Use of Interactive Response Technology (IRT) vendor-implemented randomization and dosing algorithms is an effective method to reduce the incidence of medication errors in the clinical trial setting. However, errors in the programming of randomization and dosing algorithms remains a risk factor leading to medication errors for subjects on a clinical trial. Hence, vendor oversight is important in reducing risks for subjects participating in clinical trials. Additionally, regulatory agencies have maintained that it is ultimately the sponsor’s responsibility to maintain oversight of IRT vendor’s systems used in their clinical trials. We describe a method for improved monitoring of Interactive Response Technology vendor implemented randomization and dosing systems shortening detection time and reducing impact of system errors. To augment best practice IRT system testing and vendor oversight activities, we have developed a process which enables a sponsor to continuously monitor randomization and dosing algorithms such that the sponsor will become aware of potential IRT-caused dosing discrepancies within 24 hours of first occurrence, limiting the potential for a systematic error to impact a large number of subjects. Implementing this process represents an important step in ensuring subject safety and the validity of clinical trials.

Start time: 5/22/2018 9:15:00 AM
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Reproducibility of results is a hot topic in clinical trials. While the statistical methods and results are generally the focus of such discussions, having the exact data used for the analyses is an integral aspect of reproducibility. During internal discussions concerning reproducibility, the various approaches being implemented in regards to data download, storage and final data creation were concerning. Each statistician had an individual strategy but very little commonality. The inefficient processes being utilized at our institution were increasing the time burden on faculty and staff. In order to facilitate the efficiency of trial maintenance and the reproducibility of results, we developed a strategy to minimize the repetitive steps and harmonize the data creation and storage within the unit.

The plan centers on data collected in OnCore, a commonly used clinical database management system (CDMS) used at many cancer centers in the United States. While OnCore allows for the download of current clinical trial data into SAS, the system is a multi-step process. Since cancer centers can customize OnCore eCRFs to specify explicit data points to be collected for a particular clinical trial, the data download system has to be very general. This generalizability can cause issues within the SAS code provided by OnCore when downloading data from multiple eCRFs. Our strategy begins by highlighting download selections in OnCore, creates a harmonious directory structure and finally incorporates SAS macros and %INCLUDE statements to establish the process. Applied wisely, the current process can circumvent many chaotic situations in data handling, reduce the time necessary to accomplish certain tasks by automation and standardization, eliminate duplicated effort and guarantee a level of quality in our current data reporting.

Although our specific strategy focuses on data downloaded from OnCore, the approach and practices can be generalized to other CDMS. Lessons learned and future directions will be presented. As noted business historian, Alfred D Chandler, Jr, stated, “Unless structure follows strategy, inefficiency results.”
AtRial Cardiopathy and Antithrombotic Drugs In Prevention After Cryptogenic Stroke (ARCADIA) is a multicenter, randomized controlled trial to test the hypothesis that apixaban is superior to aspirin for the prevention of recurrent stroke in patients with cryptogenic ischemic stroke and atrial cardiopathy.

Special challenges for study drug tracking in the ARCADIA trial include: 1) large multicenter trial with 120 sites; 2) slow recruitment with an estimated 4 subjects per site per year; 3) long term follow-up (1.5 - 4 years) with study drug resupply every 3 months of which a mixture of in-person and telephone/mailing visits will be used; 4) adjustable apixaban dose (5 mg vs 2.5 mg) based on bio-characteristics assessed every 3 months; and 5) double-dummy treatment masking with study drug kits containing active apixaban and matching aspirin placebo or active aspirin and matching apixaban placebo.

To ensure that the correct study drug kit is available at the time of randomization and resupply while mitigating study drug waste, a comprehensive study drug tracking module has been developed and integrated into a web-based EDC-CTMS system. This module manages the drug bottle packing, drug kit assembly, drug shipping from the central pharmacy, drug receipt by the site, drug kit assignment to a subject, drug kit dispensing, and drug removal from site inventory due to expiration/damage. The study drug module is integrated with the site management module, subject randomization module, subject study progress module, and Case Report Form data management module, so that study drug requests are automatically posted for the central pharmacy. This design ensures that each site currently released to enroll has the minimal study drug inventory to avoid loss of subjects due to drug unavailability at the time of randomization. It also ensures the correct study drug kit with the correct treatment arm and dose is available for each subject when a resupply drug kit is needed. Barcode scanning technology is used for drug bottle labels, drug kit labels, and bulk drug barrels to augment central pharmacy quality assurance procedures. Likewise, verification codes on the individual drug kits are utilized to ensure the proper drug kit is dispensed to the subject.

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Introduction

The PhenX (consensus Measures for Phenotypes and eXposures) Toolkit is a collection of high-quality standard measures for use in biomedical research that span a number of domains (www.phenxtoolkit.org). One subset of the Toolkit is the Core Tier 1 measures of the Substance Abuse and Addiction (SAA) Collection, which include 19 measures related to the use of alcohol, tobacco and other substances, demographics, body mass index, quality of life and HIV testing history. As a method of standardization of data across clinical trials, the National Drug Abuse Treatment Clinical Trials Network (CTN) of the National Institute on Drug Abuse (NIDA) encourages investigators to incorporate these Core Tier 1 SAA measures into their CTN studies.

Objective

The Emmes Corporation in its role as the Data and Statistics Center (DSC) of the NIDA CTN for the last 8 years is responsible for implementing efficient and standardized data management systems for CTN trials. In order to assist investigators in incorporating Tier 1 measures into their studies, the DSC needed to assess the nuances of the measures and then plan their implementation into an electronic data capture (EDC) system.

Methods

Implementation of these measures in our EDC system required frequent review of the PhenX website, thoughtful conversion of paper Case Report Forms (CRFs) into questions on an eCRF consistent with the network’s existing eCRF style guide, incorporation of complex parenting and skip logic, contacting the PhenX group for clarification and review with investigators to ensure study needs were being met.

Results

PhenX Core Tier-1 measures have been incorporated in 7 CTN studies across 47 sites over the past X years. Of the 19 Core Tier-1 measures, 3 were straightforward to implement across all studies. However, the remaining 16 presented challenges during implementation that included resistance from the investigators in using the standard tools that were considered not optimal to address research questions, ensuring duplicative data were not collected based on other assessments that were integrated into the study, considering mapping from similarly worded questions from other data collection instruments, implementing complex skip logic and creating a clear paper source CRF, and keeping up with frequent changes to the PhenX measures. Specific examples of our interpretation of the measures as specific eCRFs, challenges and methods of resolution will be presented.

Conclusions

Rapid, flexible and consistent implementation of Core Tier-1 measures across multiple NIDA CTN trials accomplishes the PhenX goal of collaborative research and consistent collection of high-quality data in a standardized manner across multiple studies. However, it requires careful planning, testing, review, problem-solving and communication with internal and external stakeholders. Lessons learned here with
the Tier-1 measures can be applied to other PhenX collections, and other instruments that may need to be standardized in a clinical trials network setting. Ultimately, data collected in a standardized format allows for data to be easily understood and combined across multiple studies, leading to more impactful and generalizable conclusions, both for NIDA CTN investigators as well as researchers using these data when they become publically available through NIDA DataShare.

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