THE CDISC HEALTHCARE LINK INITIATIVE

Value Proposition

Spontaneous Triggered Adverse Drug Event Reporting (ASTER)

In 2008, a pilot project was launched between CDISC, CRIX, Pfizer, Brigham and Women's Hospital, Partners Healthcare and Harvard Medical School, entitled ASTER, or "ADE (adverse drug events) Spontaneous Triggered Event Reporting." This project sought to enable automated ADE collection through the EHR using CDISC and IHE's Retrieve Form for Data Capture. The application that was developed was a novel concept – it directly downloaded data held in the EHR and allowed direct submission to the FDA, all in the correct format for the electronic reporting of individual case safety reports.[1]

The results were impressive. In the three-month timeframe that the pilot project was in progress, through the efforts of 30 ambulatory care physicians, over 200 reports were sent to the FDA, and it was found that the time to fill out a report was reduced from 34 minutes average to less an 1 minute per patient. 91% of those physicians had not even submitted ADE reports the prior year, and of those 200 reports that were filed, it was found that 20% of these ADEs were deemed serious.

The physicians involved in this study were impressed with the application and results, and 87% thought that ASTER would improve their ability to accurately report ADEs. A majority of these physicians even wanted to receive reports back from the FDA regarding actions taken based upon their sent reports and have the ability to view national data on similar reports. The ASTER project was found to solve problems for ADE reporters, patients and regulators.

HHS ONC Structured Data Capture Initiative

More recently, there are efforts going on around the globe to increase the use of EHRs for research, including the Innovative Medicines Initiative's EHR4CR and several initiatives in Japan, using RFD and CDISC standards. On 23 January 2013, the U.S. Department of Health and Human Services Office for the National Coordinator (ONC) of Health IT launched a new initiative: Structured Data Capture (SDC). This initiative seeks to address the current, limited use of EHR data outside of direct patient care due to "a lack of uniformity in the terminology and definition of data elements across EHRs." This is a first step towards Meaningful Use 3 to achieve a Learning Health System. The HHS/ONC team has specifically stated that CDISC Retrieve Form for Data Capture (RFD), which CDISC developed with Integrating the Healthcare Enterprise (IHE), and CDISC CDASH are to be leveraged to ensure that there is no duplication of efforts. More information about this initiative can be found on the ONC S&I Framework Wiki.[2]

Background and Vision

The CDISC Healthcare Link Initiative is one of the most rapidly developing areas of work being conducted by CDISC. Leveraging standards to improve the methods by which investigative sites can conduct medical research and capture data for clinical research studies is vital for a number of reasons; one very important reason is that clinicians frequently do one research study and no more due to the unwieldy nature of clinical research processes today. The increasing presence of an electronic health record (EHR) at healthcare sites opens new opportunities to integrate the processes of clinical care and clinical research. This will, in turn, expand the capacity for research and increase patient participation.

The overarching goals for CDISC Healthcare Link have been to:

a) Make it easier for physicians to conduct clinical research,
b) Collect data only once in an industry standard format for multiple downstream uses
c) Improve data quality and patient safety

[1] The ASTER Pilot Project: Improving the Reporting of Adverse Events. 2009. http://www.asterstudy.com.

