The Benefits of Electronic Informed Consent in the Age of Decentralized Trials and Beyond

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For decades, hospitals and healthcare systems have used paper for informed consent documents. Due to innovations in technology, the desire for cost savings, remote collaboration, and the need to increase participant levels in clinical trials, electronic informed consent (eIC) has become an attractive component to many investigators.

Nevertheless, adoption has been slow since eIC first came onto the scene in the 1960s. According to DrugDev, in 2016 only 28% of global sites used eIC in at least one study, with 2% of sites reporting use across all studies.[1] This was true across all countries.

Now faced with the risk of COVID-19 infection, eIC provides an alternative to traditional face-to-face consenting. Federal government institutions like the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) have recognized the urgent need for more digital health technology in our health system in light of COVID-19.[2,3] In September 2020, the NIH awarded health technology company Vibrent Health a contract to develop a "Digital Health Solutions" platform for COVID-19 that includes using the eIC process.[4]

This push for eIC is logical and something that people have been talking about for many years. Now we've been presented with circumstances that make it a necessity rather than a luxury.

To take full advantage of the promise of digital technology, researchers still have an obligation to use an informed consent process that protects human subjects. In this white paper, readers will learn the benefits of eIC and how to be fully compliant in the eIC process.

Benefits of eIC

According to the official 2016 FDA definition, "Electronic informed consent refers to using electronic systems and processes that may employ multiple electronic media, including text, graphics, audio, video, podcasts, passive and interactive web sites, biological recognition devices, and card readers, to convey information related to the study and to obtain and document informed consent."[5]

With a wide range of features, eIC has many benefits for participants, researchers, and sponsors:

Knowledge acquisition and engagement

Experts agree that consent forms are generally difficult to read and comprehend, especially for nonnative speakers and people unfamiliar with medical language. Complex terminology, limited time, and lack of readability and transparency often affect participant consent and retention.[6,7,8,9]

eIC tools have been shown to improve participant understanding of protocol by providing more detailed information — which can be customized to the participant's needs — increasing the opportunity for inclusion and diversity.[10,11] According to a 2013 study, a combination of improving the readability of consent materials and an interactive informed consent process with video, standard consent language, and an interactive quiz on a tablet improved comprehension of research study protocol.[12]

eIC can boost comprehension, providing participants with a better understanding of their clinical trials via a more interactive process. Currently, most paper consent forms are about 20 pages long. They often incorporate words that someone who doesn't have a medical background might not understand. Using pictures, videos, and diagrams adds clarity and increases comprehension about what they're agreeing to.

Less anxiety

With remote eIC, participants can also read the consent form in a relaxed atmosphere, such as their home, without feeling pressured to sign the document. Not being face-to-face with an investigator can avoid awkwardness for participants, making them more apt to click a button saying they do not understand than if they were in an office with a human waiting for them to complete the form in person, a situation where they might be more reluctant to ask questions.

Reduced costs

Theoretically, the cost savings of a digital record is clear. Funds spent copying paper documents, shipping, storing, managing archives, and validating source data are greatly reduced. That said, there can be significant up-front costs depending on the software program used and there are a myriad of choices right now. Using a multitude of systems can result in inefficiencies and a steeper learning curve. When researching paper consent versus eIC, multiple studies cite the need for IT infrastructure, including Wi-Fi connectivity, informatics personnel for development, and help desk personnel.[13] These features are not cheap.

Therefore, research on actual savings is still scant and mixed. It is likely that as eIC becomes more common, software companies will merge, simplifying their programs to the point that they are easier for large health systems with many studies in many remote locations to adopt them at scale.

Collaboration

eIC can facilitate collaboration with researchers around the world. Researchers can integrate consent directly into an electronic data capture system that all sites can access. This is important, since as of October 26, 2020, ClinicalTrials.gov listed 355,724 studies with locations in all 50 U.S. states and in 217 countries.[14] eIC enables remote study models, supports clinical trial innovation, and will potentially force interoperability and set new quality standards.

Safety

By reducing on-site recruitment and paper consent, eIC can lead to a decrease in human errors like missing forms or missing signatures.

Omni-channel

eIC can be omni-channel, meaning available on any device, while still compliant with regulatory requirements. Bring your own device (BYOD) has become a leading approach in healthcare settings. Study participants using their own devices from anywhere they want can reduce the need to buy, share, and sanitize equipment. In the age of COVID-19, such caution is imperative.

How to Set Up Your eIC Process to Be Fully Compliant

To make eIC viable, researchers still have to comply with the Health Insurance Portability and Accountability Act (HIPAA) and General Data Protection Regulation (GDPR) standards.[15,16] To protect participants with eIC, there are a few factors to consider:

Subject authentication

The biggest obstacle to eIC has been ensuring the e-signature can be attributed to the participant, and that the participant cannot delete the signature once it is entered.

