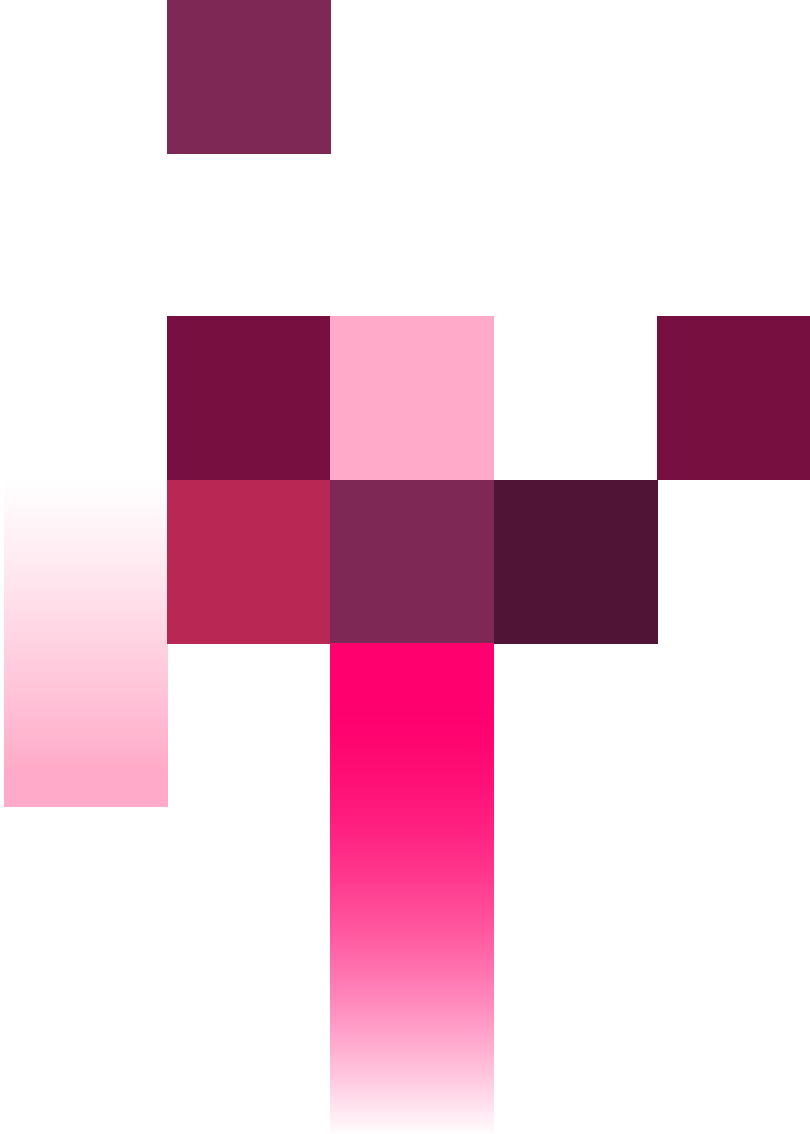
WHITE PAPER



Improve the Consent Experience for all Research Stakeholders with eConsent

August 2021

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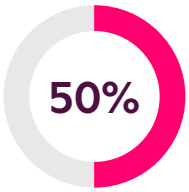
Introduction

The consent process is the first introduction to a clinical trial, but few studies take advantage of this opportunity to engage participants. Given that many clinical trials fail to recruit enough patients, it might be time to re-evaluate the way informed consent is approached and introduce digital methods of communicating study information. Electronic consent (eConsent) offers many benefits for both participants and researchers, but strategic and compliant implementation is important. Key points to consider are discussed in this whitepaper.

Are informed consent processes effective?