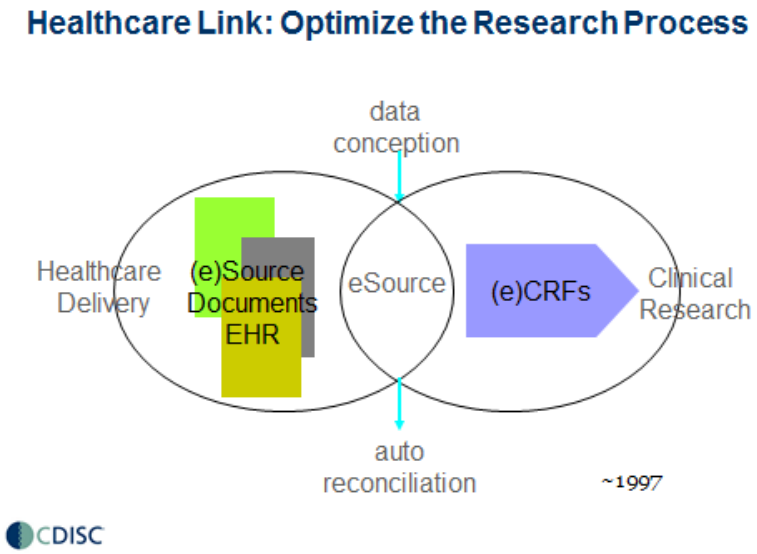
[2] http://wiki.siframework.org/Structured+Data+Capture+Initiative.

Since the CDISC Healthcare Link Initiative was conceived in ~ 1997 and officially launched in 2004, CDISC has developed: a suite of foundational standards (detailed in other chapters), various means to leverage these standards and a series of 'enablers' to improve the workflow of clinicians doing research. The Initiative has taken steps to ensure that the link between clinical research and healthcare takes into account existing regulations, privacy and security concerns, and current practices to provide practical pathways to achieve the vision through a stepwise approach. These enablers were developed in conjunctions with EHR vendors, and respect the limited amount of resource that these vendors can devote to a problem that is secondary to their main concern. These enablers are available now and have already proven to significantly decrease the time and effort to provide data for certain use cases, such as safety reporting, using EHRs.

The Problem Healthcare Link is Solving

Women's Clinic of Lincoln, NE

As can be seen in this photograph, site personnel are often the first to experience the front line difficulties of clinical research. The sheer volume of paper and forms with which they are faced are considerable and often involve painstakingly copying information from one form to another or re-entering medical chart information into a research computer application. With different research study sponsors requiring different methods of data collection and vendors supplying additional capture devices, it is unsurprising that a physician, whose primary concern is to care for patients, should choose not to take on the additional workload. The same data may be re-entered 4-7 times during the course of a study, which increases the opportunity for introducing errors. Until the development of CDASH there were no standard fields for data collection. Each time a site started a new study, the clinician or study coordinator could be faced with a variety of different requirements. So just at that vital point where sites are working for the patients' best interests, they are confronted with a new form that uses different fields and terminology. It would be simpler if the information could be captured electronically from the start, for example from electronic health record (EHR) and/or patient eDiaries. This would also reduce the time (and possibly the need) for hours spent on source data verification (SDV) by monitors or CRAs or field auditors. This was the vision in 1997 (see the picture below).



Whatever the protocol requirements for a research study or the means of collecting the patient data, at least some of it will already be stored in an EHR Clinical research data capture input to a research system. An electronic data capture (EDC) system (with the possible exception of lab data) requires copying and re-entering data from the EHR. One would think, therefore, that re-use of EHR data must be significantly better. However, much of the valuable data in electronic health records is unable to be accessed due to a disconnect between the clinical research and clinical care domains – a disconnect caused by the use of different standards and terminology systems.[3] Reaching the point where research is more closely linked to the workflow of medical professionals is the key driver behind the CDISC Healthcare Link Initiative.

While EHRs are finally being widely adopted in many countries, there are still issues with interoperability between systems and by extension finding a means of capturing data for a study. The EHR was not developed for research purposes; it was developed to ensure better patient care. Similarly, tools that are developed for research purposes are not suitable for patient care. Physicians' methods of recording healthcare information are not necessarily the same as those required for medical research and any system that is installed at a site will necessitate training and support.

CDISC is working toward the moment when the medical research workflow is seamlessly linked with the healthcare workflow. This development will significantly improve the recruitment of physicians who will conduct research and thus patient recruitment within research studies awkward, in turn bringing about more information of a higher quality and, therefore, better patient care. Outlined in this chapter are the exciting developments that have already taken place to realize CDISC Healthcare Link and work towards a Learning Healthcare System.

Existing Standards and Enablers for CDISC Healthcare Link

Well over a decade's worth of work has contributed to a set of standards and enablers to facilitate using EHRs to conduct clinical research (regulated or not). Specifically, these include the following.

- Electronic Source Data Interchange (eSDI) Document
- CDISC Clinical Data Acquisition Standards Harmonization (CDASH) Standard
- Biomedical Research Integrated Domain Group (BRIDG) Model
- Protocol Representation Model
- Interoperability Specifications
- Integration Profiles
- Testing, Demonstrations

[3] Laleci, Gokce, Mustafa Yuksel and Asuman Dogac. "Providing Semantic Interoperability between Clinical Care and Clinical Research Domains."

Each of these is briefly described in the following sections; however, there is far more information available through the links and references provided.

Electronic Source Data Interchange (eSDI) Document

The eSource Data Interchange Initiative began in 2004 when the FDA requested that CDISC assist by forming a team to explore the further use of new technologies for research in the context of the existing regulations (i.e. 21CFR11, Good Clinical Practices and Guidances related to electronic source (eSource) documentation, eSource referring to entering the data electronically initially (i.e. not first on paper). Global regulations were evaluated and analysed and a set of 12 requirements for processes to support eSource and still meet regulatory requirements was developed. The entire document can be found at: http://www.cdisc.org/esdi-document. The eSDI Document includes:

- An extensive review and analysis of the relevant existing regulations
- Twelve requirements for conducting regulated clinical research using eSource data collection in the context of existing regulations
- Five potential scenarios, three of which include the use of electronic health record systems (EHR), and associated benefits of standards
- 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
- A Good Practices Checklist for Investigators

The eSDI initiative provided the foundation and basis for the development of the CDISC IHE Retrieve Form for Data Capture (RFD) integration profile described in a later section in this chapter. The 12 requirements in the CDISC eSDI Document are now referenced in guidance for field auditors in Europe through a document published by the European Medicines Agency (EMA).[4] The FDA is soon to publish their Guidance on eSource that has had multiple comment periods. This work confirmed that it is entirely feasible to use eSource (EHRs, eDiaries, EDC) for research without breaking the existing regulations.

CDISC Clinical Data Acquisition Standards Harmonization (CDASH) Standard

The rationale for developing CDASH came from the FDA's "Critical Path Initiative: Innovation or Stagnation" article.[5] The opportunity was to create innovative and efficient clinical trials by standardizing case report forms. "Differences in case report forms across sponsors and trials creates opportunities for confusion and error." The CDISC CDASH standard can be accessed here.

The development of CDASH was a global collaborative project that resulted in a ***minimal core standard dataset*** that is common across research studies. There were 18 domains core domains (including Medical History (MH), Adverse Events (AE), Concomitant Medication (CM), Demographics (DM), Subject Characteristics (SC), Inclusion/Exclusion (IE), Substance Use (SU), Vital Signs (VS), Disposition (DS), Drug Accountability (DA), Exposure (EX), Protocol Deviations (PD), Comments (CO), Lab (LB), ECG (EG). To these, it is possible to add domains specific to therapeutic areas.

This standard enables standardization of core eCRFs and related edit checks and validation tools, thus making it possible to save significant time in study start-up by simply adding the fields/data elements unique to a given protocol to this core set. In addition, CDASH facilitates downstream production of the Study Data Tabulation Model, which is encouraged (and is expected to be mandated) for regulatory submissions. SDTM and ADaM enable aggregation of data from across multiple research sites and production of tabular data listings and analysis datasets for clinical research reporting and statistical analysis of results.

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[4] "Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials." http://www.phtcorp.com/pdf/EMAReflectionPaper.pdf. - USE EMA website directly

[5] "Innovation or Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products." http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/CriticalPathOpportunitiesReports/ucm077262.htm.

In terms of Healthcare Link, CDASH provides a logical target for an EHR to map to a defined set of research standards. One of the former barriers to using EHRs for research was that each study sponsor expected a unique set of data in a proprietary format, thus CDASH has been instrumental in removing this barrier.

