

# Healthcare and clinical research: a critical link through standards

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Collection of clinical trial data in community oncology centers is hampered by continued reliance on paper case report forms—still used in over 60% of all clinical trials—and a lack of industry-wide standardization in the tools and applications used to collect, transfer, and analyze the data. Adding to this problem is an inability to exchange data with electronic medical record systems or with other investigators, even within the same institution, leading to much duplication of effort and inadvertent errors in data entry, transcription, and re-entry of data already collected for other purposes. The Clinical Data Interchange Standards Consortium (CDISC) has developed worldwide research-industry standards and tools for the electronic capture, exchange, submission, and archiving of clinical trial data. This article describes the accomplishments and goals of this industry-sponsored nonprofit organization and its relationship with the US Food and Drug Administration and other regulatory and standards-development organizations. The goal of CDISC is to facilitate the collection and interchange of clinical research information among investigators, regulators, and clinicians, and to accelerate the process of drug development to improve patients' lives.

Clinical research is typically conducted in a community oncology clinic or cancer center quite separately from the provision of healthcare. Three distinct worlds coexist—investigator-designed protocols, protocols to support regulatory approval of new diagnostic or therapeutic agents, and patient care—that share little information. Even the tools used to collect research data, whether they be traditional case report forms (CRFs) or electronic data capture methods, are, in most cases, totally separate from the medical records, patient charts, and electronic medical files housing the institution's healthcare data. In addition, cancer centers often maintain site-wide or patient management systems, project management applications, adverse event tracking systems, and other databases or tools that collect much of the same information that is found in CRFs or medical records. This duplication results in entry, transcription, and/or re-entry of essentially the same data four to seven times<sup>1</sup>—a process that is prone to inadvertent errors and waste of human resources.

For the most part, the tools that have been developed to collect clinical trial data or to support other activities related to clinical trials are point solutions; they have different requirements for data entry, query resolution, and other procedures and do not readily connect, or share data, with other applications within the clinical trial process. Thus, training for each tool or database application is needed, and the data collected in one trial are not necessarily

readily integrated with data from other trials—even those examining the same therapy. Active investigative sites use, in addition to paper CRFs, an average

## KEY POINTS

Our current inability to readily exchange clinical trial data with other investigators and existing medical record systems is wasteful and expensive.

The transition from paper medical charts to electronic health records in medical practices is inevitable and could improve research if clinical trials are taken into consideration in the design and implementation of electronic health records.

Available now are global, vendor-neutral data interchange standards for the clinical research industry.

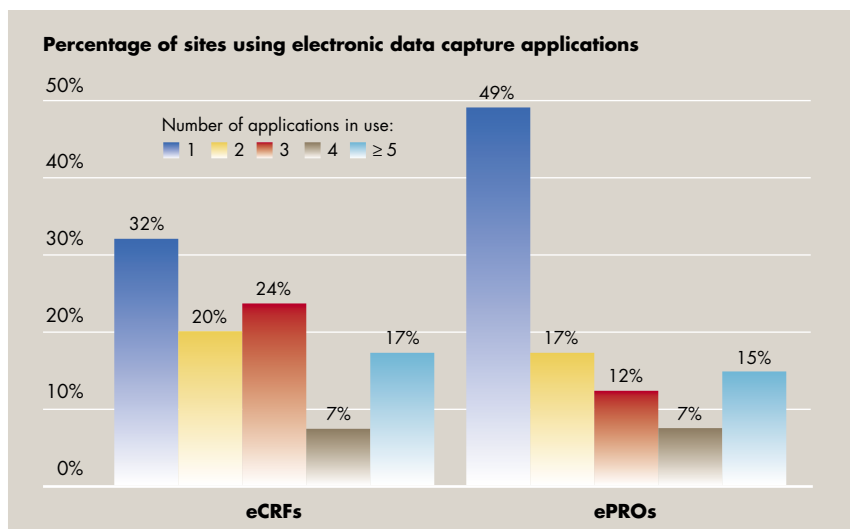
Methods to leverage data entered once for multiple purposes are key to improving the efficiency of conducting clinical trials.