Informed consent is an integral part of clinical research, as a means of protecting participants' rights and welfare when contributing to scientific knowledge. Therefore, the informed consent process should adhere to the core tenets of informedness, comprehension and voluntariness.[1]

Despite widespread recognition of the importance and components of informed consent, researchers remain challenged by ensuring research participants comprehend and agree to the requirements,[2] with approximately 50% of studies failing to ensure adequate understanding of the study purpose, voluntary nature, ability to withdraw and risks/benefits of participation.[3,4] Instead, there seems to be greater emphasis on a single-point transaction that satisfies any legal or organizational requirements than ensuring participant understanding.[5]



50% of studies fail to ensure adequate understanding of the study purpose, voluntary nature, ability to withdraw and risks/benefits of participation

These studies have highlighted the scale of the challenge that researchers face when designing effective informed consent processes, and leading experts in informed consent have stated that the "classic consent interaction is outdated."[6]

Core tenets of informedness, comprehension and voluntariness

- The participant is competent to make decisions for themselves
- Participants are provided information on the study components, including what they are expected to do and the risks and benefits of participation
- The information provided is understood
- The decision to participate is made autonomously

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Digital technologies can modernize the consent process

One way to modernize consent is to move away from traditional paper-based methods. The increasing popularity in trials that use more digital processes, accelerated by the COVID-19 pandemic, has been accompanied by a shift toward eConsent. eConsent has been defined as a technology-based patient engagement tool that uses multimedia to present the consent information and obtains a digital signature and as a "a consent process that is born digital, designed to be completed by a potential study participant on a phone, tablet, or computer screen and that assumes no interaction with a clinical research professional before or during the consent 'interaction.'"[7]

eConsent

a technology-based patient engagement tool that uses multimedia to present the consent information and obtains a digital signature.

Definitions vary to some extent, although the common theme is the use of digital, multimedia communications tools. The underlying foundation remains the same: As with non-digital informed consent, eConsent still requires providing a potential participant with enough information for an informed decision around their involvement in the research and provides opportunities to ask questions before making a decision.[8]

But the need to modernize consent goes beyond merely moving the documents to digital platforms. The Clinical Trials Transformation Initiative (CTTI) has recommended eConsent as a method to create a more effective consent process.[9] This presents an opportunity to reimagine how to engage participants in clinical research and incorporate informed consent, as one of the first key steps in the decision to participate in a trial, within participant-centric trial processes.

Participant perspective

One criticism of informed consent is that it often involves overly complex language and a lengthy format; this is reported by both research stakeholders[9] and participants,[10] with some participants stating that the consent form is "overloaded with information," a "babble of words" and "boring and made me not want to read the details."[11]

Because they can incorporate visual, auditory and tactile modes of presenting information, digital platforms are promising for their ability to improve informed consent. Participants can listen to study information, watch videos, view images and diagrams, navigate an interactive decision tree and complete quizzes intended to ensure understanding. These, often more engaging, methods of providing information improve participant satisfaction with the process.[11,12] In addition, presenting the same information in a variety of formats allows participants to choose the modality that aligns with their preferences, needs and learning style.

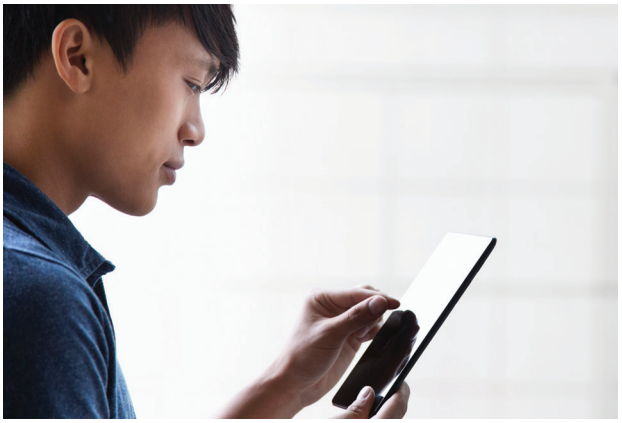
People have increased engagement with digital information, taking twice as long to review it as paper-based information.

Furthermore, digital processes that enable self-paced learning and repeated review of information provide each person with sufficient time to comprehend the information and come to a decision.[13] In fact, studies have shown that potential participants spend up to double the amount of time reviewing the same information digitally compared with on paper.[11,14]

This alignment with learning style, sufficient review time and "teach back" interactions through quizzes have been associated with

- greater comprehension of the material,[11,15-18]
- longer retention of the information,[11]
- faster recruitment[19] and
- a more diverse sample.[19]

Moreover, a greater understanding of the trial requirements and potential benefits is likely to result in greater compliance with the study overall. One study found that fewer individuals agreed to participate with the eConsent process than with the traditional consent process for stated reasons such as "worry about time," "lack of interest," "concern about pain" and "skin biopsy."[11] The authors suggested that a greater understanding resulted in participation by only those who were willing to commit to the study, ultimately resulting in fewer dropouts.