Biomedical Research Integrated Domain Group (BRIDG) Model

The Biomedical Research Integrated Domain Group (BRIDG) Model was developed for two primary reasons: 1) to ensure that all of the CDISC foundational standards are harmonized among each other (in a model that is can be understood by those who are involved in clinical research), and 2) to provide a bridge from research standards to healthcare standards.

In summary, the BRIDG is crucial to the interoperability part of the CDISC mission: *"to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare."*

BRIDG effectively enables information system interoperability by allowing the CDISC standards to work together, as well as ensuring that developers can develop applications that will work with the CDISC standards. BRIDG is a UML model that was developed collaboratively through CDISC, HL7, FDA and NCI. It is openly available at www.bridgmodel.org

Protocol Representation Model (PRM)

The protocol is the PLAN for a clinical research study. It is used by all parties involved in the study. There are certain elements within all protocols that can be standardized and tagged such that they can be re-used downstream (without re-entry) for multiple purposes. These include a) the clinical trial registration (CTR) elements that can be used for clinicaltrials.gov (US), EudraCT (Europe) and WHO International Clinical Trial Registry Platform (ICTRP); b) eligibility criteria; c) study design (study calendar); d) study design (arms, epochs, etc) as a Study Design Model (SDM).

PRM is the core of the BRIDG model and is, therefore, a UML model. However, tools are being produced to facilitate the use of PRM for clinical researchers who do not necessarily need to be IT experts to reap the benefits of this important standard. To learn more about the CDISC Protocol Representation Model and associated Toolset, please visit the CDISC website here.

Interoperability Specification and Transition Options

In 2009, a large group of public and private organizations collaborated through the U.S. HHS HIT Standards Panel activities in the U.S. in developing an interoperability specification for a use case specifically designed to enable the collection of a core set of research data elements from EHRs. The three standards identified through this work were: the Continuity of Care Document (CCD), Retrieve Form for Data Capture (RFD) and CDASH. This Interoperability Specification (IS #158) was ratified in January 2010.

The RFD is described in detail in the section on IHE profiles; briefly, it is a simple yet extremely powerful enabler for CDISC Healthcare Link. The EHR Association endorsement letter of RFD can be found on the CDISC website here.

Using RFD, an EHR can a) provide a set of structured and standardized data to the manager of a remote form; b) support pre-population of a portion of that form, depending on the content within the EHR, and c) allow for additional data to be entered anew to fill the gap between what is in the EHR and what is required for the use case. Research study protocols will, of course, vary depending on the questions being asked to serve the needs of new and innovative research.

Integration Profiles for a More Robust Process

As part of Healthcare Link, CDISC has been working closely with Integrating the Healthcare Enterprise (IHE), to develop RFD and more recently an entire set of integration profiles to support the realization of the Healthcare Link goals.

"IHE is an initiative by healthcare professionals and industry to improve the way computer systems in healthcare share *information. IHE promotes the coordinates use of established standards such as DICOM and HL7 to address specific clinical need in support of optimal patient care. Systems developed in accordance with IHE communicate with one another better, are easier to implement, and enable care providers to use information more effectively."*[6]

While IHE is not a typical standards organization, it takes a problem-focused approach, using existing standards, and integrating them into a targeted specification called an Integration Profile. These profiles are extensively tested and demonstrated before their release.

IHE has a number of domains, foremost of which, from the Healthcare Link perspective, is the Quality, Research, and Public Health (QRPH) domain. This domain focuses on the re-use of EHR data for external purposes. QRPH has developed a set of content profiles geared to research use of EHRs. These content profiles combine with more general-purpose transaction profiles from the Information Technology Infrastructure (ITI) domain to produce a comprehensive approach to the use of EHRs for clinical research.

