISC adoption. The degree to which an organization adopts CDISC falls on a continuum, as depicted below. Where an organization falls on the continuum is determined by what level of adoption best suits the organization’s goals.

To achieve its desired level of CDISC adoption, an organization must next determine the processes and subsequent roles affected by the change. For organizations seeking a lower degree of adoption (CDISC Adoption Continuum Stage 1), more emphasis will be placed on changes to vendor selection and vendor management processes, as some or all of the CDISC adoption will be done by the vendors that serve the organization.

Further along the continuum towards full CDISC standard adoption (CDISC Adoption Continuum Stages 2 to 6), the focus shifts to three key internal processes: CRF design, database management, and statistical analysis. The differences in the types of required process changes between CDISC Adoption Continuum Stages 2 and 6 are found within each of those processes. For example, an organization choosing Stage 3 would need to modify the CRF build and review subprocess, the CRF annotation subprocess within its CRF design process, and the extraction process, while an organization choosing Stage 4 would also need to revise the CRF Library subprocess. Once an organization has identified the affected processes (and subprocesses), it
can easily identify the roles that carry out those processes and will thereby be affected by CDISC adoption.

The affected roles will require both CDISC training and organizational support in order to successfully carry out their assigned task once CDISC adoption is initiated. As with determining the affected processes, determining the type and degree of training and support required will vary depending on an organization’s selected degree of CDISC adoption. The further along the continuum an organization aims, the greater the degree of training and support required. Regardless of the degree of adoption, roles participating in the implementation of CDISC standards must be trained in order to ensure standards compliance.

Once an initial round of CDISC training is completed, Campbell Alliance has found it is valuable to put an internal user support group in place. This cross-functional group is comprised of individuals who have received CDISC training and have experience using the standards. Each group member serves as a resource to their peers in their individual functional area. In this role, members both provide training to others in their functional area and bring functional area concerns and ideas up to the user support group. This dual functionality ensures knowledge transfer among functional areas and provides a means for tracking and deciding on suggested updates.

Once training and support are in place, an organization can begin the actual adoption of CDISC standards. Given the complexity of CDISC standards and the need for these standards at various points within the data collection and analysis processes, a tiered adoption approach is necessary. As with other parts of the CDISC adoption framework, the steps in this tiered adoption approach will vary based on the selected degree of adoption. The illustration below shows the high-level approach that an organization choosing Stage 4 adoption would take.

**Example of Tiered Adoption Process—Stage 4 of CDISC Adoption**

- **1.** Establish internal user group, complete training, and define governing body
- **2.** Convert legacy data using CDISC standards
- **3.** Define specifications and custom domains and establish a data extract method
- **4.** Update the global CRF library
- **5.** Define a data validation approach and select and pilot a study

Even with an aggressive timetable, the above process would take approximately a year to complete in most organizations. Just as the number of affected processes increases across the
CDISC adoption continuum, so does the amount of time needed to complete the adoption process.

No matter how long or short the adoption process for the selected degree of CDISC adoption, the adoption will only be successful if it is supported by a maintenance plan. CDISC continues to develop and enhance their published standards; therefore, continued education, awareness, and participation in the CDISC standards and future initiatives are required.

Campbell Alliance recommends that a subset of the user support group established to support CDISC adoption be identified to serve as a governing body that can both make decisions about suggested changes coming from the users and monitor the evolving CDISC standards. The following diagram illustrates a basic framework for a CDISC maintenance plan.

**Maintenance Plan Framework**

1. Identify latest available set of CDISC standards and determine timeline for adoption
2. Train required staff on standards and implementation mechanics
3. Monitor current developments within CDISC, industry, and regulatory bodies
4. Implement standards

**Conclusion**

CDISC adoption—at any level—is a complex undertaking. Standardizing the way data is presented and handled involves many processes and even more stakeholders. This means that executing a successful CDISC adoption involves both careful planning and execution. While adoption may be challenging, it is clearly the direction in which the industry and regulatory bodies are heading. Development organizations that want to achieve the efficiencies that CDISC enables must face this challenge head-on in order to stay ahead of the curve.

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Sources:


