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Clinical Data Interchange Standards Consortium (CDISC) – An Update

In the next issue of
EDC Today:

CDMS Design
Highlights

About EDC Management:

EDC Management is the leader in Clinical and Data Management and Electronic Data Capture (EDC) consulting services for the biopharmaceutical industry. EDC Management publishes well-researched and timely information about Electronic Data Capture technologies and processes through EDC Today® and EDC In Depth. We do not sell or endorse any specific EDC software application or vendor. Improve process today; position for tomorrow.

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EDC Today is an independent publication on current information and issues in Electronic Clinical Systems (ECS) strategies and technologies for the Biotechnology and Pharmaceutical (Biopharma) industry. Each month we examine topics related to ECS theory, technology, practice, or implementation.

Recently, a number of readers have requested we write about the Clinical Data Interchange Standards Consortium, better known as CDISC and discuss the current situation of this standard's setting body and any upcoming releases and events that might impact Electronic Data Capture (EDC). In particular, readers are interested in CDISC's progress with their standards models and the level of continuing support for CDISC.

In this issue, we discuss the current efforts of CDISC. We describe the models that have been released and potential updates to existing models. However, more importantly, we take a look at the purposes of, and uses for, the models and evaluate how well the models might serve these purposes. In particular, we support the Lab interchange model and the submissions models as these have well defined purposes that everyone can use. We examined the Operational Data Model (ODM) in detail, and unfortunately we feel that there is little reason for **established** EDC and Clinical Data Management System (CDMS) vendors to fully support this model.

Introduction

EDC Management considers CDISC and its efforts to be valuable and important. In fact, CDISC has been mentioned in six (6) issues of the previous twenty-seven (27) issues published to date! In *EDC Today*, Issue 8 "Data Transfer Standards: How to Leverage Your Investment in EDC" we comprehensively covered standards and CDISC's role. In *EDC Today*, Issue 13 "EDC and E-Submissions" we followed up with a fairly extensive discussion on CDISC's standards and their expected role in future, at the time, electronic submissions.



In *EDC Today* issues 3, 8, 9, and 13, we discussed how CDISC factored in the FDA and other regulatory bodies adopting standards for data transfer and/or submissions. In *EDC Today* issues 8, 13, 15, and 21, we discussed the need for easy transfers between Application Service Provider (ASP) modeled EDC vendor's databases and sponsor's clinical trials data management systems.

So what is CDISC and why does EDC Management consider them to be so valuable and important? The reason is imbedded in the consortium's name, "Data Interchange Standards". First, we deem "Standards" to be very worthwhile from the business perspective. When a business can put a "standard" into practice instead of re-inventing the wheel every time, they can see a cost savings. Unfortunately, for a variety of reasons, practical standards are as elusive as the Holy Grail to many Biopharmas. Beyond standards in general are standards specifically focused on data interchange (i.e., interchange in this context can be viewed as "the transfer of data between different computer-based systems"). For Biopharmas, clinical data interchange has been an expensive but necessary business activity. To reduce the expense of data exchange, a movement started within the DIA to create standards that would hopefully have the widespread support of the Biopharma industry.

In 1998 and 1999, CDISC was a Special Interest Advisory Committee of the DIA. In 2000, CDISC was incorporated as a separate, independent, non-profit corporation, mostly because the DIA felt that CDISC's efforts might be incompatible with the DIA's mission. The DIA, however, is very supportive of CDISC and its efforts. In fact:

All CDISC Board members, and most CDISC participants are also members of the DIA, and the CDISC President is on the DIA Steering Committee of the Americas, representing standards and technology.¹

A positive indication of the continued DIA's support for CDISC is the upcoming jointly sponsored DIA-CDISC conference entitled "e-Clinical Interchange: From Clinician to Submission" on October 20-22, 2004 in Washington DC.² The conference agenda wasn't final at press time, but the tentative syllabus indicated the conference would offer an in-depth look at the details of current and future CDISC-related activities. Certainly, a lot of EDC Management staffers plan to attend.

Clinical Data Interchange and CDISC Standards

Biopharmas have long been involved in Clinical Data Interchange. Traditionally, clinical data has been transferred from Contract Research Organizations (CROs), Central Laboratory, and Remote Data Entry (RDE) systems to the study sponsor's CDMS database. With the advent of electronic submissions to the FDA and Application Solution Provider-modeled EDC, additional needs for clinical data transfer have developed. Furthermore, the trend seems to indicate an additional interchange in the future, one between Hospital and Investigator Sites to Sponsor databases. To enable these interchanges, transfers of metadata might also be performed between the various databases that store clinical data over the life of a trial. Finally, when a study is over and all analysis is complete, the clinical data might be archived for undetermined future use.