Collaboration in the development of open standards and adoption of these standards by the industry will result in the most valuable global industry standards, for the benefit of all—and especially our patients.

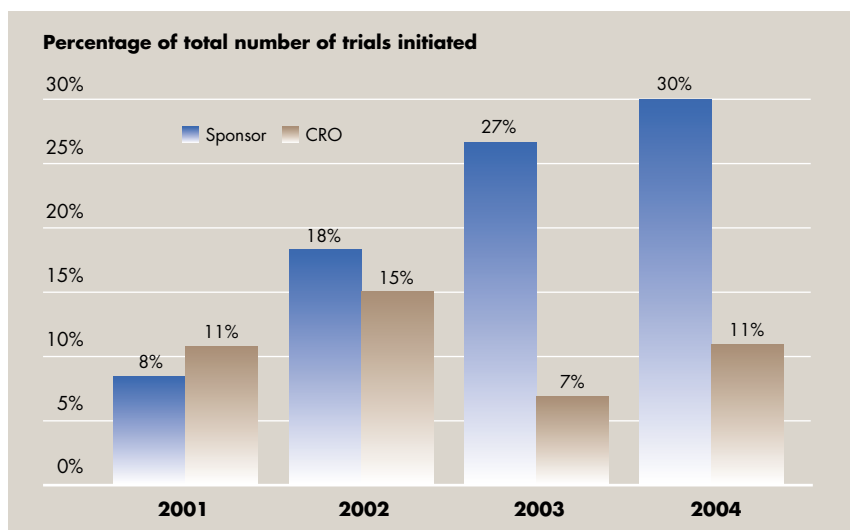
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**FIGURE 1** Percentages of sites using one, two, three, four, or five or more electronic data capture applications at investigative sites. eCRFs = electronic case report forms; ePROs = electronic patient-reported outcome tools, such as eDiaries.



**FIGURE 2** Percentages of overall trials conducted by sponsors and contract research organizations (CROs) using electronic data capture (electronic case report forms or electronic patient-reported outcomes tools, such as eDiaries) from 2001 through 2004.

of three disparate tools for clinical trial data collection at any given time, and this number can reach as high as 10–12 tools per site (Figure 1).<sup>2,3</sup>

Although the solutions currently available for electronic data capture in clinical trials are not yet optimal, they do allow for more rapid access to the data when compared with paper-based processes. Furthermore, they encourage error resolution at the point of data entry, which is more cost

effective than error resolution downstream. Unfortunately, even by the end of 2004, over 60% of trials were still conducted using paper-based processes (Figure 2).<sup>3</sup> A new survey is underway in conjunction with the Tufts University Center for Drug Development to assess the adoption of electronic data capture in 2007.

If we are to improve the availability of information and the effectiveness of clinical research to assess pa-

tient safety and therapeutic efficacy, ready electronic exchange of information among different systems and organizations is essential. Patients are at the core of this effort—and we are all patients.

**Potential to improve the current situation**

Three key opportunities are emerging to improve the current clinical research situation by moving from clinical trials using electronic data capture as a point solution to “eClinical” trials. An eClinical trial is defined as “a study in which primarily electronic processes are used to plan, collect (acquire), access, exchange, and archive data required for conduct, management, analysis, and reporting of the trial.”<sup>4</sup> These opportunities include increasing support for and awareness of the value of health information technology; global, vendor-neutral data interchange standards for the clinical research industry; and methods to leverage data entered once for multiple purposes. Each of these changes is explored in more depth in the following paragraphs.

*Health information technology* is coming—on a global basis. Countries around the world have initiated projects to encourage the implementation of electronic health records in physicians’ offices and hospitals. According to the Medical Records Institute,<sup>5</sup> the top factors driving the need for electronic health records (EHRs) in medical practices include the following:

- Efficiency and convenience to physicians (81.7%);
- Savings and increased revenue (60.0%);
- Satisfaction of patients and physicians (52.6%);
- Need to survive and thrive in a much more competitive, interconnected world (44.4%);
- Value-based purchasing/pay for performance (33%).