Researcher and site perspectives

Moving informed consent to a digital platform does not replace the site-participant relationship. There is still an important role in ensuring that participants understand the study and protecting participant safety. However, eConsent can facilitate communication between the site and participant.

In a recent survey, site representatives reported supporting the use of multimedia components for improved participant understanding.[22] For site staff, eConsent reduces the time-consuming tasks of:

- describing the study,
- obtaining signatures on multiple pages,
- maintaining a paper trail and
- reconsenting when there are trial amendments as well as the risk of unintentionally introducing bias and pressure to participate.[13,22]

Instead, there is an opportunity to have more meaningful interactions with dedicated, informed participants early in the study. Electronically available individual participant data as well as metadata enable the site-participant engagement to be more tailored in advance of the first interaction. Site representatives also recognized the potential for fewer site visits and therefore participant burden.[22]

With digital systems, the ability to capture participant feedback, view incorrect responses to quizzes and analyze the time spent on certain sections provides insight into the overall experience:

- Are there sections that can be improved?
- What are the commonly missed questions, and should that information be revised?
- Should certain terms be explained more clearly?

Real-time updates to the system are possible (after institutional review board [IRB] approval), including for mid-study amendments, and participants can be notified of any changes that may affect their willingness to continue to participate.[8]

Built-in version control and audit trails ensure participants are always presented with the latest version, and a timeline can be derived for all interactions (e.g., date reviewed, date signed, versions), improving both data quality and regulatory compliance.

For these reasons, an enhanced digital process is useful not only for remote or decentralized clinical trials, but also to improve the participant and site experience in traditional, in-person trials. For these benefits to be realized, government and industry organizations have recommended the inclusion of a set of key features.

eConsent recommendations from industry experts

Considerations for eConsent include expectations from participants as well as regulatory requirements. Participants expect understandable, convenient, easy-to-use, professionally designed and tailored digital solutions, and these must be delivered in a secure environment that protects patient identity and safety and ensures autonomous, informed decisions.

Recommendations in this section originate from:

- government/regulatory agencies,
- collaborative industry organizations such as the eConsent Initiative at TransCelerate Biopharma Inc. (participants, sites, global health authorities and global ethics committees)[22] and
- a recent survey of eConsent stakeholders (technologists, ethicists, physicians, researchers, patient advocates and patient representatives).[21]

Language and supporting elements

No different than paper-based consent, the information presented in eConsent must be in language understandable to the potential participant (fifth-grade reading level is recommended[20]) and presented in a way that minimizes the possibility of undue influence on their decision to participate.[8] Participants themselves, have also requested simple language because they find lengthy consent forms difficult to understand.[22]

Unique to eConsent is the ability to support simple, concise explanations with audiovisual and "teach back" components, as outlined in the Agency for Healthcare Research and Quality's (AHRQ) Informed Consent and Authorization Toolkit for Minimal Risk Research.[20] To choose appropriate and representative multimedia components, the first step is understanding the target participant population (e.g., age, culture, socioeconomic status, region, therapeutic area, culture) and their learning preferences.[22]

Tips

- Use a fifth-grade reading level.
- Incorporate audiovisual and "teach back" components.
- Understand the target participant population and their learning preferences.

Format and navigation

The ability to proceed forward and backward within the system and stop and continue at any time are crucial to providing participants enough time to review and revisit information to improve comprehension. Hyperlinking to additional material can help keep the primary information brief while providing additional explanation for those who need it.

One of the cultural challenges with digital interactions is the tendency to accept legalese without fully reading it — we tend to hit "Agree" as soon as possible.[7] Therefore, it can be useful to design methods to ensure that all material is accessed and read before consent can be provided.[8] These can include providing supporting images, incorporating interactive elements and limiting concepts to one per screen, which have been shown to slow down readers.[21] Use of more images than text, limiting the amount of text on each screen and providing audio files are helpful for visually impaired participants.[14]

Participants have requested the ability to review the eConsent content, including multimedia components, throughout the entire trial.[22] Moreover, according to the FDA, the participant must have the ability to review amended consent information and determine whether they wish to continue participating in light of any study changes.[8]

Tips

- Allow forward AND backward navigation.
- Include the ability to stop and continue at any time.
- Hyperlink to additional information, as needed.
- Design methods to ensure all information is reviewed before consent can be provided.
- Allow participants access to the eConsent information throughout the entire trial.

