Lessons learned along the journey to merge electronic platforms in clinical research and health care.

In April 2009, President Barack Obama announced an initiative to create a new electronic health record (EHR) system that would transfer data held by the Department of Defense (DOD) to the Department of Veteran Affairs (DVA). Clearly frustrated by the lack of standards and differing medical systems within the two departments, President Obama tasked DOD and DVA with creating the Joint Virtual Lifetime Record that could serve as a model for a national EHR system.

President Obama followed up this initiative with one tied to the American Recovery and Reinvestment Act (ARRA): Hospitals and physicians who demonstrate “meaningful use” of certified electronic health records will qualify for incentive payments through Medicaid and Medicare starting in 2011. Estimated pay-outs through 2016 are as much as $45 billion.

The federal government’s spotlight on EHR has had a galvanizing effect on both the health care and pharmaceutical R&D industries. Historically within the health care setting, keeping patient records has been a manual, laborious, paper-based process. Most records have been “physical” media such as film (x-rays), paper (notes) or photographs—making the storage and sharing of these records problematic. EHR, or an individual patient’s medical health record in a digital format, was developed to streamline the storage and retrieval of these records.

Marked progress
The federal government’s push for EHR adoption has had a ripple effect in the pharmaceutical industry. With the Obama administration’s keen interest in reducing drug costs as part of an overall plan for affordable health care, additional pressure has been placed on drug developers and manufacturers to find ways to both reduce costs and accelerate the time to market for new therapeutics. One significant step toward alleviating some of this pressure has been the integration of R&D and electronic data capture (EDC), which is currently used in more than 40% of all trials.

Not surprisingly, the increasing adoption of EHR within...
health care organizations has accelerated the industry’s interest in finding a single system that could simultaneously be used for patient care in both the hospital/clinic and clinical trial settings. Since the collection methodologies are similar, the conventional thinking is that a platform that merges EHR principles with the functionality of EDC would improve efficiency, eliminate data transcription errors, and ultimately help speed new drugs to market.

“Widespread adoption and availability of electronic health information has the potential to create additional opportunities for physicians and other care providers in clinical research as well as in population health improvement,” observed Judy Hanover, a research analyst with IDC Health Insights. “The EDC applications used in clinical trials perform many of the same functions as EHRs, and capture similar point-of-care patient information, albeit for restricted use during clinical trials. Leveraging parallel data capture activities in health care and clinical trials as EHR adoption becomes widespread has the potential to drive efficiencies in both areas and create financial opportunities for providers as well as patients.”

Everyone involved in research stands to gain from EHR–EDC integration. Having a single user interface that could populate common data into both sides of the equation—including 21 CFR Part 11 validated systems—would tremendously streamline workloads. Physicians would be able to provide a better continuum of care for patients by having direct access to clinical trials inclusion criteria, allowing them to identify and enroll applicable patients into active studies without significant data entry. Similarly, the benefit to patients would be increased opportunities to participate in leading research. For life sciences companies, for example, EHR–EDC integration means quicker study starts through easier access to larger pools of available candidates and faster enrollments.

**Mutual respect**

But there are some hurdles that need to be overcome before electronic platforms in use within the health care setting and those in use within clinical trials can be merged. Health care and pharmaceutical industries have separate regulatory requirements in place that must be followed to ensure systems are validated and controlled. These regulations protect the integrity of the data within these systems, as well as the privacy rights of patients. Integration of EHR and EDC systems requires that both systems adhere to the applicable regulations from each industry.

In order for the merger of the two to be successful, both the EHR system and EDC system must completely understand and respect the requirements and priorities of the other to ensure that the data meets all regulations, particularly in situations where applicable data may exist between the two systems. For health care, patient privacy is paramount and patient data that has been entered into the EHR system is subject to the health care industry’s rules, such as the Health Insurance Portability and Accountability Act (HIPAA) related to patient privacy and security. For clinical research, data integrity is key and systems for the electronic collection of data are subject to a number of federal regulations and guidances, such as Title 21 of the Code of Federal Regulations (CFR) Part 11 related to data integrity, validation, and security.

During EDC–EHR integration, processes and technologies must be in place to protect patient privacy and ensure data integrity. This is accomplished by strict control on data that is sent from the EHR system through an SSL-encrypted connection (Secure Sockets Layer) to the EDC system. The EDC system then provides an encapsulated response that the EHR system can surface within its own interface, all the while maintaining the validated processes and components of the EDC system.