While EHR systems are being integrated into society, it is now time to include support for regulated clinical

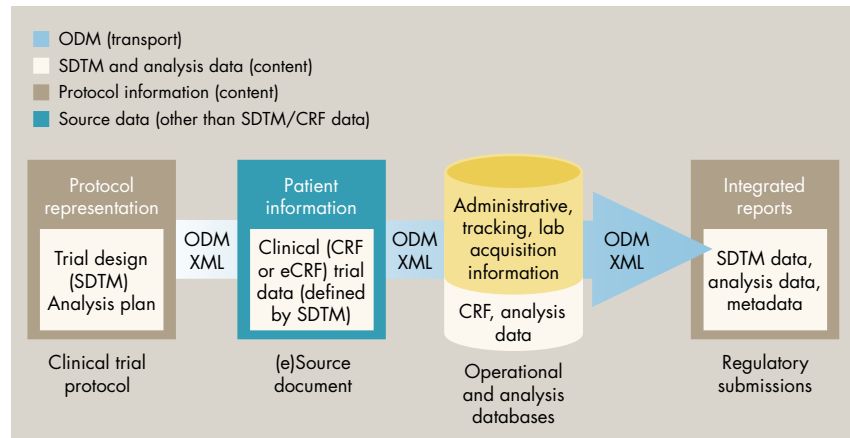
research. It will be much more difficult to incorporate support for this important area once these record systems are in place.

*Global, vendor-neutral data interchange standards for the clinical research industry* are available and ready to use today. There is a clear opportunity to leverage these standards now. The non-profit Clinical Data Interchange Standards Consortium (CDISC), through a consensus-based process and the efforts of numerous volunteers, has established standards to support the acquisition, exchange, submission, and archiving of electronic clinical trial data.

The CDISC Study Data Tabulation Model (SDTM) has been acknowledged by the US Food and Drug Administration (FDA) to facilitate regulatory reviews of submissions for approval of new drugs for marketing. The SDTM is also proving its value for clinical trial reporting and integrating data from various trials into data warehouses, regardless of whether they are used to support regulatory submissions.

The CDISC Operational Data Model (ODM) is a data-interchange standard that is being implemented by companies providing global services, including a number of electronic data capture vendors and contract research organizations in the United States and Europe. Service and technology providers are beginning to bring the reporting standards of the SDTM upstream to define the way data are collected; the data can then be transported by the ODM standard, which can automatically generate electronic data collection forms.

In addition, the ODM supports a complete electronic audit trail and provides an efficient means of archiving electronic data in a standard format for ready review (Figure 3). Through a project named Clinical Data Acquisition Standards Harmonization (CDASH, described in the following sections), CDISC is currently leading the development of data collection standards for CRFs.



**FIGURE 3** Data flow using the CDISC Study Data Tabulation Model (SDTM). ODM = operational data model; XML = extensible markup language, a standard for exchanging data electronically; CRF = case report form; eCRF = electronic CRF.

Having production standards for clinical trial data interchange in place allowed CDISC to expand its scope and explore how best to develop a link with healthcare data standards. The CDISC mission thus became “to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare.”

*Methods to leverage data entered once for multiple purposes* are key to improving the efficiency of conducting clinical trials at investigative sites. Such methods can also help to improve quality by eliminating transcription or data re-entry steps. There are certainly issues to be addressed in doing this type of clinical research, not the least of which are regulations; however, recognizable progress has occurred in this direction, as noted in the next section.

As clinical trials require more and more investigators and subjects, it is crucial to consider how to facilitate the participation of the investigative site in research. Entering data once for use in medical records and clinical research, applying more standard means of entering such data, and using one system (the EHR) versus many point solutions are a few of the key goals that form the basis for many of the current CDISC initiatives.

## Progress and ongoing initiatives

A number of current projects are making strides toward achieving the CDISC mission and, in turn, streamlining clinical trials in the context of healthcare. Many of them are collaborative projects. All involve invaluable contributions from CDISC supporters and volunteers. These initiatives include, but are not limited to, the Biomedical Research Integrated Domain Group (BRIDG) model and harmonization between CDISC and Health Level Seven (HL7) standards<sup>6</sup>; analysis of requirements for eSource data collection and the CDASH project for data collection standards; and standard integration profiles for using EHR systems in research activities, such as data collection for clinical trials, safety reporting, and biosurveillance.

