Whitepaper – electronic Informed Consent: Considerations for Implementation in Clinical trials

Background

Since medical guidelines established in the Nuremberg Code (1) and later the Declaration of Helsinki (2) were imported into the ethical guidelines for the social sciences, informed consent became a common part of the research procedure. The informed consent process has been an area of debate ever since and over recent years has in many cases become a lengthy legal document of 30 or more pages that covers research sponsors from a legal perspective rather than being an informative and concise way of providing useful information to the potential study subject. Furthermore, the quality of the actual consent process at the study site is vastly dependant on the site's motivation and time constraints and can vary between individuals, sites and countries depending on local customs and often patient understanding is not documented. Site-based collection of source data to document the process and the information given as well as the filing and storage of this documentation beyond the actual study is often inconsistent across sites and requires an increasing amount of resources. Alteration, loss and delay in filed paper data may result in inspection findings or even compromise submissions to regulators.

In an era where data acquisition (eg. ePRO), capture (EDC) and storage (eTMF) are done electronically, it is the logical consequence to do the same for the informed consent process as all the advantages of the electronic modality equally apply to this process.

Informed Consent requirements

Electronic informed consent includes a number of different ways of obtaining informed consent from supportive electronic information, to a complete computer/tablet-based process at site to a completely remote Internet-based process. As with other forms of research, the consent/assent process for Internet research should be tailored to the risks and complexities of the research. The absence of direct, in-person contact can add complications to the consent process. Three often-cited concerns with consent in Internet research are verifying identification, ensuring comprehension, and obtaining appropriate documentation when needed. Adequate identity verification may in some cases be handled by the hosting survey provider; in other cases, with minimal risk research, it may not be a critical issue. Comprehension of the consent materials may be addressed by a checkbox ("I understand and agree") for low risk research, or by mandatory quizzes as a comprehension check.

A designated contact for questions and to provide additional information may have to be available to subjects at all times. Applications such as Skype® or LiveChat® have also been used to enable direct communication between researcher and subject during the consent process (3).

Now some countries e.g. India are calling for increased transparency of the consent process by using audio-video documentation, which in the case of India has been a legal requirement since October 2013 (4), adding additional operational challenges.

Virtual eConsent Solution

In the Research on Electronic Monitoring of OAB Treatment Experience (REMOTE) study (5), the first completely virtual trial conducted under an Investigational New Drug (IND) application; there was a need to find a new way to conduct the informed consent process in a remote setting.
The goal was to find a patient-centric informed consent process that leverages multi-media to thoroughly and consistently explain a study in order to achieve a more knowledgeable and engaged patient, which would ultimately lead to enhanced recruitment and retention and better quality for clinical trials. It was essential to have a well-documented, centralized process enhancing the ease of retrieval of source data for inspections, audits and monitoring, which was compliant with ICH GCP and acceptable to regulatory agencies and Institutional Review Boards (IRBs)/Ethics Committees (ECs).

The solution was a web-based, multi-media informed consent process consisting of a computer-based platform allowing for a study-specific video, followed by the presentation of the written informed consent document and a multiple choice quiz, which was documented and version controlled to allow a consistent, patient-oriented and well documented consent process with electronic sign-off facility and centralized storage. This was followed by a compulsory telephone call with the investigator. If the investigator was satisfied that the subject was eligible he or she would countersign the Informed Consent document and at this point the subject was considered enrolled in the study.

A recent study has shown that information recall by study participants based on an multimedia electronic Informed Consent process was significantly better compared to the conventional process (6) and supports the motion to use this new and improved process for the majority of clinical trials and is by no means limited to virtual studies where subjects a consented in a remote setting.

System requirements

Stand-alone electronic Informed Consent solutions have been available for a number of years and have seen considerable improvement over time.
In order to provide a consistent and engaging experience for clinical trial participants a suitable platform should be able to incorporate visual media like video clips or animated slides as well as text documents and tools that allow an assessment of the understanding by the participant. In order to have an engaging, patient orientated consent process the system should allow for a multi-media IC process on a flexible computer tablet based platform, which is compliant with all legal and regulatory requirements.