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**Table 1: Clinical Data Transfer**

Data Interchange		Data Source	Data Target
	Data Capture To Clinical Database	CRO, EDC	CDMS
Data Interchange	Laboratories To Clinical Database	LAB	EDC, CDMS
	Clinical Database To FDA	EDC, CDMS	FDA
Metadata Interchange	Data Capture To Database	EDC, CDMS, LABS	EDC, CDMS, LABS
Potential / Possible Future Interchanges	Hospital and Investigator Site Database To Clinical Database	HOSP, INV	EDC, CDMS
Archive	Database to Archive	EDC, CDMS, HOSP, INV, LABS	ARCHIVE

Given that there are several different clinical data interchange requirements, it is not surprising that there are a number of interchange standards being developed (or being fine-tuned) by CDISC.³ Amongst these standards is the Operational Data Model (ODM) that supports the exchange of clinical data between databases. The ODM supports not only the transfer of clinical data, but also the transfer of metadata describing the database structures needed to store the clinical data that will be transferred. Obviously this model is a complex one as it is not only expected to cover the complete range of clinical data's intricacies (or is it idiosyncrasies?), it is expected to cover the metadata too. The only "shortcut" being taken in the development is that the model is vendor neutral and "only" supports metadata and data in a generic way. That is, metadata that contains vendor proprietary information (due to system architecture) like data entry screen layout data (X-Y locations, font, question wrapping, and so on) and record identifiers are not included in the model, and EDC Management believes there are good reasons for doing this.

What motivates the refinement of the ODM is its large potential. Potential uses include "simplified" interchanging of data between CROs and sponsor EDC and/or CDMS database; between EDC and CDMS databases; and possibly in the future, between Investigator Sites and CRO, EDC, and/or CDMS databases. The ODM is currently at version 1.2 which was released in January 2004.

Another standard is the Laboratory Standards (LAB) model that supports the exchange of information between "central labs" and (either or both) the sponsor's database(s) used by their EDC or CDMS applications. The obvious benefit of a combination of "built-in" vendor support for both the laboratory's data capture application and the sponsor data management application(s) would greatly simplify transfers and make obsolete a large number of data loaders developed in-house by Biopharmas. The LAB model is currently at version 1.0.1 which was released in April 2004. Work is in progress on microbiology components and ECG extensions.

Two other standards that are being refined by CDISC that should be of interest to those that work with clinical trials data are the Submissions Data Standards (SDS, which includes the Study Data Tabulation Model (SDTM)) and the Analysis Dataset Model (ADaM). These

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models cover different aspects of an electronic submission. The FDA has been piloting tools that enable reviewers to work with data that was formatted using these models. If nothing else, this has a big benefit of standardizing, and clarifying what data are submitted to the FDA in a New Drug Application (NDA) and/or Biologics License Application (BLA.) The FDA has shown great interest in SDS, specifically the Study Data Tabulation Model (SDTM) and has approved the latest version of the model. This action should prod the current CDMS as well as EDC vendors to provide support for data extraction in this format.

One or more of these models might be used for data archival purposes. One might use the ODM model and/or the SDS model for long-term data on electronic media. The LAB model might even be useful for long-term storage of central lab information if this data is unaltered after being uploaded into an EDC or CDMS. It is, in part, the formatting and structure of the data within the CDISC models that makes them ideal for archiving clinical trials data. That is, they use platform independent files (XML - eXtensible Markup Language) containing a widespread character-coding scheme (ASCII - American Standard Code for Information Interchange).

There are other CDISC models, for instance those produced by the Protocol Representation Group (PRG), as well as the Standard for Exchange of Non-clinical Data (SEND Version 1.4) both of which are outside the scope of this issue.