Currently, the health care and pharmaceutical industries are working on joint recommendations that would help the federal government harmonize regulatory requirements. Both parties are working internally to define how the chain of custody is controlled and at what point each system's rules should affect a joint solution, as well as any additional auditing and validation transactions needed to ensure the data can be verified and audited at any stage of the process. The health care and pharmaceutical industries are already united, however, in their dedication to maintaining patient privacy throughout the entire data exchange process.

**Leading the way**

As background, on the pharmaceutical side, the Clinical Data Interchange Standards Consortium (CDISC) has worked toward developing standards to support the electronic acquisition, exchange, submission, and archiving of clinical trials data and metadata for medical and biopharmaceutical product development. CDISC is known for developing standards such as Clinical Data Acquisition Standards Harmonization (CDASH), which focuses on streamlining data collection in a way that promotes improved data interoperability throughout the biomedical research and product development processes, and enhances the interface with health care and EHR.

In health care, Integrating the Healthcare Enterprise (IHE) is an organization driven by health care professionals and the industry to improve the way computer systems share information. IHE played a key role in building upon the Continuity of Care Document (CCD) to develop the Clinical Research Document (CRD), an XML-based markup standard intended to specify the encoding, structure, and semantics of a patient summary (including patient demographics, medications, and allergies) for seamless
exchange between disparate health care systems. In creating the CRD, IHE used standards proposed by the CDASH initiative that were based on the structures certified EHRs must comply with.

Together, IHE and CDISC have supported the development of standards that allow an EDC data entry screen to be displayed within the EHR system and be prepopulated with routine patient information (i.e., demographics and patient histories) from the EHR. One outcome of this has been IHE’s Retrieve Form for Data Capture (RFD), an integration profile that addresses the problem of integrated data capture for patient care and clinical research. This has been particularly essential in integration efforts because RFD enables EHR applications to directly request study-specific forms for clinical trials and public health reporting.

Using this technology to mine EHRs within medical and health care facilities, pharmaceutical R&D teams could potentially shorten the timeline and cost for initiating new studies by creating access to an enormous pool of potential participants. This would also reduce the need for source data verification and in some cases allow for electronic or automated source verification, lowering costs associated with study monitor visits.

“There are also benefits to utilizing RFD in the health care industry, in particular, for clinicians who are interested in doing research but are concerned about the administrative burden,” noted Rebecca Kush, CDISC President and Chief Executive Officer. “Two clear benefits are the reduction in time for data entry and increased data accuracy. By collecting patient data at a single source—the point of care EHR system—physicians and staff need not re-enter data into specialized research and surveillance systems. Avoiding this redundancy and transcription step reduces data errors and saves the care provider’s valuable time.”

Kush added that another benefit of using the RFD with CRD is that it allows for adherence to 21 CFR 11 without the necessity of validating the entire EHR system, which can be nearly impossible (the eSDI document for requirements is found at www.cdisc.org/esdi-document). “The beauty of this new standards-based process is that workflow for clinical research is integrated into the clinical care workflow,” she explained. “With this facilitated workflow comes also an accelerated and streamlined process of sharing records across multiple locations/sources. Last, but far from least, the benefits to patients will be increased opportunities to participate in research that may find new therapies for their diseases.”

Pilot project
In October and November 2009, clinical research software and services company Nextrials, Inc., and Greenway Medical Technologies Inc., a supplier of an EHR health care business solution, initiated a multisite retrospective study on the use of birth control method for the treatment of dysfunctional uterine bleeding known as “The NextGreen Pilot Project” in hopes of successfully mapping data from Greenway’s PrimeSuite EHR system into Nextrials’ Prism EDC system.

Both early proponents of EDC–EHR integration, the two companies had already integrated RFD into their respective software prior to the start of the pilot project. In fact, before partnering with Nextrials, Greenway had previously worked with Outcome Sciences to produce a commercial implementation of the common RFD technical specification. During this early demonstration, Outcome’s system provided a direct, standards-based link for a registry study with Greenway’s PrimeSuite EHR.

However, the NextGreen Pilot Project was the first time outside of staged, high-profile interoperability demonstrations where multiple sites were able to enroll in real time and collect live patient data through a single interface. This pilot project overcame two major problems long noted by industry leaders: duplicate data entry and workflow issues, which have been traditionally associated with disparate EDC and EHR systems.

