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2 Abbreviations

BYOD  bring your own device
CAPA  corrective action preventive action
CRA   clinical research associate
CRO   contract research organization
CRF   case report form
CSF   critical success factor
CTMS  clinical trial management system
CTTI  Clinical Trials Transformation Initiative
eCOA  electronic clinical outcome assessment
eCRF  electronic case report form
EDC   electronic data capture
EHR   electronic health record
eICF  electronic informed consent form
ePRO  electronic patient-reported outcome
EU    European Union
GCP   Good Clinical Practice
GxP   good practice (guidelines)
HA    health authority
ICF   informed consent form
ICH   International Conference on Harmonization
IEC   independent ethics committee
IRB   institutional review board
IT    information technology
IVRS  interactive voice response system
LAR   legally acceptable representative
NPRM  Notice of Proposed Rule-Making
PHI   personal health information
QA    quality assurance
ROI   return on investment
SAE   serious adverse event
SOP   standard operating procedure
UAT   user acceptance testing
3 Introduction

3.1 Purpose of This Document

This document provides both insight on eConsent and practical guidance for sponsors and other stakeholders to facilitate more efficient and effective implementation of eConsent in a clinical study.

eConsent includes multimedia components, which can be used to develop an interactive and engaging informed consent experience, offering flexibility for diverse learning styles (e.g., auditory, visual). This document does not provide sample consent language, standards, or requirements, but rather provides information about various considerations and alternatives that sponsors may encounter in determining whether eConsent is a feasible approach and/or which eConsent multimedia components are a reasonably good fit for a specific study. This guidance document describes several eConsent multimedia components that can be used and provides guidance for sponsors to facilitate voluntary adoption of eConsent.

The language herein is purposefully generic so that sponsors may apply the information to their individual organizational structures and practices. Furthermore, unless otherwise stated, the order that information is presented does not indicate or prescribe a linear process or suggest any order of priority. Company standard operating procedures (SOPs) and other considerations may require activities to be performed in a specific order. In addition, vendor selection is not covered in this document; sponsors should follow their internal processes for vendor selection.

As eConsent becomes more widely used, the guidance may evolve. Industry adoption practices, information technology (IT) considerations and advancements, and any new regulatory requirements may require changes. Users of this guidance should defer to their internal subject matter experts in considering future changes.

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.

3.2 Quick Reference Guide for This Document

The topics discussed herein are shown in the table below and can be accessed via the hyperlinks.

<table>
<thead>
<tr>
<th>Question/Topic</th>
<th>Section</th>
<th>Link</th>
</tr>
</thead>
<tbody>
<tr>
<td>Could my company and its trial participants gain any benefits from eConsent?</td>
<td>Benefits and Considerations</td>
<td>Section 3.4</td>
</tr>
<tr>
<td>What multimedia components are potentially available for use in an eConsent solution?</td>
<td>eConsent Multimedia Components</td>
<td>Section 4</td>
</tr>
<tr>
<td>What issues might I face regarding adoption of eConsent at my company?</td>
<td>eConsent Pre-Implementation Considerations</td>
<td>Section 5</td>
</tr>
<tr>
<td>What are feasibility considerations for eConsent?</td>
<td>eConsent Feasibility Considerations</td>
<td>Section 6</td>
</tr>
<tr>
<td>What operational considerations need to be addressed?</td>
<td>Operational Considerations</td>
<td>Section 6.3 Error! Reference</td>
</tr>
</tbody>
</table>

DRAFT eConsent Implementation Guidance

V0.1
### 3.3 Introduction to eConsent

The foundation of an effective informed consent for clinical research studies is to provide study participants with the information that they need in order to make an informed decision as to whether they want to participate in the study. This includes an open discussion between the investigative site staff and potential clinical research study participant, with the informed consent form (ICF) serving as a tool for enhancing that dialogue and documenting that the participant provided consent.

The principle of informed consent, based on the Nuremberg Code and Declaration of Helsinki, is key to ethical conduct in clinical research. The Declaration of Helsinki, as originally published in 1964, stipulated that valid consent should be properly and freely provided, without pressures, threats, or persuasion. Consent is therefore not a simple yes or no response to a question, but a process by which potential research participants can decide if it is appropriate for them to participate in a study despite the potential risks and associated costs, and should ultimately ensure that the potential research participant completely understands what to expect.

International Conference on Harmonization (ICH) Good Clinical Practice (GCP) defines informed consent as a process by which a potential participant voluntarily confirms his or her willingness to participate in a particular study, after having been informed on all aspects of the study that are relevant to the participant’s decision to participate. Informed consent is documented with a written, signed, and dated informed consent form.

Due to many factors, informed consent (ICF) documents have become increasingly complex/technical, and more difficult for study participants to understand. Complicated study designs and specialized study participant populations make conveying the research objectives clear to the study participants more challenging. Inconsistent literacy levels and cultural diversity also complicate the development of ICFs. Study sponsors must find new ways to ensure that potential study participants are fully informed, despite the complex information provided.