On demand information should be available for patients e.g. hyperlinks in order to get relevant information for individual needs and reduce question time with site personnel. There should also be an option to flag unfamiliar terms or sections or an ask-a-question button in order to discuss them with the site personnel.
Furthermore there needs to be flexibility in the system that allows for different versions of the Informed Consent document based on local or regional IRB/EC feedback to be presented to the subjects at individual sites. Revisions and updates to the documents need to be accommodated with strict version control allowing only the latest approved version to be signed and there have to be documentation and tracking capabilities of such a re-consent in compliance with regulatory requirements. The platform should also enable storage of or access to video documentation of the actual consent process, which is a regulatory requirement in some countries. There must be a validated and acceptable signature process (e.g. signature capture directly from a tablet device) and the ability to capture additional signatures like counter signature by the doctor, assent, witnesses or separate HIPAA consent on the same page in order to comply with legal/regulatory requirements as well as the ability to link several consents to the same individual (e.g. several versions of IC and bio-banking consent) in order to track completeness and to allow for efficient access during inspections. There also has to be an option to print the signed IC document from the device or a web-portal in order for the participant to print at home or take a copy home to comply with regulatory requirements.

All data should have a documented audit trail for all changes, be encrypted and stored at a secure, validated, HIPAA compliant, central place with search options by participant, site, country or study in order to allow monitors, auditors and regulators real-time access to the signed forms, which will greatly reduce regulatory and legal exposure.
The system should allow to define different user groups to get access to relevant information and to de-identify patient information in order to allow sponsor access to IC documents and remote, user controlled access to all IC documents to enable off-site monitoring and auditing.
It is essential that the system is compliant with all local rules and regulations and if it is used for a study under an Investigational New Drug Application (NDA) under the auspices of the FDA it needs to be compliant with 21 CFR part 11.

Even though there is often a focus on point solutions it is important to keep focused on the data flow in the whole study to avoid multiple hand off processes, which increase complexity and are often sources for errors. To make the Informed Consent system more efficient for the overall study conduct seamless integration into a cloud-based clinical trial management system (CTMS) is highly desirable. This will allow the site and the sponsor to track the progress during subject recruitment and confirm completeness of the Informed Consent documentation in real time. It also enables the seamless transfer of data into an eTMF or into long-term storage.

Advantages of Electronic Informed Consent

This new process has clear advantages over the conventional way of obtaining informed consent. Now we have a multi media-based informed consent process with real-time tracking options, which provide more consistent and better understanding to study subjects. Not only can we document the information provided to subjects but also their resultant understanding. There is one standardised process with a pre-defined standard across sites, which allows for real-time remote monitoring and audit access. This minimizes legal exposure, reduces potential regulatory findings and may even avoid more restrictive external regulation of the process. Ultimately it will enable remote study models, support clinical trial innovation and potentially set new quality standards.

Conclusion

The new electronic Informed Consent process has been reviewed by a number of regulatory agencies in the US and in Europe and has also been approved by IRBs and ECs.

There is definitely a strong push from innovative pharmaceutical companies to adopt this new concept in the conventional clinical trial setting and the implementation is fairly straightforward. In the virtual trial space there are still a few hurdles to overcome as there is a lack of defined regulatory requirements and a number of country-specific laws and regulations on the acceptability of electronic signatures, witnesses to the consent, the need for video documentation and the use of telemedicine, which require a case-by-case assessment.

As on many previous occasions, the supporting technology is not the limiting factor. In fact there are readily available flexible platforms that allow adoption of country- and site-specific requirements waiting to make this innovation happen in the global clinical trial environment. Clearly the technology adoption has already started and is likely to accelerate.

By Miguel Orri

References

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