CDISC Healthcare Link Profiles	**Description**
Core Profiles	
CDISC/IHE Retrieve Form for Data Capture	Retrieve Form for Data Capture provides a method for gathering data within a user's current application to meet the requirements of an external system. RFD supports the retrieval of forms from a form source, display and completion of a form, and return of instance data from the display application to the source application.
CDISC/IHE Clinical Research Document	The Clinical Research Document Profile (CRD) describes the content and format to be used within the Retrieve Form Request described within the RFD Integration Profile and an additional Archive CRD Data transaction. The purpose of this profile is to support a standard set of pre-population workflow data in which the Form Filler provides for use in Clinical Research.
CDISC/IHE Drug Safety Content Profile	The Drug Safety Content Profile (DSC) describes the content and format to be used within the pre-population data transaction described within the RFD Integration Profile. The purpose of this profile is to support a standard set of data in the Continuity of Care Document (CCD) format that the Form Filler provides for use in reporting adverse events as it relates to drug safety.
Supplemental Profiles	
CDISC/IHE Redaction Services	The Redaction Services Profile (RSP) provides a method for redacting data from a document within a user's current application to meet the requirements of an external system in preparation for exporting the redacted document to the external system. RSP supports the redaction of a document according to an extraction specification provided by the external system.
CDISC/IHE Retrieve Protocol for Execution	The Retrieve Protocol for Execution Profile (RPE) provides an automated mechanism for an EHR to retrieve a complex set of clinical research instructions (Protocol Definition) from an Electronic Data Capture (EDC) system to execute within an EHR.
CDISC/IHE Clinical Research Process Content	The CRPC is to specify content, which is appropriate to help automate the sharing of information among systems during the clinical research process. Using the transactions from the RPE profile, the proposed content profiles will improve the recruitment for, setup and performance of clinical trials.
Security Profiles	
CDISC/IHE Consistent Time	The Consistent Time Integration Profile (CT) provides a means to ensure that the system clocks and time stamps of the many computers in a network are well synchronized. This profile specifies synchronization with a median error less than 1 second. This is sufficient for most purposes.
CDISC/IHE Cross Enterprise User Assertion	Cross-Enterprise User Assertion Profile (XUA) provides a means to communicate claims about the identity of an authenticated principal in transactions that cross enterprise boundaries. To provide accountability in these cross-enterprise transactions there is a need to identify the requesting principal in a way that enables the receiver to make access decisions and generate the proper audit entries. The XUA Profile supports enterprises that have chosen to have their own user directory with their own unique method of authenticating the users, as well as others that may have chosen to use a third party to perform the authentication
CDISC/IHE Audit Trail Node Authentication	The Audit Trail and Node Authentication (ATNA) Integration Profile establishes security measures which, together with the Security Policy and Procedures, provide patient information confidentiality, data integrity and user accountability.

[6] IHE Website: http://www.ihe.net.

IHE profiles are built upon core standards from CDISC and other standards development organizations. The profile development process begins with the identification of a use case, and proceeds through a yearlong process of development and refinement followed by another six months of testing and demonstration. For Healthcare Link, the initial use case was the population of an electronic case report form using data and workflow from an EHR. The first Healthcare Link profile to go through this process was Retrieve Form for Data Capture (RFD). RFD is an ITI domain profile within IHE.

As with Electronic Source Data Interchange (eSDI) and BRIDG, the aim of the Retrieve Form for Data Capture (RFD) profile is to share data between healthcare and clinical research. Physicians or site investigators often repeat the same data entry into the EHR and case reporting form (CRF) for research purposes. Clearly this break in physicians' workflow is a barrier to their working with medical research. RFD is the first step towards harnessing vital data needed for research out of an EHR and transferring this data automatically into the CRF, which the investigator can then confirm is correct for the research study. RFD, combined with the first of the QRPH content profiles, Clinical Research Document (CRD) offers a real world solution that can be implemented now. While it may not be perfect, or a *total* solution, it is a practical resolution to the tricky problem of semantic interoperability between EHRs and research systems RFD is the result of collaboration between technicians from healthcare and clinical research that have considered the challenges associated with integrating cross-industry workflow, and therefore provides significant opportunity for process improvement.