In current practice, the ICF is generally presented on paper. **Electronic informed consent (eConsent) provides the same information, but in an electronic format using an array of multimedia components, as shown in Figure 1 (below). It is important to note that eConsent is not meant to replace the important discussion between the participant and site staff, but support it. As with traditional consenting, the site will continue to own the consenting process.**
Current informed consent practices make it challenging to meet the ethical obligation to adequately inform potential research participants, and thus sponsor companies are working to improve the informed consent process by adopting patient-centric tools to increase understanding and incorporating new technologies that participants can use to learn about potential research options. eConsent can serve these purposes by including elements that aid understanding of clinical research and study participation, in addition to the information provided in a paper ICF. Well-designed eConsent can better describe study features and procedures with videos or glossaries and other interactive components. These interactive components of eConsent, designed to meet the particular needs of a study population may provide many added benefits when combined with the conversation between the potential study participant and the research site. While this has broad benefit for study participants, eConsent may be particularly beneficial for children and individuals with lower literacy levels.

In addition to the benefits for potential study participants, eConsent may be advantageous for sponsors, sites, IRBs/IECs, HAs as described in the section below (Section 3.4).

### 3.4 Benefits and Considerations for eConsent

#### 3.4.1 eConsent Benefits

Some research has shown that paper-based ICFs do not promote consistent quality dialogue and informed decision-making. eConsent has the potential to improve the consent experience, increase quality, and reduce regulatory inspection findings. eConsent also complements risk-based monitoring of studies by enabling risk assessment through central and remote monitoring of consent activities. These potential benefits are described in greater detail below, some of which apply to more than one stakeholder (e.g., sponsor, site). The degree of benefit will be directly related to the components selected and their fit within a specific context.
Potential benefits of eConsent for study participants:

- Multimedia format increases readability and comprehension compared to a lengthy and complex paper document.
- Presenting the information with different multimedia components allows the study participant to choose their preferred method of learning.
- Study participants who are better informed about study procedures and requirements are more likely to make an informed decision about whether to participate in the study, can better manage their own study expectations, and can become active partners.
- Increased understanding
  - Better preparation for discussions on ICF content with site staff
  - Increased compliance with study procedures
- Special functionalities can be included to help special populations (e.g., visually impaired, children)
- Attractiveness of new technologies
- More engagement with consenting process
  - Empowerment
  - Ownership

Potential benefits for sites:

- Reduces audit and inspection findings
- Provides information about study participants’ level of understanding during the consent process
- Provides information about study participants’ perspectives of the quality of the informed consent process
- Reduces the need for complex and time-consuming explanations and supplementary study explanation tools
- Reduces paperwork and quality risks
- Lowers burden on site staff, allowing a focus on high-value activities, including specific study participant questions and concerns
- Reduces administrative burden of on-site monitoring activities by providing an increased amount of information within eConsent (e.g., glossary) to the study participant and also enabling some activities to occur remotely
- Ensures a consistent and complete explanation is given to all study participants
- Less administration time (e.g., automated reminders for consent amendments, potential for paperless systems)
- Improves management of overall consent tracking (e.g., re-consenting, consent withdrawal)
- Easier to check understanding of study
  - More time to go into more detail of the sections that are not well understood
  - Easier to help study participant’s understanding by answering the right questions
- Alert messages to site in case of eConsent errors or re-consenting need
- Increases participant compliance

Potential benefits for IRBs/IECs and health authorities as applicable:

- Reduces audit and inspection findings
- Improves the review/approval process
• Increases confidence in the informed consent process
• Improves development of a regulatory perspective on informed consent

Potential benefits for sponsors:
• Increases retention due to better understanding, in other words reduced drop-out rate
• Reduces audit and inspection findings
• Improves study participant compliance and may also improve recruitment, depending on study design/therapeutic area
• Streamlines on-site monitoring activities and complements risk-based monitoring by providing data in real time and enabling some activities to occur remotely
• Enables continued improvement of consent content based on information about what is not understood by study participants and concerns that prevent potential participants from enrolling
• Improves management of overall consent tracking (e.g., re-consenting, consent withdrawal)
• Improves timely/immediate identification of consenting issues by the monitor (rather than discovery after the fact)
• Increases quality and consistency
  o Data validity and protection (e.g., access controls and passwords)
  o Follow-up on errors can be achieved more easily/quickly and remotely
  o Identification and prevention of recurring errors (e.g., version control)
  o Timely re-consent notification linked to protocol amendments and safety updates
  o Fewer transcription errors (e.g., ICF date copied automatically into the electronic data capture [EDC] system) if this functionality is being used
• Improves productivity
  o May reduces site visit time monitoring ICFs so that Clinical Research Associates (CRAs) can concentrate on other site duties (e.g., safety monitoring).
  o CRAs can check data remotely without visiting the site to check details
  o Central team can review data in core systems/case report form (CRFs) for all sites
• Enables possible automated reporting of data in sponsor systems
  o Partial pre-population of monitoring visit reports prior to the site visit
  o Automated edit checks on completeness of ICF
  o Interdependency with core systems, e.g., interactive voice response system (IVRS), CRF, clinical trial management system (CTMS)
  o Alert messages to sponsor in case of eConsent errors