The platform used should ideally enable storage of video or photo documentation of the actual consent process so that signature verification can be verified by research staff. This is a regulatory requirement in some countries. The signature process should also include an ability to capture additional signatures by the investigator, witnesses, or separate HIPAA consent on the same page. This links several consents to the same individual. Because of COVID-19, Zoom and other consumer teleconference programs have been widely adopted. Zoom itself is developing an end-to-end encrypted version and it is likely other programs will follow.[17]

FDA regulations permit a wide variety of methods to create electronic signatures, including using computer-readable ID cards, biometrics, digital signatures, and user name and password combinations. All eIC documents, information, and processes must be approved by an independent research ethics committee.

Two popular forms of digital signatures include 1) using a stylus or finger or 2) a validated electronic signature on platforms with password entry. Validated signatures require an identity and password within an electronic system. Methods to further identify a subject include verification of a state-issued identification, other identifying documents, personal questions, biometric methods, or visual methods.

Data privacy

For FDA-regulated clinical investigations, the electronic system that supports the eIC must be secure, with restricted access, and should include methods to ensure confidentiality regarding the subject's identity, study participation, and personal information after informed consent has been obtained. The subject's information within an electronic system must be encrypted, unless the entity documents why encryption is not reasonable and implements an alternative. The system should be able to de-identify participant information in order to allow sponsor access to eIC documents to enable off-site monitoring and auditing.

Clear responsibilities

The clinical research site and sponsors should clearly define the eIC process and the roles and responsibilities of stakeholders. A few questions to ask:[18]

- How is version control managed?
- How are different languages managed?
- Who is hosting the eIC software application?
- Where is the data backed up?
- How is website access controlled?
- How are questions created and answered?
- What happens if the website is down temporarily?
- Who is managing the user accounts?

Oral explanation
The researcher should be available, virtually or otherwise, to describe the study and answer questions.

Accessibility
After signing, the study subject must have access to the eIC document. It should be printable from the device or web portal or sent to them electronically.

Source document storage
Since the eIC document is a source document, it should be stored in an electronic repository with user management and access controlled by the study site.

Version control
There needs to be flexibility in the system to allow for different versions of the eIC document as the study evolves and based on local or regional regulations. The system must allow for re-consenting and/or for keeping the participants in the trial based upon the original consent. It also must lock the content on the form to prevent it from being altered post-signature. eIC allows for a date and time stamp of consent forms, theoretically making tracking versions for each participant easier than with paper forms. Tracking also makes remote monitoring and audit access easier.

For clinical trials not yet launched, consider the following:[19]

- Determine if your electronic data capture (EDC) system can take eIC, or if a separate system is needed
- Confirm the system and signature process are compliant with FDA requirement 21 CFR Part 11, especially if it is FDA regulated research
- Obtain IRB approval for use of eIC; some IRBs have preferred vendors
- Define how the sponsor and its representatives will have access to review the signed eIC
- Include eIC guidance on study training materials and monitoring/data management plans

For studies currently running, consider the points above and these three questions:

1. Will currently enrolled participants be re-consented electronically?
2. Will eIC be available for all participating sites or for a limited set?
3. Will the same language from the original consent be applied, or will there be changes that need to be reviewed and approved by the IRB?

Key Takeaways
Less anxiety
Digital consent helps participants access information in their own environment, without feeling pressured to sign a document straightaway and without feeling self-conscious if they don't understand something.

Theoretically more accessible

eIC can theoretically reach more people in remote locations or whom are mobility-impaired. However, computer literacy and access to technology are still factors affecting use of eIC. For example, in a 2014 study investigating eIC for biobanks, there was strong interest among researchers but they found participants with low computer literacy, not surprisingly, were less eager.[20] In a 2018 focus group study, minorities and rural area residents expressed concern about access to computers and the internet, computer literacy, privacy, and confidentiality as they related to the use of eIC.[21] It is important to consider how accessibility to devices could affect inclusion of diverse populations.

Greater comprehension

eIC can offer greater comprehension than the traditional paper consent process. For instance, the eIC may still contain the long consent form we are familiar with, but include embedded links to further explanations of medical jargon, illustrations that can run through study scenarios, spoken text, and quizzes that help participants gain a clearer understanding of the study protocol.

Paper and people will not go away

People learn in different styles — what works for one participant might not work for another. There will always be participants who can't use eIC or do not want to. Participants may also have difficulty navigating eIC because of a lack of familiarity with electronic systems, poor eyesight, impaired motor skills, or if the eIC is badly designed.

eIC usage will increase

As a result of COVID-19, eIC will increase out of necessity. The industry is moving toward decentralized trials on the whole because COVID-19 has served as a catalyst for a quicker adoption of eIC.

Each study and subject population is unique, so consider that when looking at how to use eIC. With an understanding of these basics, you are better positioned to determine if eIC is right for your study.

About Clinical Research and Informed Consent

When scientists want to determine if a new study drug Is safe and effective, they go through a long and careful research process.

Study drugs that work well in computer simulations or in animals don't always work the same way in people.

So doctors and scientists work together to design research studies to understand how the new drugs work in humans, in the safest and most effective way possible.

To include participants in a research study, doctors need to explain what to expect and ask for their permission.

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