CDISC has had a formal relationship with HL7 since 2001. A key goal centers on harmonization of the standards for healthcare and clinical research. This goal prompted CDISC to initiate the development of a domain analysis model, in the clinical research domain, following the HL7 Development Framework. This model became a joint project under the leadership and support of CDISC, HL7, the FDA, and the National

Cancer Institute (NCI). The BRIDG model that is now connecting standards, organizations, and healthcare with research.<sup>7</sup> Although still in development, collaboratively, this model is currently serving as a basis for development of tools and applications that will allow for interoperability with other tools or applications for exchanging healthcare information and clinical research data.

Another CDISC project was encouraged by the FDA because of its interest in broadening the use of technology for clinical trials. The project is called eSource Data Interchange (eSDI); its purpose is “to facilitate the use of electronic technology in the context of existing regulations for the collection of eSource data in clinical trials for regulatory submission by leveraging the power of the CDISC standards, in particular the ODM.” The eSDI group comprises multidisciplinary representation from the industry (including academic centers) with five FDA liaisons.

The product of the eSDI project, a document entitled “Leveraging the CDISC Standards to Facilitate the Use of Electronic Source Data Within Clinical Trials,” went through seven reviews and comment periods. It is now posted on the CDISC website along with an analogous document developed by the Pharmaceutical Research and Manufacturers of America (PhRMA) and the eClinical Forum. The eSDI document includes an analysis of clinical research regulations in the United States and Europe, a set of 12 requirements to follow in implementing eSource systems (ie, those that capture data electronically initially, without paper) for regulated clinical research, five scenarios as examples (three of which are based on EHRs as the eSource application); an Appendix on Responsibilities of each of the various functional groups conducting clinical research; a template for evaluating an eSource data-collection process against the requirements; and a Good

Practices Checklist for Investigators.<sup>8</sup>

A related CDISC project is leading the development of CRF standards. This project is one of the FDA’s Critical Path Initiative Opportunities. It was initiated in 2005 by the Association of Clinical Research Organizations (ACRO), after which the CDISC was requested to take the lead as a standards development organization with a proven process and existing standards that can be leveraged. This is now a collaborative project seeking participation from site personnel and anyone involved in data collection for clinical research.

A fourth CDISC project began with a proof-of-concept called Single Source. Conducted in 2004, this project actually formed the basis of one of the scenarios in the eSDI document. It was an industry-sponsored initiative that successfully demonstrated clinical information inter-operability between physician-managed clinical systems (eg, EHRs) and pharmaceutical clinical trials systems (eg, electronic data capture) based on open standards. An important aspect of this project was that data were collected once for use in both the EHR (HL7 standards) and clinical trials system (CDISC standards) to streamline workflow at the investigative site. Single Source creates one “source record” for medical data collection regardless of purpose (ie, patient care or research).

This project opened the door for semantic interoperability between healthcare and biomedical research. Single Source has now become the basis for an integration profile developed by the CDISC through Integrating the Healthcare Enterprise (IHE). This integration profile is a vendor-neutral standard that will allow for four usage scenarios that can be supported through an EHR system:

- Investigational new drug trials (EHRs linked to electronic data capture for clinical research), including laboratory and imaging information;
- Biosurveillance (EHRs linked to

local and national bio-surveillance systems);

- Pharmacovigilance (EHRs linked to adverse event reporting); and
- Registry (EHRs linked to clinical trial registries).