3.4.2 eConsent Considerations

Some limitations to eConsent include:
• eConsent is a new technology and not all components may not be acceptable in all countries. For example, country-specific regulations on eSignature validity and acceptance may result in some regions using paper for collecting the signature.
• Significant initial investment cost and resources needs
• Inexperience and lack of processes for health authorities, ethics committees, sponsors, and investigators in many countries/institutions
• Study participants’ limited experience and discomfort with the technology
• Setup time will be longer for eConsent compared to paper ICF.
• Approval times may temporarily be longer for eConsent due to initial IRB/IEC unfamiliarity with the technology
• Increased upfront work to tailor eConsent to special subject groups (e.g., children)
• Electronic distribution of signed consent form (compliance/IT security/data privacy)
• Subjects opting for the paper version might limit return on investment
• Need for backup system in case of failure and maintenance periods
• Other stakeholders (sites, sponsors, IRB/IEC, HA) may be reluctant to use new technology
• The need for additional translations of multimedia components may impact cost and timelines

4 eConsent Multimedia Components

This section provides an overview of generally available eConsent multimedia components and a non-exhaustive list of benefits, considerations, and guidance for implementation for each. The decision about whether and how to implement any one of these components rests with the sponsor at the design stage.

Various multimedia components that potentially could be used in eConsent are described along with benefits and considerations for each. The benefit/consideration for each potential component is focused on identifying impacted stakeholders. While the components may include examples of sample text or content, the examples are provided for illustration only and are not meant to propose or suggest model language that sponsors should use in their ICF or eConsent. Further, the components included here represent those currently available and mainstream at the time of publication. As technology evolves and matures, the depth and breadth of these multimedia components will also grow.

Where possible, it is generally considered a good idea to develop the components to minimize the need for non-value-added changes. For example, variability around topics such as birth control specifics and genetic risks may create complexity and increase cost by creating the need to have multiple versions of multimedia components (e.g., video) to meet local requirements.

Refer to Section 10.1 to view some publically available standardized ICF templates with examples of how eConsent multimedia components could be incorporated. These will demonstrate some practical application tips that may be considered.

The table below includes a summary of the multimedia components included in the section, as well as a brief definition.

<table>
<thead>
<tr>
<th>Multimedia Component</th>
<th>Definition/Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multimedia Tiered Approach</td>
<td>Tiered consent consists of a consent form that includes essential elements in a concise main section and more detailed information in later sub-sections</td>
</tr>
<tr>
<td>Video</td>
<td>Video provides a visual and potentially auditory overview of the study and promote participants’ better understanding of the selected content</td>
</tr>
<tr>
<td>Audio</td>
<td>Voice-over of consent document or other components, voice response elements</td>
</tr>
</tbody>
</table>
## 4.1 Multimedia Tiered Approach

### 4.1.1 Description of Multimedia Tiered Approach

Tiered consent consists of a consent form that includes essential elements in a concise main section and more detailed information in later sub-sections.

Tiered consent has recently been endorsed in the Notice of Proposed Rule-Making (NPRM) regarding the Common Rule in the U.S. It is also a Clinical Trials Transformation Initiative (CTTI) official recommendation and is already being used in the paper format in several countries including Belgium, the Netherlands, and Sweden.

A multimedia format for tiered consent, like eConsent, is particularly useful, because it allows study participants to move between different sections to learn more about specific items as needed, while tracking their movements between and within sections. Enhancements such as hyperlinks can facilitate this.
Example Tiered Consent

What will happen if you take part in this research study?

The study begins once you have received the first dose of the study drug and will end when you and the investigator agree that you should stop the study treatment. You will have 10 visits. The visits may include the following activities:

- A physical exam
- Discussion with the study site that will include an assessment of your ability to perform daily study tasks
- Measurements and imaging of your tumor that could include:
  - X-ray
  - CT and/or MRI
- Blood draws
- Questionnaires about your well-being

For more information, please refer to the detailed study treatment visit schedule. The detailed schedule will explain what you will do at each visit including what tests of samples will be taken, and what will be done with them. The study doctor will discuss the schedule in more detail with you.

<table>
<thead>
<tr>
<th>Screening Visit</th>
<th>On the Study Drug (Treatment Phase)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Visit 1</td>
<td>Visit 2</td>
</tr>
<tr>
<td>Procedures:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical History</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Physical Exam</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>ECG</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Urine collection</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Receive Study drug</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Blood collected</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Approximate blood draw amount in mL</td>
<td>45</td>
<td>70</td>
</tr>
</tbody>
</table>

May include physical exam, weight, vital signs, pulse, or blood pressure.