SDS and ADaM

In 2002, the FDA's Patient Profile Pilot was started. Its premise was that standardized data would ease the development of a standardized data review tool. Furthermore, it was anticipated that the use of a standard review tool would both improve the quality and expedite the review. Lastly, it was hoped that the use of standardized data and a universal review tool would make it easier for Biopharmas to package e-submissions. As of the end of last year, the data review tool was to be updated to support the most recent CDISC SDS version (version 3 at the time). The FDA was to pilot another project to test submission data formats and tools. This year there are expectations that the installation, training, and support for both the standard and the review tool will take place. "The resulting version of these standards (SDS Version 3.1) is scheduled to be directly referenced by FDA Guidance by mid 2004."⁴ On July 21, the FDA announced that the Study Data Tabulation Model (SDTM) developed by CDISC is to be the standard format for data included in NDA submissions to the FDA.⁵ On July 27th, 2004, the FDA posted "Electronic Common Technical Document: Study Data Specifications" which do indeed directly reference CDISC's SDS model 3.1.⁶ When looking for information regarding CDISC, SDS, and SDTM, use the eCTD (electronic Common Technical Document) keyword.

In conjunction with the FDA's acceptance of SDTM, is its acceptance of the Submission Data Manager tool or viewer application. This application can be downloaded from the FDA's website at <http://www.fda.gov/cder/OIM/ESI/evsweb/index.htm>. Complete instructions on how to install and use the software are also posted.

"The Analysis Data Modeling (ADaM) team has developed a guideline and several examples for analysis datasets used to generate the statistical results for a regulatory submission."⁷ This model is a work in progress and still evolving. It should not be confused with the SDTM / SDS model. The ADaM guidelines are currently at version 1 and were released in February 2002.

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Vendors

Along with the FDA's support for CDISC, CDMS and EDC vendor support is also critical to the CDISC initiative. It is up to these vendors to build support for the various models into their software. EDC Management would expect support for LAB, SDS, and ADaM to be included in future releases of any data management software. As for support for the ODM, it remains to be seen how it is in any vendor's own self-interest to support this standard, especially if they already provide for transfer of data in and out of databases built on their own solution. An example of this functionality is eResearch Technology's "metadata send/receive" function that, within eResearch Technology-based CDMS of the same version, would always be superior to an ODM-based metadata transfer. The vast majority of those in the EDC market deem the adoption of data interchange standards as critical.⁸ But while the Biopharma industry might benefit from being able to select the best of breed of CDMS and EDC solutions from different vendors, it would seem that the vendors themselves gain little by providing it.

That said however, all of the major CDMS vendors and most of the better-known EDC vendors are members of CDISC. Most of the major CDMS vendors say they will implement unspecified CDISC exchange functionality in the indeterminate future. It is believed that this support will be slow in coming however, as the functionality will need to be designed in such a way to support continuously evolving standard(s) with a minimum amount of software modification. Add in the complexity of the CDISC ODM and it easy to see that incorporating this ill-defined enhancement will be a challenging, highly technical, problem – especially for vendors with large and complex CDMS offerings. The new-to-the-scene EDC vendors are more likely to be able to implement CDISC support since their products use newer development tools, and are less likely to be encumbered by "legacy code". The marketplace is testimony to this, as only three vendors are known to have extensive CDISC support and all of them are relatively new and small.

Table 2 shows CDISC's vendor membership and the amounts of monetary support they provide the standards body.⁹

Of this illustrious list of vendors, only three have extensively implemented CDISC standards in their products to date. All of these vendors, DataLabs, Inc, etrials, and a relative newcomer on the scene, the Glasgow, Scotland-based Formedix, offer EDC applications.¹⁰

DataLabs offers the DataLabsXC product suite which includes three modules, Designer, Clinical, and Connect. The Designer module is used to design, prototype and implement clinical trials. The Clinical module is a portal-based, fully featured, web collection tool. The Connect module supports the integration of DataLabsXC Clinical with other Clinical applications including CDMS.¹¹

etrials offers a system for generating ODM formatted data from its data-entry database. It also offers an ODM Request application that supports scheduled (e.g., daily) data exports of selected patient data.¹²

Formedix, like DataLabs, offers a suite of three products. They are the Origin Study Modeller, used to design study databases; Transform, used to build EDC databases; and Express, an electronic data capture solution that can be used in on-line (connected to the internet) and off-line (unconnected) modes.¹³

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Finally, a couple small firms not listed as CDISC members, Target Health Inc.¹⁴ and Visitrial¹⁵ claim to offer an EDC solution completely based around the CDISC ODM. Interestingly, Visitrial offers their software free to the academic research arena, hoping to license the same code to biopharmas.¹⁶ Target Health offers CDISC Lab and other data transmission support that meet CDISC standards in addition to having database configurations built upon CDISC standards.