RFD was created using the criteria as stated and supported by the eSDI document. Bringing the investigator workflow and the research workflow together has implications for where the source will lie. This approach allows enough separation for EHRs to be minimally impacted, enabling the physician continued ease of workflow and also avoiding the scenario where the EHR (in and of itself) has to become 21 CFR Part 11 compliant. Rather, the process itself meets 21CFR11 and eSource regulatory requirements and, included in the process is an eArchive step at the site (thus ensuring that the investigator retains an important electronic record of the research results at the site). By collecting data at a single source, this being the point of care EHR system, physicians and staff need not re-enter data into specialized research and surveillance applications. Avoiding this redundant data entry reduces data errors and saves the care provider's valuable time while allowing key data to be reported in a timely and accurate manner.

CRD creates a data export process within an EHR session by importing a CRF from the appropriate clinical research system (Forms Manager) while exporting a pre-population dataset. The content of the CRF, defined as a set of CDASH data elements, can receive data elements from the EHR that are defined by the HL7 export specification Continuity of Care Document (CCD). CRD provides a minimal set of medical research data to collect from an eSource application (EHR). In other words, RFD and CRD allow the CRF or other form to gather key data directly from the EHR, thereby avoiding the redundant data entry that is so prevalent in many current systems. RFD also combines with another QRPH content profile, Drug Safety Content (DSC), to enable similar form completion for safety reporting.

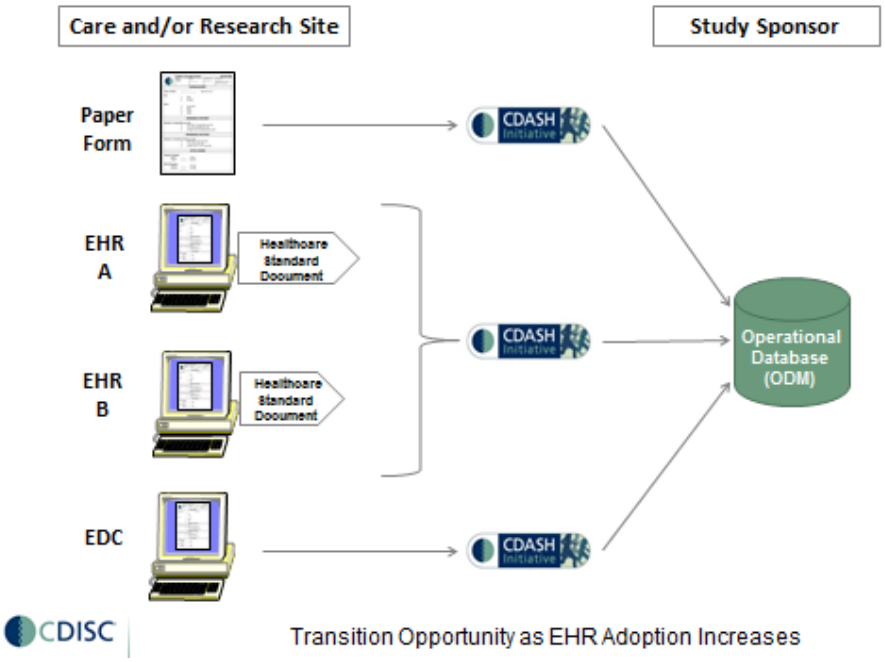
Using the CDASH standard means that a sponsor can easily use SDTM to create tabulations for raw, clean data from various sites, ensuring that there is a seamless flow of data from healthcare to a regulatory submission, if that is the end product. There are many benefits to the RFD process, including greater accuracy, reducing the time required by the care provider to complete mundane tasks, and real time responses of the physician being added to the research data.