4.1.2 Benefits and Considerations for Tiered Consent

Potential benefits and considerations for tiered consent are described in Table 1.

**Table 1** Tiered Consent Benefits and Considerations

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increases readability, comprehension, and ease of use, and allows embedding of other multimedia components</td>
<td>Study participants, sites, IRBs/IECs, Health Authorities (HAs), and sponsors</td>
</tr>
<tr>
<td>Flexible method of learning that allows participants to choose how they want to use the material</td>
<td>Sites and study participants</td>
</tr>
<tr>
<td>Supports progressive, incremental disclosure</td>
<td>Sites and study participants</td>
</tr>
<tr>
<td>Mitigates against overloading incremental disclosure</td>
<td>Study participants</td>
</tr>
<tr>
<td><strong>Consideration</strong></td>
<td>Stakeholders Affected</td>
</tr>
<tr>
<td>Limited regulatory guidance and experience with the concept in some countries</td>
<td>Sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
</tbody>
</table>

When the study participant clicks on ‘detailed study treatment visit schedule’, the full visit schedule appears.
4.1.3 Guidance for Implementation

Discussion of informed consent content placement (e.g., main versus sub-sections) should include all relevant stakeholders. These may include medical, legal, and the study team.

4.2 Video

4.2.1 Description of Video

Videos can be used for different purposes, with an overall aim to provide a visual and potentially auditory overview of the study and promote participants' better understanding of the selected content.

Several video clips can be prepared independently, and then displayed separately or linked. The most common video sections/clips include how to use eConsent and a high-level summary of the study, which are outlined in detail below. Other video types may include complex procedures and disease-specific videos.

**How to Use eConsent Video**

The eConsent video should explain how to use eConsent and may include:

- What to expect from the eConsent process
- How to use the device (if applicable)
- How to navigate through the content
- How to use the different eConsent components, e.g.:
  - How to play the video
  - How to obtain glossary definitions
  - How to access hypertext links for additional information
  - How to tag content for later discussions with staff

**Study Summary Video**

The Study video should include a high-level overview of the study and explain key study participant rights. Consider that later changes during the study may be costly and time consuming and design the video to reduce the need for changes. Key topics may include:

- What is a clinical trial
- Purpose of the study
- Study design (duration, type of control [e.g., placebo], procedures)
- That the study has risks
- Participation is voluntary
- Data are kept confidential
Example of a video that explains certain study aspects:

Source: https://www.healthit.gov/providers-professionals/video/can-i-change-my-mind

4.2.2 Benefits and Considerations for Video Components

Potential Benefits and considerations for video components are described in Table 2.

Table 2 Video Components Benefits and Considerations

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>May provide more detailed information on general clinical research and study-related topics without increasing the length of the informed consent document</td>
<td>Study participants, IRBs/IECs, and sponsors</td>
</tr>
<tr>
<td>Study participants may better understand the study and could have more effective and tailored discussions of their questions and concerns with the site staff</td>
<td>Sites and study participants</td>
</tr>
<tr>
<td>Consistent approach to key concepts essential to making an informed decision</td>
<td>Study participants</td>
</tr>
<tr>
<td>Improved understanding on how to use the device</td>
<td>Study participants</td>
</tr>
<tr>
<td>Considerations</td>
<td>Stakeholders Affected</td>
</tr>
<tr>
<td>Some participants may only pay attention to visual aids and fail to read the full informed consent</td>
<td>Study participants, sites, and IRBs/IECs</td>
</tr>
<tr>
<td>Considerable cost/time impact due to site/country variability, protocol amendments, and translations</td>
<td>IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Visually impaired participants might not be able to use videos</td>
<td>Study participants and IRBs/IECs</td>
</tr>
<tr>
<td>Some study participants might prefer one video type over another (e.g., animation vs videos of people), or for example find animated videos too juvenile</td>
<td>Study participants and IRBs/IECs</td>
</tr>
</tbody>
</table>

4.2.3 Guidance for Implementation

- Introductory videos such as how to use the device may be included up front to ensure understanding of general concepts before starting the consent process.
- When determining which video types to use, consider the study participant population (age, gender, disease state, clinical study knowledge level, legally authorized representative involvement, caregiver involvement, and other factors).
- Videos should be clear, simple, and engaging and provide relevant information.
- Consider whether video text should be made available as a transcript.
- Specific segments of video could be used to reinforce key messages/information on an ongoing basis.
• Additional videos could be used to describe the disease state or other concepts (e.g., DNA, PET scan). These could be optional and accessible from the main part of the consent.
• Total video time should follow standard user engagement limits for the video medium to maintain engagement.
• Use diagrams and pictures more than text and language.
• Voiceovers and animation instead of live action videos may be easier to edit and thus less expensive.
• Use regionally acceptable practices and tools; for example, a study in Africa might benefit from a song format.
  o This example in a different context reflects this: http://www.takeandtell.org/#video
• Consider if previously created video clips such as standard company videos on what is a clinical study, disease, or compound-specific video clips from previous applicable eConsents may be re-used.