Assessment

One method of ensuring comprehension is assessments/quizzes built in to the eConsent platform, or what the AHRQ calls a "teach back" interaction.[20] If questions are answered incorrectly, the user can be redirected back to that section for further review before answering the question(s) again.[8,14]

Tips

- Build assessments and quizzes (e.g., "teach back" interactions) into the platform.
- Redirect the participant back to review information when he/she answers a question incorrectly.

Option for paper-based information

Some people might prefer to read information on paper, have difficulty navigating electronic systems or want a hard copy to reference throughout the consent process. And participants have reported a preference for a combination of paper documents and electronic information related to consent.[22]

Therefore, both paper-based and eConsent methods should be made available.[8] This can be as simple as providing a printable pdf within the eConsent platform.

Tips

- Provide both paper-based and eConsent methods.
- Allow a PDF version to be downloaded or printed.

Interaction with researchers

Inherent to the informed consent process is the ability to ask questions of the researchers before agreeing to participate. The FDA suggests that this can be accomplished in person, electronic messaging, telephone calls, video conferencing or live chat.[8]

In a recent survey, a participant panel thought it would be useful to be able to highlight text or graphics they did not understand and then discuss these items with the site staff.[22] Similarly, the majority of the respondents reported that the opportunity to electronically record their questions within the eConsent platform and to ask study staff general questions about the trial would be valuable for improving their understanding and making an informed decision.[22]

Tips

- Allow participants to ask the researchers questions about the study.
- Allow participants to highlight text or graphics they don't understand.

Verification

The FDA states that, if any or all of the consent process takes place remotely, eConsent must include a way to ensure the person signing is the participant.[8] Suggested methods include verification of state-issued identification or use of personal questions, biometric methods or visual methods. Then, the participant must receive a copy of the informed consent form, whether electronically or in hard copy.[8]

Tips

- Verify a state-issued identification, or use personal questions, biometric methods or visual methods of verification.
- Provide the participant with a copy of the informed consent form.

Integration with other eClinical systems

Sites desire integration with other eClinical technologies such as randomization trial supply management (RTSM) and electronic data capture (EDC), improving efficiencies and making sure that the patient trial journey is documented from start to finish.[22] In addition, they would like to see implementation of eConsent more broadly, such as with other eClinical apps on a single device or in a bring your own device (BYOD) scenario. If BYOD is being used, practical issues such as impact on smartphone battery life and data usage plan should be included in the consent materials.[21]

Tips

- Build easy integrations with other eClinical systems.
- Enable eConsent with other eClinical apps on a single device or as BYOD.

Security

Participants have expressed some concern over data security, particularly when it is not clear who will have access to their data.[22] And the FDA requires that eConsent systems are secure, have restricted access and ensure confidentiality of the participant's identity, participation and personal information.[8]

To alleviate concerns and ensure compliance, data handling (e.g., where data are stored, who controls the data, how data are being used, how long data will be stored) should be transparently explained.

Tips

- Ensure the eConsent system follows all regulatory requirements for security.
- Clearly explain how data will be handled.

Site training and assessment

To ensure sites have a full understanding of how eConsent will be implemented within a trial, it is important that sponsors communicate early and often with sites in addition to providing adequate training, documentation and helpdesk support.[22]

Depending on site capabilities, as determined during an appropriate feasibility assessment, a hybrid approach combining eConsent with traditional consent processes might be required.

Tips

- Provide sites with training, documentation and helpdesk support.
- Consider a hybrid approach of eConsent and traditional consent processes.

IRB and ethics committee review and approval

All consent documents, supporting multimedia components, quiz components, navigation and mid-study amendments need to be approved by the appropriate regulatory agencies.[8] IRB and ethics committee representatives have requested that the review occurs as early as possible to avoid any unexpected issues.[22]

There is some concern about the review process of electronic formats, specifically regarding technological capabilities, timing of the review and the amount of time it might take to review all components.[22] Submitting material that reflects the participant experience but is still open for comment can be a difficult balance to achieve. For example, reviewing a completed video does not allow for any significant feedback to be incorporated without major rework, expense and time. At the same time, submitting a storyboard might allow for earlier feedback but not fully represent the intended content or interaction.

