Electronic Informed Consent: A New Industry Standard

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Introduction

The past two decades have seen incredible changes in the way we manage clinical research trials. The advent of electronic document management systems (EDMS), electronic data capture (EDC) systems, electronic trial master file (ETMF) systems, and other automated solutions have significantly enhanced access to critical information meant to improve the quality of clinical trial data and provide greater protections to study participants. Until now, the process of obtaining clinical trial participants’ informed consent is one of the only areas of clinical research operations that has remained largely paper-based.

Electronic informed consent, or eConsent as it is commonly referred to, is gaining greater acceptance and adoption as a standard. A recent review of the 2012 top 50 pharmaceutical companies (as ranked by Pharmaceutical Executive Magazine1) indicates that 66% of these companies are engaged in or are planning an eConsent initiative.2 Within the top 25 companies, this number is approximately 88%, and 100% of the top ten companies report they have an eConsent initiative in place for 2013–2014.2 Amongst biotechnology and medical device manufacturing companies, this number is lower, but quickly increasing. The benefits of eConsent are manifold, including advantages to prospective research participants, operational improvements for research sponsors and clinical site administrators, and streamlined oversight for ethical review.

A properly-designed eConsent solution replaces the paper informed consent document with an interactive electronic tablet, such as a native iPad® application, preloaded with the consent form and explanatory materials. Building on years of research on how people learn and more recent research into successful new interventions for improved understanding of the informed consent process, the electronic platform includes multimedia approaches for the presentation of information, and feedback mechanisms to test and reinforce participant comprehension.3 Prospective research participants can still read the text of the informed consent document on the device, but the interactive properties of the platform allow them to access additional explanatory materials. For example, they can click on an unfamiliar term and connect to an on-line dictionary or a study-specific glossary, or mark the concept for further discussion with the research staff. Prospective research participants can view animations with descriptions of tasks, laboratory tests, or actual procedures to be conducted during the study. They can access explanations of unfamiliar concepts and critical details of study participation, such as randomization and blinding. Programming features can assist the site staff with a more comprehensive assessment of an individual’s understanding of the aspects of a study, enabling them to provide any necessary clarification before the participant proceeds with consent for participation.

eConsent and the Ethical Premises of the Consent Process

Informed consent is a process to ensure the voluntary consent of human subjects for clinical research,4 and the process should be ongoing throughout a study. It has
three essential components: 1) information for the participant; 2) face-to-face discussion between the participant and clinical research staff; and 3) ample time for the participant to consider participation or continuation in the study.

A paper informed consent form fulfills just the first requirement by providing a written description of the study. In all cases, it remains incumbent on the clinical research staff to engage prospective participants in discussion about their potential role in the study, and then grant them ample time for reflection before they decide whether to enter the study. It can serve as a vital framework for the face-to-face discussion with staff. Initially, to provide prospective participants time for consideration and the opportunity to view the consent materials for discussion with their families, the system can allow both web-based access to the consent materials from home and the option to print out the information. Built-in, individualized assessments ensure prospective participants’ comprehension of the aspects of the study before they decide whether to enter. If they require more explanation of a concept or do not answer correctly, they can open a window that displays key information, reinforcing their understanding. They can use interactive links to explanatory audio and video material and glossaries. Study staff can access the annotated form to review prospective participants’ responses and address any issues that need clarification.

The interactive eConsent solution offers participants the chance to review materials as often as they wish before and after entering the study, giving them time to reflect on their choices over time. In advance of conversations with staff, prospective and active participants can bookmark any aspects of the study they may wish to discuss further.

The eConsent solution addresses the ethical tenet of respect for individual autonomy in multiple ways. The interactive approach is oriented toward the individual participant. It allows access to as much or as little explanation as required. The use of animation, visual imagery, audio, and written text in clear language for presenting information accommodates multiple learning styles. The presentation can be paused, backed up, and watched as many times as desired. The interactivity and potential for the repetition of difficult concepts enhances participants’ retention of information. The process supports participants’ self-determination. Fully informed, they are empowered to make personal decisions about their participation.

**Operational Benefits of eConsent**

The eConsent solution is centralized, which offers multiple advantages to sponsor organizations, clinical sites, and ethical review boards.

Because data from all sites is collected in a centralized, secure server, stakeholders can have real-time access to current data from the consent and enrollment process across a single or multiple studies. Data can be sorted and shared based on individual access rights to show participant-identified data for the site staff and site monitor, and de-identified data for sponsors, research ethics committees (RECs), and institutional review boards (IRBs).
Sponsors that have previously had to rely on manual systems for reporting screening and enrollment from paper-based systems can now track screening and enrollment rates remotely in real-time across large, multi-site studies. Metrics derived from the data collected can provide quick dashboard views of what is happening on a study, such as the number of participants consented, countersigned, or withdrawn from the consenting process.