4.3 Audio

4.3.1 Description of Audio
Audio components could serve the following main purposes:
• Voiceover of consent document: provides an alternative for the participant to reading a long document; the study participant can opt to have the consent document read to them
• Voiceover of video content: supports comprehension of visual information
• Voiceover of other eConsent components: instructions and callout boxes may include voiceover

4.3.2 Benefits and Considerations for Audio Components
Potential Benefits and considerations for audio components are described in Table 3.

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provides alternative access to consent information and increased autonomy for visually impaired, blind, and low literacy study participants</td>
<td>Study participants, sites, IRBs/IECs, and sponsors</td>
</tr>
<tr>
<td>Allows study participants to choose how to receive the information (independent from actual literacy level)</td>
<td>Study participants and IRB/IECs</td>
</tr>
<tr>
<td>Potentially reduces time spent to ensure comprehension</td>
<td>Sites</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Literate participants who can read quickly may be frustrated by the slow audio pace</td>
<td>Study participants</td>
</tr>
<tr>
<td>Participants may be too embarrassed to use the functionality</td>
<td>Study participants</td>
</tr>
<tr>
<td>Voiceover translations if required may incur additional costs, time, and resources</td>
<td>IRBs/IECs and sponsors</td>
</tr>
<tr>
<td>Additional verification step required to ensure alignment to written consent text</td>
<td>IRBs/IECs and sponsors</td>
</tr>
<tr>
<td>May require additional space (isolated viewing areas) to avoid noise pollution</td>
<td>Sites and sponsors</td>
</tr>
<tr>
<td>May impose additional cost for equipment (e.g., headphones)</td>
<td>Sponsors</td>
</tr>
</tbody>
</table>
4.3.3 Guidance for Implementation

- Consider complete voiceover as an option for visually impaired, blind, and low literacy study participants.
- The study participant should be able to turn the audio on or off.
- Consider accent, pace, and gender of voiceover.
- The study participant should be able to adjust the volume and repeat/replay content.
- Assess upfront with sites whether a separate area is available for consents and/or if headphones may be used. If needed, consider who is providing headphones.

4.4 Pictures and Diagrams

4.4.1 Description of Pictures and Diagrams

Studies have shown that visual aids can help explain and reinforce key trial components or complex topics. Example topics include risk percentages, explanation of a serious adverse event (SAE), specific study procedures, and the study schedule.

Example Pictures
4.4.2 Benefits and Considerations for Pictures and Diagrams

Potential benefits and considerations for pictures and diagrams are described in Table 4.

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increases understanding of complex information and simplifies ICF information</td>
<td>Study participants, sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>May support processing of information through different modes</td>
<td>Study participants and sites</td>
</tr>
<tr>
<td>Might facilitate discussion of relevant topics</td>
<td>Sites</td>
</tr>
</tbody>
</table>

**Considerations**

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some information (e.g., risk percentages &lt; 10%) is difficult to show graphically and pictures could be misleading</td>
<td>Study participants, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Some participants might be intimidated or not feel comfortable looking at graphics/schedules</td>
<td>Study participants, sites, and IRBs/IECs</td>
</tr>
<tr>
<td>For studies with a wide age range, graphics that are acceptable for all age groups may be difficult to achieve</td>
<td>Study participants, IRBs/IECs, and sponsors</td>
</tr>
<tr>
<td>Some study participants may feel this is too juvenile or not beneficial</td>
<td>Study participants</td>
</tr>
</tbody>
</table>

4.4.3 Guidance for Implementation

- Ensure graphics are acceptable for the target population and are emotionally neutral.
- Ensure graphics are clear and not misleading.
- Ensure consistent format of visuals/graphics in eConsent and paper consent
- Limit graphics to places of maximum benefit.
- For multinational studies, ensure graphics are inter-culturally acceptable.

4.5 Callout Boxes

4.5.1 Description of Callout Boxes

Callout boxes can be highlighted text within the consent document (e.g., color highlights, framed text) or textboxes within the document or margin that summarize key information in 1 or 2 simple sentences to highlight and reinforce key ideas. Example topics include:

- The study is voluntary.
- Duration of the study
- There are risks to the study.
- Data are accessed and shared.
- Explain complex required language
Example Callout Boxes

This study has risks. The most common and severe risks are A, B, and C. Talk to your study doctor if you have questions.

Your information will be sent outside the country. Your information will be kept private.

4.5.2 Benefits and Considerations for Callout Boxes

Potential benefits and considerations for callout boxes are described in Table 5.