There is also a new integration profile that expands the scope and power of the Healthcare Link processes - Retrieve Process for Execution (RPE). This new profile leverages CDISC's Protocol Representation Model and the Study Design Model and could therefore define the workflow integration between an eClinical and EHR system at the start of the clinical research process. Like RFD, RPE is a transaction profile that defines the actors and transactions required to automate cross-industry business processes. And like RFD, RPE requires content specifications to meet its full potential. The content profile that extends the use of RPE is Clinical Research Process Content (CRPD), which uses the CDISC Study Design Model to define the research processes that an EHR can ingest and execute. RPE and CRPC are in the trial implementation phase of development, but despite their newness, early adopters will find much value in their use today.

At some point it became evident that the healthcare link set of profiles required a more rigorous security framework. Fortunately, IHE's infrastructure group had a set of security profiles ready to fill the bill. These profiles, Consistent Time, Cross-enterprise User Assertion, and Audit Trail and Node Authentication, have now been grouped with CRD to provide greater security.

Testing, Demonstrations and Implementations

The power of RFD includes the opportunity for researchers to engage sites that are using a variety of EHRs (and even those that have not yet adopted EHRs). (See the figure below.) One study could be using EHR "A," another using EHR "B," and yet others may not yet be using EHRs but rather EDC or paper. This allows for a transition period that should be anticipated as adoption and evolution of EHRs within the healthcare realm increases. We can also appreciate the need for different but complementary standards in clinical care and clinical research and focus on the Healthcare Link that bridges these two worlds. Of course, the ultimate goal is for all sites to have EHRs and for EHRs and research systems to be largely interoperable. However, the current methods and profiles are available to realize a significant improvement even today. (See the following section on available Integration Profiles.)



A long list of EHR vendors, EDC vendors, CROs and others have tested Healthcare Link at IHE connectathons and have demonstrated the utility of CDISC Healthcare Link at trade shows and professional meetings over the past decade. One of the first proof-of-concept tests was done at Duke; this was a successful collaborative industry pilot based upon open standards, demonstrating that the EHR could be used to access a remotely managed form, prepopulate areas of this form, collect additional data and provide this from one entry source to multiple users (healthcare and research).[7] The methodology was significantly simplified after this and the profiles, standards and opportunities described above have now been implemented for actual use cases, including the reporting of H1N1 virus outbreaks by the U.S. Centers for Disease Control, Phase IV studies and for spontaneous adverse event (safety) reporting.[8][9]

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[7] Kush, Rebecca, PhD, Liora Alschuler, Roberto Ruggeri, Sally Cassells, Nitin Gupta, Landen Bain, Karen Claise, RN, Monica Shah, MD, and Meredith Nahm. "Implementing Single Source: The STARBRITE Proof-of-Concept Study." *Journal of the American Medical Informatics Association* 14 (2007): 662-73. Print.

[8] Linder, Jeffrey A., Jennifer S. Haas, Aarthi Iyer, Michael A. Labuzetta, Michael Ibara, Michael Celeste, George Getty, and David W. Bates. "Secondary Use of Electronic Health Record Data: Spontaneous Triggered Adverse Drug Event Reporting." *Pharmacoepidemiology and Drug Safety* 19.12 (2010): 1211-215. Print.

[9] Dal Pan, Gerald J. "Commentary on "Secondary Use of Electronic Health Record Data: Spontaneous Triggered Adverse Drug Event Reporting" by Linder Et Al." *Pharmacoepidemiology and Drug Safety* 19 (2010): 1216-217. Print.