More in-depth reporting of this data reveals key information, including words or concepts commonly marked as unfamiliar by participants and knowledge assessment questions indicating topics participants have difficulty comprehending. The system enables remote monitoring of how much time the participants spend with the consent material. Metrics, stripped of participant identifiers, can provide sponsors with mean and individual review times of the consent materials, as well as results of comprehension assessments and those terms most frequently defined. This data can help the sponsor refine the consenting process and target sections of the eConsent that might be improved with revision, even as the study is on-going.

Central review of the eConsent solution metrics can allow for more remote monitoring activities, reducing the number or length of trips by site monitors and reducing the cost to the sponsor for these activities. In addition, many of the metrics can be used to develop or improve risk-based monitoring activities to reduce risk of non-compliance with regulatory statutes.

Whenever an amendment to the eConsent is issued for a change in study information or renewal of REC/IRB approval, central version control ensures that the older version is immediately made unavailable. Version control can be applied to individual sites for site-specific consent updates, or across all sites. With eConsent, it is effectively impossible to obtain a signature on an incorrect or outdated version. The central version control and regulatory-compliant signatures ensure regulatory compliance by preventing protocol deviations and violations study-wide.

**Potential Benefits of eConsent to Research Practices**

A recent study comparing the comprehension level of participants who provide consent using paper documents versus eConsent provides empirical evidence that the eConsent solution is more effective at eliciting more fully informed consent. Participants who have a higher comprehension of the goals of research, the risks and benefits, and the key concepts of randomization, blinded studies, and placebo are more likely to remain on research studies for the duration of the study, resulting in better information about the drug, device, or procedure. If participants are unaware of what study participation actually involves, they are at increased risk for dropping out of a study due to the burdens of participation; such preparation for discussion can ultimately contribute improved participant retention.

eConsent also has the potential to standardize the informed consent process and make it more accessible to more participants. This could better educate the general public about the implications of participation in clinical research studies and appeal to individuals’ altruistic goals to help others. If more people could be recruited to
participate, medical research could be furthered to the potential benefit of future patients and society overall.

**Challenges of Incorporating eConsent as a Default Process**

**Cost**

The cost of managing the paper-based consent process is highly misunderstood and often under-reported in clinical research. Many organizations consider only the cost of developing the informed consent document, the review process, printing paper copies at sites, and the 30 to 60 minutes of investigator or clinical staff time to meet with the participant at the site. Each of these costs is often represented as a line item for a CRO or site and assumed to be “the cost of consent.” However, the consent process also intrinsically includes the time and resources of managing the versions of the consent form, tracking consenting participants’ information, managing re-consents for protocol amendments, reporting to sponsors, and hosting monitors for site visits. Costs that do not get evaluated or are less tangible are costs associated with risk of protocol deviations and non-compliance (reporting deviations to RECs/IRBs, and potential loss of data for a study), costs of participants who are not retained on the study for the full research period, and the costs of developing reporting mechanisms during the term of the study.

eConsent development includes computer programming costs, graphic design, and audio script and video production. Review times for the interplay among the different media and for consistent messaging across them are marginally longer than for straight text. To evaluate a true cost/benefit for eConsent, an organization must take into consideration all of the benefits of an eConsent solution that are not easily available with a paper-based process.

**Site Start-up Timing**

The production of an eConsent solution currently requires about 8 to 12 weeks from the completion of a near-final written consent document and protocol. When taken into consideration and planned for, this timeframe can run concurrently with other study tasks such as site identification and site planning and will not affect study start-up timeframes.

**eConsent as an Unfamiliar Concept**

In their attempts to implement an eConsent solution, sponsors may initially encounter resistance to change among their own staff, as well as clinical research site staff, who may be accustomed to their current process and unaware of its inherent weaknesses. This can be especially true among departments that are already stretched thin. Sponsors may also encounter RECs/IRBs that are unfamiliar with the concept of eConsent and focus on review of the technology rather than the content.
A Fully Integrated Process Addresses the Challenges of eConsent Implementation

Reduces Overall Cost

Production costs of the eConsent solution and added costs for review can be offset over time by the operational savings of a fully integrated, centralized system. As outlined above, these savings include efficiencies in the oversight of participant enrollment, the revision and version control of consent material, and improved monitoring of regulatory compliance while reducing the cost of risk. In addition, it would be reasonable to expect that improved participant comprehension of all of the aspects of a study improves overall retention, helping to keep recruitment costs down. As an organization standardizes their eConsent initiatives and adopts eConsent as an enterprise solution for all studies, greater efficiencies can be achieved, significantly reducing costs.