### Collaborations with other organizations

CDISC has been collaborating with a number of organizations in this work, including the FDA, HL7, and the NCI on BRIDG. There are also several other areas of CDISC collaboration with NCI and its cancer biomedical informatics grid program, including terminology to support the SDTM (which has been mapped to and is housed by the NCI’s Enterprise Vocabulary Services [EVS] and Cancer Data Standards Repository [caDSR]); implementation of the FDA’s cross-trial database as a cross-trial warehouse for SDTM data submitted to the FDA; protocol representation standards for a machine-readable protocol; and the CDASH project, for which a collaborative group of 16 organizations provides strategic input and addresses resource needs.<sup>9</sup>

Collaborations and joint development of open standards and open source models are the only way that standards will become real global industry standards (versus proprietary in-house “standards”) that will benefit the entire clinical research industry. When implemented at the initial stages of a clinical research study, the CDISC standards can result in an overall 60% resource savings, with over half of this savings being realized in the start-up stage.<sup>10</sup> Global, industry-wide standards have a potential value to the industry of \$5.8–\$6.6 billion annually,<sup>11</sup> but even more importantly they can help us to more efficiently and effectively assess the safety and efficacy of new therapies to the benefit of all—a priceless value.

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### Commentary

# Electronic medical records and standardized data could mean a boost in clinical trials enrollment

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Currently, the pharmaceutical industry is spending billions of dollars on developing promising new drugs and trying to bring them to market quickly. Many of these dollars are spent on recruiting patients into clinical trials and on monitoring data management. The shift from paper data collection to electronic data capture has increased the rapidity of data retrieval, reduced the number of queries to sites, and reduced the need to travel to clinic sites (and the costs entailed) to monitor data. Still, there is only limited success getting physicians and patients involved in clinical trials. According to Gotay,<sup>1</sup> only 1.7% of adult cancer patients participate in studies.

Dr. Kush's article is certainly well timed: Because the clinical research industry faces barriers to recruitment and data management turnaround is slow, the need for a better system is evident. Her manuscript is informative and up-

dates the progress that the Clinical Data Interchange Standards Consortium (CDISC) has made toward standardizing clinical research and electronic medical record (EMR) language.

### Raising awareness

Dr. Kush accurately describes the positive outcomes that could result from using this system. She addresses the drain on our resources caused by paper case report forms. Not only does her article have immense value for research, it also raises awareness among investigators and oncologists as to what is in the pipeline for electronic medical records and electronic data capture.

In addition to the CDISC, there are other initiatives in place to merge research with EMRs. FasterCures, a nonprofit organization, focuses on the process of medical research to accelerate discoveries and treatment. Currently this group is focusing on using the National Health Informa-

tion Network, not only as an EMR, but also as a system to support clinical research. Barriers to getting the project underway include the duty to protect privacy and ensure data security while building in the access and flexibility needed to conduct research.<sup>2</sup>

United BioSource (UBC) is already using an oncology EMR. Through a partnership with Varian Medical Systems, UBC has access to oncology patient records collected from cancer clinics across the United States.<sup>3</sup> The system captures information without patient identifiers. Elements of the database include the visit, diagnosis, treatment, and outcome. All this EMR seems to need is a way to flag patients who might be encouraged to join a clinical trial.

### How will it happen?

Although Dr. Kush discusses how CDISC has been working to create models for clinical research data-

base exchanges, there is no mention of how a merge of EMRs and clinical research databases would occur. Various initiatives and concepts seem to be in place, and yet there are no plans or timeframe for carrying out this concept. It appears that the models for interchanging data among research groups are still evolving, continuing to standardize their own language. As Dr. Kush says, as we integrate EMRs into all practices, we should simultaneously include this data interchange standard for clinical research.

There are still a number of steps that must take place. According to the American Medical Association, only 11% of community hospitals have fully implemented EMR systems, while 57% have “partially” implemented systems and 32% have not started.<sup>4</sup> The addition of a clinical research database would need to be seamless to avoid disruption. There

is still the question of whether this standardized research database can, in fact, be melded into the various—and varied—EMRs now available.

Another consideration is fulfilling the requirements of good clinical practice (GCP), especially 21 CFR Part 312.62(b).<sup>5</sup> This section pertains to maintaining adequate case histories and recording all pertinent clinical data trial. Also, capturing data must fall within the GCP and HIPPA privacy regulations of the US Food and Drug Administration. However, if a way can be identified to incorporate a standardized data capture into every EMR in medical practices, this could be a very efficient way to exchange clinical research data globally. Being able to flag all potential research patients for clinical trials in the community setting and streamline data in a more cost-effective, efficient, and progres-

sive manner could change that 1.7% to a more robust number.

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