Table 2: CDISC’s Vendor Membership⁹

Corporate Sponsors (\$5,000 to \$111,000 initially; \$5,000 to \$30,000 annually depending on size of company)	
EDC	CDMS
ClinPhone	eResearch Technology, Inc.
Compleware	Oracle
CRF Box	Perceptive Informatics
DataTrak International	Phase Forward
eResearch Technology, Inc.	
Formedix	
ICTI	
Oracle	
Outcome Sciences	
Phase Forward	
PHT Corporation	
ViPs Biomedical Services	
Corporate Members (\$5,000 to \$15,000 initially; \$5,000 to \$15,000 annually depending on size of company)	
EDC	CDMS
LifeTree Technology	None
Relysis	
Synteract, Inc.	
Associate Members (\$2000 annually)	
EDC	CDMS
Clinsource	Clinsource
DataLabs, Inc.	
etrials	
Gereq	
Industry Dynamics Associates	
InvivoData	
Medidata Solutions	
Mini Mitter	

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Conclusion

As one can see, CDISC continues to be an important organization affecting the biopharma industry. Since the FDA has adopted CDISC's SDS model as part of its electronic submissions guidance, CDISC will likely be an increasingly important factor in the foreseeable future. EDC Management considers it essential for professionals in the biopharma industry to keep abreast of CDISC's efforts.

EDC Management views CDISC's efforts in the laboratory and submissions areas to be the most significant for all parties involved with clinical data. The LAB model will help reduce the cost requirements for supporting data transfers from central labs. The SDS submissions model, with the blessing of the FDA, will help facilitate both the submission of data to the FDA and the review process the FDA performs.

EDC Management feels that vendor support for the LAB and SDS models should be quickly forthcoming as it is in the vendor's best interest to support these models. Certainly vendors that have a large and / or mature code base will face the largest hurdles in developing support for CDISC. Newer vendors that have started developing their applications based on the CDISC standards will find it easier going and should have more support already built-in to their applications.

The ODM model has taken considerable effort on CDISC's part. While biopharmas have a definite interest in the ODM including the potential ability to use more than one EDC and / or CDMS products and transfer metadata and data amongst them, there is no compelling reason for the vendors to support the ODM without necessary vendor specific additions to the model. That said however, it would be in the interest of an EDC vendor with a new, or nearly new, product to incorporate ODM support in the hopes of capturing customers currently running studies using another EDC vendor's software. Unfortunately, development of the ODM may unintentionally offer new EDC vendors a business advantage over their established competitors.

It remains to be seen how much true support EDC and CDMS vendors give to the CDISC models. It may be a decision with profound business implications for these vendors in any eventuality.

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References:

- ¹ <http://www.cdisc.org/faq/index.html>
- ² <http://www.diahome.org/Content/Events/04032.pdf>
- ³ <http://www.cdisc.org/standards/index.html>
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- ⁵ <http://www.fda.gov/bbs/topics/news/2004/NEW01095.html>
- ⁶ <http://www.fda.gov/cder/regulatory/ersr/5640studydata-v1.pdf>
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- ⁸ <http://www.eyeforpharma.com/index.asp?news=34923>
- ⁹ http://www.cdisc.org/sponsors_members/index.html
- ¹⁰ http://www.bio-itworld.com/news/041604_report4890.html
- ¹¹ <http://www.data labs.com/dldescription.html>
- ¹² <http://www.challengeyourdata.com/wp1.html>
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- ¹⁴ <http://www.targethealth.com>
- ¹⁵ <http://www.visitrial.com>
- ¹⁶ http://www.bio-itworld.com/news/061704_report5380.html

Who's behind the research?

Our lead researcher, Kirk Mousley, PhD received BS and MS degrees in Electrical Engineering from MIT and a PhD in Computer Science from Lehigh University. He has been the President of Mousley Consulting, Inc. since its founding in 1993 and has directed the company's efforts in the areas of clinical database design, data editing/cleaning, document management, and submissions.

Karl Mousley received his BS in Mechanical Engineering from Rose-Hulman Institute of Technology and a MS in Computer Science from Villanova University. He has been a senior member of the technical staff at Mousley Consulting, Inc. since 1993. Among his significant accomplishments are the investigation, evaluation, and implementation of new computer technologies for clinical data management systems and developing strategic plans for integrating these technologies into current systems. He has extensive experience preparing Standard Operating Procedures (SOPs).



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