“We wanted to definitively prove whether or not EDC–EHR integration would give sponsor companies more accurate and up-to-date patient information and encourage more research within the health care arena,” noted Jason Colquitt, Director of Research and Outcomes for Greenway Medical Technologies. “We knew that many of our PrimeResearch site network had avoided research scenarios in the past due to resource demands. With the NextGreen Pilot Project, we hoped to validate our belief that an integrated EDC–EHR platform for a study was not only possible but more efficient in order to support RFD’s use in future studies.”

First hand experience
The retrospective NextGreen Pilot Project posed the following question: What percentage of patients placed on oral contraceptives (any brand) for the treatment of dysfunctional uterine bleeding changed their therapy within the first year of treatment? The study design included two visits: one to enroll the patient, collect demographics, and record the initiation of therapy, and a second to assess the efficacy and safety of the therapy.

During a period of four weeks, four sites across the United States pulled data on 40 patients who were enrolled and whose data was submitted within minutes via electronic Case Report Forms (eCRFs) that were hosted within PrimeSuite. Over 75% of the data required for the pilot was auto-populated from matching data that had already been collected previously as part of the patient’s routine care.

“Initially, the retrospective pilot study experienced a few problems around the mapping of the data from the EHR to the EDC system in a process we call prepopulation,” explained Robert Barr, Chief Technology Officer for Nextri-
als. “This is where the EHR provides the EDC system with relevant data to the eCRF form that is being opened. This allows us to populate the form with existing data so the user is not required to enter it again. We found that the data type collected in an EHR system might not be an exact match to the CRF design; for example, sites may have entered a patient’s birth date, but we needed the patient’s age instead. This required us to look at our prepopulation step and create a derived value option where we can either adjust formatting or choose from multiple source fields to populate a target data point. Since we expect to encounter similar problems with varying data points in future studies, the NextGreen Pilot Project really helped us understand how to add product functionality to make an integrated EDC–EHR platform a viable option for live studies going forward.”

For Greenway, initiating the study meant it programmatically queried its PrimeResearch sites using the inclusion and exclusion criteria to identify sites that had a sufficient number of patients to complete enrollment. After site selection, each site was configured to point to Nextrials RFD-enabled Prism eCRFs. Next, the sites were able to harness the fact that their patient data was electronic and quickly qualified patients flagged as meeting the protocol.

Since one of the goals of the pilot study was to show how health care organizations not normally known for participating in research could easily be integrated into clinical trials, Greenway Medical tapped Birmingham-based OB/GYN Associates of Alabama as one of the pilot’s participating sites.

“We are an average sized, five physician OB/GYN practice that is new to the world of research,” said Stephanie Grooms, study coordinator. “At first we were a little timid, but after we received training and got our feet wet, our outlook changed tremendously. The ease of data capture and the capability to query patients eligible for active studies within our system is amazing.”

Vendor challenges
When the pilot study was completed in November 2009, the challenges for EDC and EHR vendors looking to add integrated function to their products were obvious. On the EDC product side, vendors will need to:

• learn to overcome the differences in EHR systems and compensate for those differences
• resolve connectivity issues in multisite studies, since accessibility will vary
• establish a common methodology for saving data, whether it’s within EHR or EDC
• create interfaces capable of seeing and understanding mismatched data (i.e., birth date or patient age)

Vendors offering EHR technology will have to meet a similar set of challenges on the road to integration, such as:

• determining how to configure different application level security mechanisms across EDC systems
• overcoming the varied ways in which EDC systems define their eCRFs granularity and how that translates to the investigator/coordinators interaction with those CRFs during a study visit
• tapping into the study design to more closely know the order in which to execute the study events
• establishing a standard mechanism to synchronize the status of an eCRF between the EHR and EDC
• educating the clinical research community on the encoding, structure, and semantics found within CRD

While the pharmaceutical R&D industry is still mid-shift toward EHR–EDC integration, the NextGreen Pilot Project has proven its viability. Additionally, the underlying support of the Obama administration has forced the creation of a more holistic approach to the secure and reliable exchange of medical health data by bringing together many different players within the health care/pharmaceutical realms, such as medical imaging, medical hardware and devices, laboratories, accounting, and more. Changes are swiftly occurring; Duke University Medical Systems has already instituted a single source EDC/EHR product within its Clinical Research Information System.

The NextGreen Pilot Study is one more proof point that streamlined data processes can save time, labor, costs, and most importantly potentially give patients broader access to future clinical trials.

References

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