eCONSENT: VULNERABLE POPULATIONS
Foreword

This document is intended for sponsors and other interested stakeholders to introduce and facilitate the implementation of eConsent. Every company is free to decide and must decide for itself whether, to what extent, and in what manner to implement eConsent and to rely on the guidance set forth herein. This Guidance merely is intended to help those companies that decide to adopt eConsent to do so in an efficient and effective manner. It is not intended to provide specific standards or specific guidance directed to sites or vendors, or specific regulatory references. It does not provide specific guidance to the content of informed consent or the process of administering informed consent.

Disclaimer: Nothing in this document constitutes legal advice. Users are responsible for ensuring their own compliance with all applicable laws and regulations in the jurisdiction in which they are conducting the research, associated with the informed consent process. Any party using this document bears sole and complete responsibility for ensuring that any materials or programs developed or any actions undertaken as the result of its use complies with all applicable laws and regulations.
eConsent: Vulnerable Populations

1 Table of Contents
1 Table of Contents ...............................................................3
2 Abbreviations ........................................................................4
3 Vulnerable Populations ........................................................5
  3.1 Better Practices ..................................................................6
  3.2 Considerations for Specific Vulnerable Populations ............6
4 Background Resources ........................................................14
2 Abbreviations

ICF  informed consent form
IRB  institutional review board
LAR  legally acceptable representative
US   United States
3 Vulnerable Populations

Findings from numerous studies confirm that interactive, multimedia-assisted informed consent with vulnerable populations may:

- Improve participant understanding
- Reduce some health literacy-related barriers
- Increase participant and researcher satisfaction with the consent process
- Result in longer recall times of comprehension-related items
- Simplify the process of declining to continue, both at the beginning and during the study

Vulnerable populations may have additional considerations impacting their ability to make a voluntary and informed decision, and thus require extra care and special considerations for their protection in clinical research.

Vulnerable populations considered here include:

- Pediatric
- Economically and educationally disadvantaged
- Physically and intellectually challenged individuals
- Pregnant women
- Vision or hearing impaired

Other vulnerable populations (e.g., prisoners, fetuses, active military) are not specifically addressed here, as benefits with eConsent are unknown or unlikely. Other vulnerable populations may have other considerations that the sponsor should evaluate.

eConsent may help improve understanding compared to paper consent for some vulnerable populations, e.g., by:

- Making it easier to ask questions
- Embedding links to pictures/videos of procedures, medical equipment, or explanations of key terms

A set of simple questions may be added at the end of the eConsent to assess study participant comprehension, which may provide more autonomy to these populations.

The sponsor should assess how eConsent and use of multimedia components may enhance the consent experience for the targeted vulnerable populations.
3.1 Better Practices

Some suggested better practices for using eConsent with vulnerable populations include:

- Weigh benefits of multimedia components against population characteristics, including age, education, health literacy, the health problem, cultural values, and health beliefs.
- Ensure people involved (e.g., site staff) understand how to use metadata to address possible challenges with vulnerable populations, such as how to encourage participant questions.

3.2 Considerations for Specific Vulnerable Populations

3.2.1 Pediatric Populations

Pediatric populations (birth to the age of majority) are vulnerable for multiple reasons, including parental pressure, low literacy, brain development, and incomplete physical development. Pediatric populations may also be more susceptible than adults to advertising and multimedia tools may mislead a child into thinking the consent process is a game. Pediatric participants must be made aware as much as possible of what it means to be in a clinical study and what to expect. Their assent to the procedures and risks of participation should be obtained in the most appropriate manner for their cognitive ability. Specific benefits to the use of eConsent in pediatric populations include:

- The legally acceptable representative (LAR) consents to the study on the child’s behalf, but the child’s assent must be independent of the LAR’s desire for the child to participate. Pediatric participants who strongly resist participation should be respected by clinical trial staff, overriding the LAR’s wishes when necessary. eConsent enables easy tracking of signatures and linking the assent to the consent.
- Many children are very accustomed to multimedia content, for both entertainment and educational purposes. Multimedia content may include interactive and game-like content, including game-style rewards such as points, progress bars, and comparative statistics to encourage interaction and continued participation. These features, when added to eConsent, may help children understand and retain information more easily and completely. eConsent can be a useful tool to help pediatric participants understand clinical study information and provide their full assent to participation.
Considerations when using eConsent with pediatric populations:

- The attractiveness of the content might lead to concerns of overselling the study’s possible benefits, making the study appear to be a game, or over-rewarding the child’s participation through game-like or storytelling elements.
- Research on eLearning vs traditional learning is mixed; there is some suggestion that paper-based materials may be superior to electronic materials for complex information. However, some research shows the opposite and suggests that eLearning is superior for those with conditions like dyslexia.³
- Coercion is a key concern with pediatric participants; content cannot appear to suggest that the pediatric participant will make others happy (parents, other patients, the study staff) through participation or will be punished or disliked for non-participation.