Maintains Target Start-up Timelines

The focus is on eConsent programming from the time of initial protocol development. Much of the platform and boilerplate aspects can be prepared before study specifics are worked out. The metrics from previous eConsents can facilitate on-time study start-up. Using identified successful aspects and correcting flaws to build new eConsents saves time at the outset. Sponsors new to the process can learn from the experience of others who have used the platform.

An experienced eConsent provider will have an integrated review process that is efficient and saves time. eConsent providers will also have IRB partners whose members are experienced in the review of their platform. They will have an operational system that allows the review and approval of the eConsent components by the sponsor and by the IRB along the development process, so that all necessary changes can be made to consent scripts and storyboards before production.

Builds Trust and Comfort with the New Platform

A successful eConsent solution is fully integrated across all aspects of a study, from the sponsor's clinical operations and regulatory departments to clinical research site administrators and staff to the IRB. Proper training in the new process allows all members of the clinical research process to feel confident in the use of the technology, and the value it represents to the team. By working with an experienced and trusted partner to introduce an eConsent solution and helping staff to understand how it works and the benefits it will provide to stakeholders, this initial change process can become a positive and productive exercise.

From a regulatory perspective, the IRB's assessment for informed consent approval is the same for all technologies. For eConsent, IRBs will pay special attention to data security and confidentiality. To address these concerns, a fully integrated eConsent solution has a secure, cloud-based system where all data is stored and access control lists define the type of view of data each group is afforded. The electronic
tablet is only a conveyance for such data and no personal health information (PHI) or personally identifiable information (PII) is stored on the tablet. Data is never compromised or lost if the tablet is lost, stolen, or broken.

Research Results of a Randomized Comparison of eConsent with Paper-based Consent

A prospective study, conducted at the California Pacific Medical Center (CPMC), compared comprehension of consent materials among two populations randomized in a 1:1 ratio by computer to receive consent material either via an interactive iPad or a traditional paper-based form.

The first population included clinical research professionals, primarily IRB panel members from the CPMC Research Institute, for the purpose of pilot-testing the two consent methods for differences in comprehension and to collect data on the function of and user experience with the interactive eConsent solution. For this purpose, the target sample size was set low at 15; 14 of the original 15 completed the study.

The second population was drawn from individuals attending medical appointments at several CPMC clinical practices. The sample size was determined based on an estimated 20% difference in comprehension scores between those randomized to the paper-based consent and eConsent. With 27 subjects per group (N = 54), there would be 95% power to detect this level of difference at the p < .05 level. Participants who failed to complete a follow-up online survey provided no evaluable data and were not included in the statistical analysis. Estimating a 25% to 30% failure rate in completing the follow-up online survey, a target sample size of 75 participants was set. A total of 75 agreed to participate; 55 completed the online survey.

Study outcome measures included comprehension, delayed recall, and acceptability of the respective consent method to the user. Depending on the outcome measure, chi-squared, unpaired t-test, and Wilcoxon signed ranks tests were used to determine if significance was present at the p < .05 level.

The complete consent form from a previously approved longitudinal study of the possible nerve damaging effects of chemotherapy was used. It was felt the consent provided a level of complexity required for the assessment of the performance of an interactive eConsent solution. According to their assignment, participants received a paper consent form or accessed the eConsent.

For the eConsent group, an iPad presentation began with an informational video outlining the main features of the study, then presented a series of screens of the same consent form as the paper form in the same font. At the end of the presentation, the eConsent group was asked to complete quiz questions. If the participant marked the wrong answer on the iPad, the device would signal the answer was incorrect and return to the screen relevant to that particular question before allowing the subject to answer again. Participants had three chances to answer correctly before the device moved to the next question.
All participants were encouraged to fully review their respective forms and signal to the research coordinator at the point they would make a decision whether to sign it.

Between 18 and 36 hours after reviewing the consent, all participants were to complete an online survey testing the three outcomes. Among the 14 research professionals, comparing eConsent with paper-based, there was a trend (p = .07, chi-squared test) in the direction of eConsent participants scoring better on the online follow-up survey (mean correct = 77%) compared with paper-based (mean correct = 57%). Among the 55 individuals enrolled from the CPMC clinical practices the eConsent group had significantly higher test scores than the paper-based group (mean correct = 75% vs 58%; p < .001). This study demonstrates that combining an introductory video, standard consent language, and an interactive quiz on a tablet-based system improves comprehension of research study procedures and risks.

2 Source: Personal Conversations between Mytrus and Company representatives, March 2013- October 2013