Table 5 Callout Boxes Benefits and Considerations

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>May increase knowledge and awareness of key concepts essential to making an informed decision</td>
<td>Study participants, sites, IRBs/IECs, and sponsors</td>
</tr>
<tr>
<td>May facilitate finding key information without having to re-read whole sections</td>
<td>Study participants, sites, and IRBs/IECs</td>
</tr>
<tr>
<td>Supportive tool to drive the discussion with a potential study participant</td>
<td>Sites</td>
</tr>
<tr>
<td>Considerations</td>
<td>Stakeholders Affected</td>
</tr>
<tr>
<td>Study participants may not read the other material or access the detailed reference sections</td>
<td>Study participants, sites, and IRBs/IECs</td>
</tr>
<tr>
<td>Discussions with the participant might focus only on the highlighted topics</td>
<td>Study participants, IRBs/IECs, and sponsors</td>
</tr>
<tr>
<td>Simplified or interpretive text may require additional review and/or time</td>
<td>IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Highlighted elements might be regarded as biased</td>
<td>IRBs/IECs and sponsors</td>
</tr>
<tr>
<td>Additional effort required within the study team to identify areas to be highlighted</td>
<td>Sponsors</td>
</tr>
</tbody>
</table>

4.5.3 Guidance for Implementation

- Ensure appropriate balance between regular text and callout boxes.
- Ensure language is simple.
- Should be limited to a few words or phrases (1-2 sentences).
- Only key information should be flagged.
- Recommend using one type of callout box rather than a mix of styles within one document.
4.6 Knowledge Review

4.6.1 Description of Knowledge Review

The knowledge review is a short set of questions that the potential study participant is asked to answer to highlight key information and concepts. While questions can be provided on paper, multimedia components allow for reinforcing the relevant content (e.g., by linking back to key content). Multimedia components may be useful for the knowledge review for several reasons:

- May promote active engagement and learning
- Incorrect answers direct the study participant to the relevant source information.
- Inform the site staff of information that could be discussed directly with the study participant

The knowledge assessment is intended to assess comprehension and guide the potential study participant to areas that may be worthwhile to re-review and/or discuss further with their study doctor. The intention is not to quiz study participants as a criterion for study entry.

Example of Knowledge Review

Question 1 of 4

Once I decide to participate in this research study, I can stop my participation...

- Only when the study is over
- After visit #5
- At any time/whenever I choose
- Between week #5 and week #10

4.6.2 Benefits and Considerations for Knowledge Review

Potential benefits and considerations for knowledge review are described in Table 6.

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helps to demonstrate that the study participant understands core concepts</td>
<td>Study participants, sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Potential for better structured and focused discussion between site staff and study participant based on real participant’s needs</td>
<td>Study participants, sites, and IRBs/IECs</td>
</tr>
<tr>
<td>Continuous improvement of consent language is easily possible based on real study participant experience and feedback</td>
<td>Study participants, IRBs/IECs, and sponsors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>May create anxiety or cause study participants to have negative opinions/embarrassment or to fear exclusion from the study or judgment by the study staff or third parties</td>
<td>Study participants, sites, IRBs/IECs, and sponsors</td>
</tr>
<tr>
<td>Expectations might arise regarding how to document the rationale to enroll participants who failed the knowledge review</td>
<td>Sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
</tbody>
</table>
May prevent a detailed discussion with a participant who answered all questions correctly | Study participants, IRBs/IECs, and HAs

Increased burden/approval delays due to change requests from individual IRBs | Sites and sponsors

### 4.6.3 Guidance for Implementation

- Limit the number of questions to focus on key concepts.
- Ensure that the language used to describe the knowledge review does not imply that this is a test or an assessment, for example “Let’s Recap”
- Consent of the questions should focus on key concepts to reinforce may include the study purpose, that the study has risks, voluntary nature, and confidentiality. If applicable, consider reinforcing that invasive and/or high-risk procedures/drugs are part of the study.
- Use true/false or multiple choice question formats; aids should be provided if the study participant answers incorrectly. The answer should be provided after a certain number of tries, and this information should be retained within the metadata.
- Communicate the purpose of knowledge review (to ensure key elements of the consent have been effectively provided and reinforced) to both the site and study participant.
- Communicate the purpose of the knowledge review up front and reassure potential participants that knowledge review results do not impact study participation.
- If a study participant answers incorrectly, the relevant source information should be displayed (e.g., screenshot popup, hyperlink). The study participant should be allowed to try again, if appropriate.
- Site staff should review metadata to identify any gaps in study participant understanding. The site staff should document in their site files or within the eConsent system (such as via a site comment section or checkbox) how they ensured the study participant understood key concepts.
- **Example questions:**
  - Does this study have risks? True or False
  - Common side effects that may be experienced while taking this compound might be a) increased urination b) dizziness c) constipation d) all of the above
  - Can you stop the study at any time? True or False
  - Once I decide to participate in the study, I can stop a) only when the study is over b) after being in the study for at least 2 months c) whenever I choose d) only if I’m having a side effect
  - Will your data be kept confidential? True or False
  - How long will the study take place? a) 10 weeks b) 20 weeks c) 30 weeks

### 4.7 Dictionary/Glossary

#### 4.7.1 Description of Dictionary/Glossary

While these terms are often used interchangeably, for the purposes of this document:

- A dictionary provides existing definitions of words.
- The glossary is a custom set of words/phrases defined by the sponsor and/or vendor.