Better practices:

- Include:
  - Simple, direct sentence structure using age-appropriate language
  - Video content that clarifies key concepts visually
  - Interactive or game-like elements that encourage a child to learn the information and reward correct answers during the consent process

- Do not include:
  - Video content that uses coercive language or images when explaining concepts (e.g., must, should, punished), oversells possible benefits, or makes the study appear to be a game
  - Interactive or game-like elements that imply rewards for study participation

3.2.2 Language Access and Cultural Competency

Cultural differences and language barriers may also make a study population vulnerable. Considering the study participant point of view is important to delivering equitable care throughout the research study experience. Both paper consent and eConsent should be health literate, culturally competent, and in an appropriate language for study participants and their families. The sponsor must obtain necessary translations for either paper consent or eConsent.

- Cultural competence: the ability of an organization and/or individual within the health care delivery system to provide effective, equitable, understandable, and respectful quality care and services that are responsive to diverse cultural health beliefs and practices, preferred languages, health literacy, and other communication needs of the patient.
Professional interpreters and certified translators become key in implementing eConsent in global studies, especially because multiple eConsent components may need translation. Poor translations may cause the failure of the study participant to act as instructed and disparities in prescription and administration of the study treatment. It may also reduce the likelihood for appropriate follow-up and treatment of the underlying conditions and/or of side effects of the study, plus physical or emotional damage, mistakes in conduct of the study, and wasted time and money.

3.2.2.1 Translation and Localization

Both translation and localization may be needed to ensure eConsent tools are appropriate for the intended study population.

Translation involves the written word and typically takes place long after the text is created, which gives the translator time to access resources (dictionaries, glossaries, subject matter experts, etc.) to produce an accurate and effective end document.

Localization involves cultural adaptation and addresses the norms and style that are familiar to the local population. Localization can account for changes in information (e.g., time/date format) and eConsent design and functionality, thereby helping to provide quality assurance and control. This is particularly true for studies in technologically emerging countries and countries culturally distant from the country where the study was planned.

Better practices:

- Use localization and globalization expert service providers that include content, cultural, and technical issues in addition to language translation, e.g., consider skin tones, clothing, and audio voiceover accent. Global videos and graphics may not always be appropriate.
- Multimedia components such as graphics may assist in non-verbal comprehension
- Consider linking to live, certified interpreters within the eConsent system such as via video chat or direct link

Considerations:

- eConsent may have increased translation needs (e.g., voiceovers or glossary terms)
- Particularly where the participant is not fluent or comfortable in the dominant language, eConsent does not replace the involvement of the study site staff and translator in the consent process
• Study sites may have a study participant who speaks a language they were not expecting and are not prepared for. The language may not be immediately available in eConsent.
  o Consider using paper ICFs for initial consent instead of delaying the participant’s entry to await translation of all eConsent components
  o In the US (or other locations where allowed), consider using generic pre-translated paper short forms that could made available within eConsent. Multimedia components would need to be translated to be used.

3.2.2.2 Language Access vs Language Assistance

Vulnerable populations may need language assistance in addition to access. Language access is achieved when non-native speaking participants can communicate effectively with study staff and participate in consent. Language assistance includes all oral and written language services needed to assist non-native speaking participants in communicating effectively with study staff and gaining meaningful access and equal opportunity to participate in research studies. eConsent may be advantageous for vulnerable populations in facilitating language assistance.

3.2.3 Low-literacy Population in Typical Research

Several eConsent components might be considered for low-literacy populations, such as video, audio, glossaries, and dictionaries, which may create a more user-centered environment where the study participant has more control. The ability to flag content and ask questions may also increase control and reduce anxiety. Some researchers have also found that these approaches offer more consistency among individuals in the study.¹

• Advantages:
  o Audit trail
  o Consistency
  o Lowered anxiety
  o Perceived control
  o Reduced staff time and costs
  o User-centered

• Considerations:
  o Age dependent
  o Dependent on education level
  o Computer experience needed
  o Mixed findings
Multimedia components do not always improve effective communication and adding components could increase the time needed to consent, which could be problematic for site personnel.

Research on low health literacy has not yet found solid evidence that alternative formats such as video and audio have been effective, as they depend on education level, age, and computer experience.\(^5\)

In the absence of consistent findings, the consent format could depend on the level of risk.\(^4\) For example, observational studies may be better suited to using only multimedia components or other less well studied methods.

Consider:

- For those unable to write due to illiteracy, physical disability, or other reasons, evaluate if other documentation of consent options such as video or thumbprint methods may be used
- Evaluate if the population is comfortable using electronic devices (understand how to move between sections, etc.)
- Multimedia components do benefit certain audiences. Consider and test alternative approaches for eConsent to increase chances of comprehension by the target population.
- Allow a shared electronic link to the eConsent so the study participant can review information about the study with friends and family, which may make some participants more comfortable
- The use of a tiered consent may allow the participant to focus on the basic information without being overwhelmed

Additional information can be found in the Health Literacy guidance.