Therefore, sponsors should work with the ethics committees regarding a review process that will accommodate the committee's needs and work within any constraints. Designing a technology-enabled review process within the eConsent platform could address some of these issues.

Tips

- Submit eConsent materials for IRB approval as early as possible.
- Consider when the materials reflect the participant experience but will still allow room for feedback.
- Design a technology-enabled review process within the eConsent platform.

eConsent: the accepted and expected method for the future

There is general consensus across research stakeholders that eConsent is beneficial to participant understanding, true informed consent, site-participant relationships and oversight. As a result, broader implementation of eConsent in the future is not only accepted but expected. To take full advantage of digital capabilities for better engagement, a shift in thinking is required. This depends upon collaboration across all impacted groups to ensure that needs are met and the implementation complies with local regulations. Working with an experienced technology partner can streamline this process and help with a smooth transition to an eConsent process that transforms the way the industry engages with participants from the very beginning.

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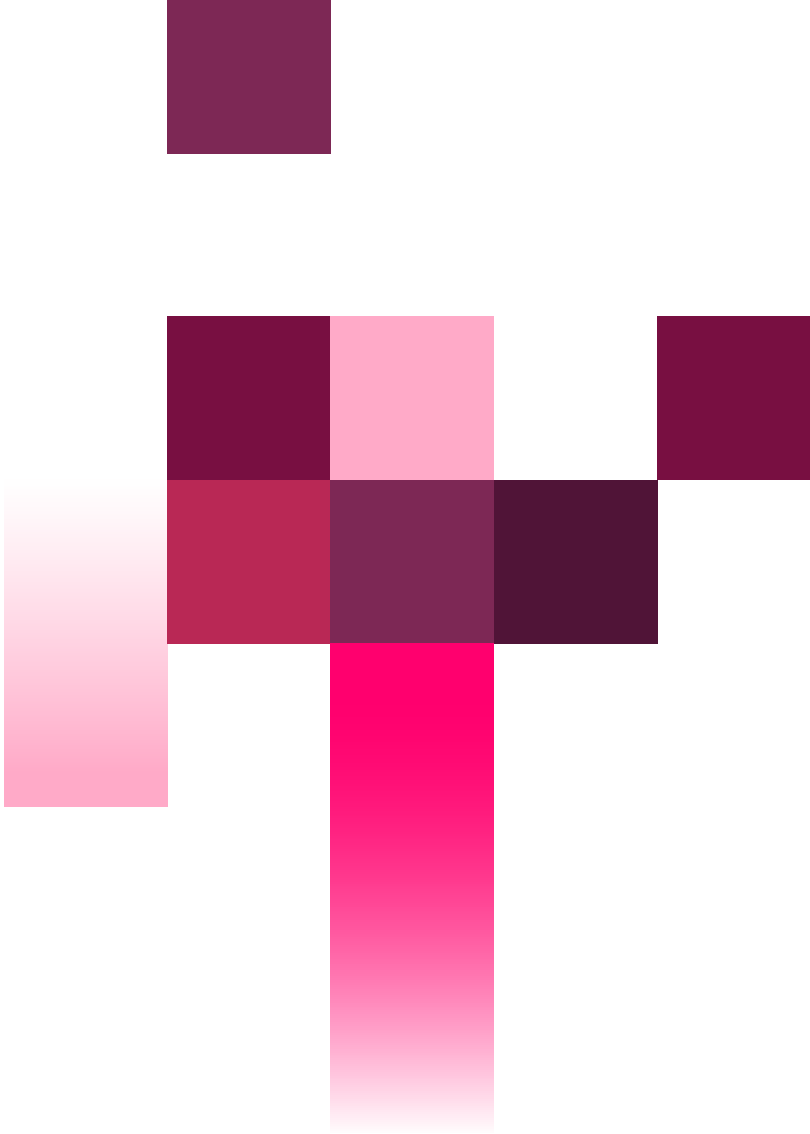

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