Both dictionary and glossary terms are made available through standard user interface cues, including hover-over and highlight.
While explanations of complex words and phrases can be provided on paper, this is not as easy to use and lengthens the document.

**Example Dictionary Component**

<table>
<thead>
<tr>
<th>Definition</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gmail</td>
<td><img src="image" alt="Gmail Example" /></td>
</tr>
</tbody>
</table>

**Example Glossary Component**

<table>
<thead>
<tr>
<th>Glossary Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Study</td>
<td><img src="image" alt="Research Study Example" /></td>
</tr>
</tbody>
</table>

### 4.7.2 Benefits and Considerations for Dictionaries and Glossaries

Potential Benefits and considerations for dictionaries and glossaries are described in Table 7.

<table>
<thead>
<tr>
<th>Table 7 Dictionary and Glossary Benefits and Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benefit</strong></td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>Glossary provides definitions for unfamiliar words or phrases</td>
</tr>
<tr>
<td>Glossary terms can be tailored to the protocol/population needs</td>
</tr>
<tr>
<td>Glossary terms can be defined with graphics, color, video, etc., to provide optimal descriptions</td>
</tr>
<tr>
<td>Metadata created from use of the dictionary/glossary may help to improve overall ICF language</td>
</tr>
</tbody>
</table>
Facilitates document understanding and focus on content questions during the face-to-face discussion | Study participants, sites, and IRBs/IECs

Dictionary provides definitions through the operating system | Study participants and sites

Can review words at their own pace, without fear of judgment and without intervention from site staff | Study participants

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Words or phrases in a dictionary may have a study-inappropriate or no definition</td>
<td>Study participants, sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Dictionaries are not available in all languages</td>
<td>Study participants, sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Some words or phrases the participant does not understand are not defined in the glossary</td>
<td>Study participants and sites</td>
</tr>
<tr>
<td>Dictionaries are presented in text only</td>
<td>Study participants and sites</td>
</tr>
<tr>
<td>Creating a glossary is a time- and cost-intensive activity and might require internal discussion to arrive at the right definition</td>
<td>Sponsors</td>
</tr>
</tbody>
</table>

4.7.3 Guidance for Implementation

- Key words/phrases for clinical studies should be defined in the glossary for all studies (e.g., placebo, research study, sponsor, genetics/DNA, study treatment).
- Key words/phrases for the specific study should be defined in the glossary (e.g., disease state, study procedures, drug name).
- Glossary words, and when possible, dictionary words that are reviewed should be tracked by the sponsor to look for opportunities to simplify text.
- Glossaries may use videos, icons, or animation to define terms.
- When selecting vendors be mindful of the difference between dictionaries and glossaries and review sources for each.

4.8 Content Flags

4.8.1 Description of Content Flags

Content flags are used to mark or flag content or words/sentences where a study participant would like to ask a question to ensure his/her comprehension on the specific text. The participant could place an icon or highlight the content. Thus the participant does not have to recall questions and the flags provide a focus for follow-up conversation with the consent coordinator. Study staff should address each content flag prior to signatures. Sponsors should review the trends for flagged items to improve consent content and presentation for future consent activities.

Content flags may be combined with a comment box, described in Section 4.12, in which the study participant can document a specific question.

4.8.2 Benefits and Considerations for Content Flags

Potential Benefits and considerations for content flags are described in Table 8.

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creates metadata indicating where questions arose</td>
<td>Study participants, sites, and IRBs/IECs</td>
</tr>
</tbody>
</table>
## 4.8.3 Guidance for Implementation

The site should develop communication strategies to share information on flagged items and ensure that participant questions are answered.

### 4.9 Chapter/Section or Continuous Content Views

#### 4.9.1 Description of Chapter/Section or Continuous Content Views

Some vendors divide content into discrete sections, with scrolling available within the section, while others allow scrolling through the entire content.

#### 4.9.2 Benefits and Considerations for Chapter/Section or Continuous Content Views

Potential benefits and considerations for chapter/section or continuous content views are described in Error! Reference source not found..