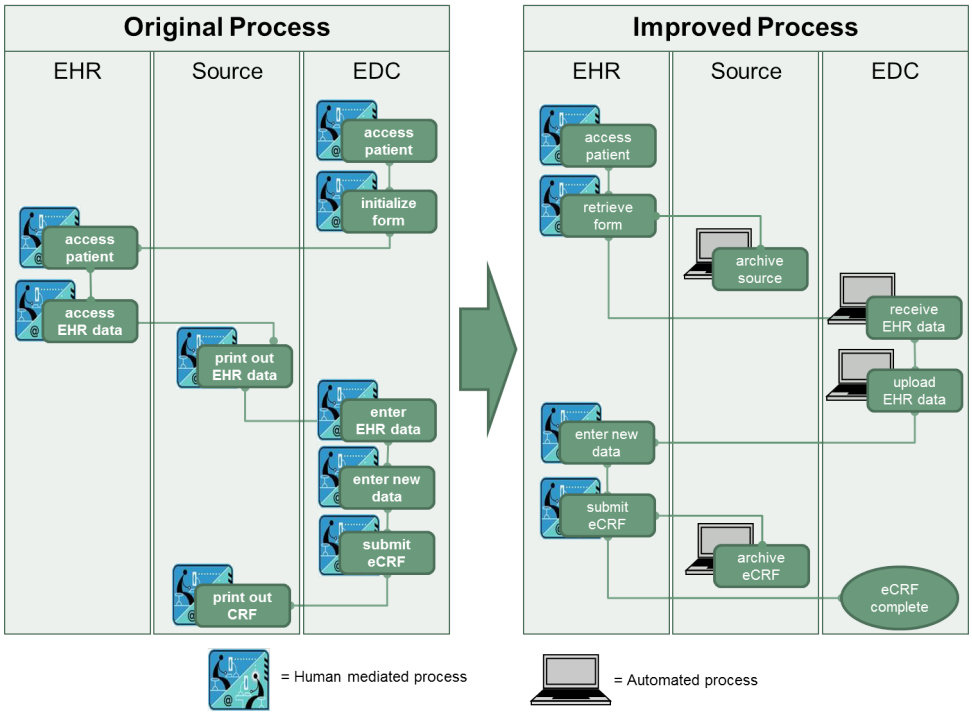
A proposed Learning Health System (LHS) would accelerate the means by which clinical research is conducted and subsequently informs clinical care decisions, thus facilitating the information flow to improve healthcare decisions by clinicians and by patients themselves.[10][11] Achieving this vision would translate to more cost-effective and efficient processes that would improve the quality of care and speed safe and effective therapies to patients.

Further opportunities are awaiting those who do not fear change and relish a viable means to truly transform the way that clinical research is conducted. Expanding the available pool of researchers and patients by making it easier to conduct research such that we can more readily gain additional knowledge from patient care will benefit patients – and we are all patients.

Impact of Healthcare Link on Investigative Sites, Monitors and Auditors

Healthcare Link promises to simplify research processes at healthcare sites while improving the quality and usability of data. In addition, it has the potential to significantly decrease the time and effort required for source data verification and auditing at investigative sites.

The figure below illustrates the improvement (automation opportunity) in completing a case report form.



Note that the number of human processes is reduced from 9 to 4, and that all of the remaining human processes take place within one system, the EHR.

Even greater simplification results from the creation of an electronic source document, which are defined by the two core healthcare link profiles RFD and CRD. The onsite storage of archived electronic source documents from the EHR, along with electronic copies of the completed case report form as submitted to the research system, opens the possibility of monitoring or auditing from afar. If monitors no longer have to perform routine source document verification at the sites, there would be significant cost savings to the processes of clinical study execution.

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[10] Friedman, Charles P., Adam K. Wong, and David Blumenthal. "Achieving a Nationwide Learning Health System." *Science Translational Medicine* 2.57 (2010): 1-3. Print.

[11] Kush, Rebecca D., PhD. "What the Patient Should Order." *Science Translational Medicine* 1.3 (2009): 1-5. Print.

Healthcare Link continues to expand its scope and depth through additional profile development. Research Matching extends the process automation to the matching of prospective subjects to appropriate research studies using patient context and a clinical study database. And Data Element Exchange brings Healthcare Link to the use of semantic web solutions by leveraging semantic metadata registries such as CDISC's SHARE to more uniquely match research and healthcare at the common data element level. This profile promises to fundamental change the pre-population step first addressed by simple XML transfers.