### 3.2.4 Other Vulnerable Populations

Other vulnerable populations may include those with physical disabilities (such as blindness or hearing loss) or with cognitive impairments (such as Alzheimer’s, brain injury, or Trisomy 21). They may also include those with diminished decision-making capacity that may be temporary, permanent, or progressive due to cognitive impairment illness, injury, or stress. Some of these populations require the consent of a LAR on behalf of the study participant (who then may provide assent). These variances in vulnerable populations lead to difficulties in using a paper-based form to consent all participants. Paper consent may increase the vulnerability of these participants by not providing adequate resources.
eConsent could possibly reduce the vulnerability of these study participants. Multimedia components could increase autonomy while alternative documentation options could decrease the likelihood of coercion.

Consider using certain multimedia components that may increase autonomy\(^7\) such as:

- Audio:
  - Listening to a recording of the consent instead of reading
  - Listening to and following along with a narrator reading the content
  - Advantageous for literate, blind populations
- eSignature:
  - Signature alternatives such as video recording or fingerprinting would improve the autonomy of certain study participants
  - Some populations, such as those with multiple sclerosis or arthritis, may not be able to hold a stylus or use their own finger to sign their names

EConsent would allow assents to be linked to the main consent signed by the LAR, improving tracking of consent completion. Refer to the Implementation Guidance for more information on the multimedia components and operational considerations.

### 3.2.5 Pregnant Partners

There is a special risk during pregnancy of possible birth defects or other sequelae with an experimental intervention. Partners of potential participants may need to consent when there is a possible risk with pregnancy or lactation during the study. Partners must be informed of the possible risks for pregnancy, birth, and lactation, and of the need for follow-up on the outcome (requirements may vary based on local regulations). Partners may be involved at the beginning of the study or later if the partner becomes pregnant.

EConsent is particularly suited to obtaining remote consent when necessary. For example, if the consent of a partner cannot be obtained because the partner is not available, efforts must be made to notify the partner of the study participation and possible risks through remote consent or other notification. If the partner is concerned but the study participant still wishes to participate, the partner should be told how to protect herself during the study and any safety follow-up period. Both of these activities can be made easier through eConsent.

If the study staff becomes aware of a partner pregnancy, birth, or lactation during the study, an effort should be made to reach the partner and inform her of the possible risks, and to ensure appropriate medical and safety follow-up of the pregnancy, birth, or lactation, and of any affected children. In these cases, the
partner consent can be electronically linked to the participant consent, aiding in the pursuit of follow-up safety information.

### 3.2.6 Legally Authorized Representatives

Some vulnerable population study participants may be unable to consent, such as pediatric participants (see Section 3.2.1). In these situations, a LAR, typically a parent, spouse, child, or legal guardian, makes a decision for the study participant. The LAR has an important role and information about the study must be easy for the LAR to understand. Multimedia components (described in The Guidance) may increase the ease of obtaining and comprehending this information.8

It may be possible to upload supporting documentation to the eConsent as evidence of the specific LAR relationship, e.g., adoption papers, birth certificate, or court decree. The added benefit is that the monitor can remotely monitor the documentation, if allowed within the specific country.

### 3.2.7 Study Partners (teachers, spouses, caregiver, etc.)

In some studies, additional people may be asked to provide insight and data about the research participant. Examples of study partners may include teachers providing educational and behavioral feedback on pediatric study participants in attention-deficit disorder studies, caregivers providing quality-of-life feedback on study participants in Alzheimer studies,9 or spouses providing feedback on physical interactions in erectile dysfunction studies. Study partner consent is key to ensuring that they have agreed to provide such important data.

A full, lengthy consent on paper may not be optimal, as study partners typically need only a reduced amount of information (e.g., no need to view original medical records, no need to provide drug or procedural risks). Study partners may be unable to attend the initial consent visit or their presence may not be appropriate. Obtaining documentation of study partner consent may be challenging for sites as they may have to rely on mail, email, fax, telephone, or the study participant.
Some suggested multimedia tools for use with study partners include:

- **Video:**
  - Because consent is simpler, a video can convey only the information needed for the study partner to decide to complete questionnaires, etc.

- **eSignature and remote consenting:**
  - Remote consent may be used with the study partner’s identity verified electronically, eliminating the need for a paper consent document to be sent home to the participant, have it signed and witnessed as required, returned by the participant, counter-signed by the site, and then a copy returned to the study partner. This reduces the burden on the study participant, the study partner, and the site, as well as the likelihood of issues with the consent documentation, as it is easily trackable and monitored.

Refer to The Guidance for more information on multimedia components and operational considerations and Section 3.2 for considerations related to vulnerable populations.
4 Background Resources


Institute of Medicine and Healthy People 2020


Lorenzen B, Melby CE, Earles B. Using principles of health literacy to enhance the informed consent process.


5. Aldoory et al. 2014