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shorter sections may facilitate navigation within the document and lessen intimidation due to complex content (chapter/section view)</td>
<td>Study participants, sites, IRBs/IECs, and sponsors</td>
</tr>
<tr>
<td>Supports easier comprehension of material, allows for continuous improvement using metadata, and enables remote monitoring (chapter/section view)</td>
<td>Study participants</td>
</tr>
<tr>
<td>May require less pre-production editing (very useful for amendments), which may affect the cost of changes (continuous content view)</td>
<td>Sites, IRBs/IECs, and sponsors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consideration</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous scrolling may not support tiered consent (continuous content view)</td>
<td>Study participants, sites, IRBs/IECs, and sponsors</td>
</tr>
<tr>
<td>May be little value in forcing section breaks and may be more distracting than a continuous flow (chapter/section view)</td>
<td>Study participants and sponsors</td>
</tr>
</tbody>
</table>

#### 4.9.3 Guidance for Implementation

- If the sponsor prefers to have the user acknowledge that each page was read and understood, it may be preferable to use a section-based approach.

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Sites can use metadata to better frame informed consent discussion when segmented. Sites will have to document, e.g., how they ensured that study participants understood when they only spent 1 minute on the risk section. However, time spent should not be used out of context. For example, some people may speed through certain elements of the consent because they had a copy to review prior to initiating the eConsent.

### 4.10 Section-based Participant Attestation

#### 4.10.1 Description of Section-based Participant Attestation

Some vendors have developed a sliding tool for the participant to indicate “yes, I understand” or “no, I have a question” at the end of each section. This requires that the informed consent content be split into separate sections and is different from a blanket attestation, essentially a signature at the end of the document. Section-based attestations do not replace a signature.

#### 4.10.2 Benefits and Considerations for Section-based Participant Attestation

Potential Benefits and considerations for section-based participant attestation are described in Table 10.

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decouples information from consent; enables application development, improved education, and a movement toward progressive consent</td>
<td>Study participants, sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Metadata indicate which sections raised the most concerns and enables remote monitoring of long each participant spent per section, allowing queries</td>
<td>Sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Ensures no segment of the consent is missed</td>
<td>Sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td><strong>Consideration</strong></td>
<td><strong>Stakeholders Affected</strong></td>
</tr>
<tr>
<td>Requires ongoing interaction from a study participant that may feel redundant or time-consuming</td>
<td>Study participants, sites, and sponsors</td>
</tr>
<tr>
<td>Edits to consent language may be challenging to incorporate, increasing time and cost</td>
<td>IRBs/IECs and sponsors</td>
</tr>
</tbody>
</table>

#### 4.10.3 Guidance for Implementation

Development and reuse of modular sections supports efficient consent development and reduces redundancy and inconsistencies.

### 4.11 eSignature

#### 4.11.1 Description of eSignature

When considering the use of eConsent on-site, the authentication/confirmation of study participant identity by the site is unchanged. However, the number of signature types that are available in eConsent increase. Each sponsor will need to evaluate the use of the different signature options with local requirements. The following are European Union (EU) signature categories:

- **Electronic signature**: electronic data attached to or logically associated with other data and which serve as a method of authentication
Advanced electronic signature: meets the following requirements: uniquely linked to the signatory, capable of identifying the signatory, created using means that signatories can maintain under their sole control, linked to the electronic document to be authenticated. This ensured that any subsequent change in that document is detectable.

Qualified certificate: must include an indication that it is issued as a qualified certificate, identification of the certification-service provider, the name of the signatory, the possibility to include a specific additional element of authentication of the signatory such as a date of birth (depending on the intended purpose of the certificate), signature-verification data that correspond to signature-creation data under the control of the signatory, beginning and end dates of the certificate’s validity, identity code of the certificate, and the advanced electronic signature of the issuing certification service provider.

Example eSignature

4.11.2 Benefits and Considerations for eSignature

Potential benefits and considerations for eSignature are described in Table 11.

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date and time of consent are automatically recorded, reducing the risk of human error and number of audit/inspection findings</td>
<td>Study participants, sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>The signature is embedded in the eConsent process on the device and therefore reduces the probability that the consent signature is forgotten</td>
<td>Study participants, sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Populations with motor skill issues or certain physical impairments can sign electronically more easily</td>
<td>Study participants, sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>The site monitor can remotely monitor the consent process and ensure more quickly that the consents are appropriately signed</td>
<td>Sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>No need for a pen</td>
<td>Study participants and sites</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consideration</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electronic signatures are not universally accepted for signing ICFs though often accepted for other legal matters</td>
<td>Sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Countries/IRBs/IECs may have varying requirements</td>
<td>IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Participants may have objections to eSignature (lack of trust, privacy concerns)</td>
<td>Study participants, sites, and sponsors</td>
</tr>
</tbody>
</table>
4.11.3 Guidance for Implementation

- Allowing study participants to sign via eSignature in all countries would create significant efficiencies, but given differing views around the world on the acceptability of eSignatures, initially workarounds will be needed in some countries. If not using eSignature, it is more difficult to enable risk-based monitoring; a dual system (paper and electronic) must be maintained, and there may be increased risk for audit findings.
- eConsent can be printed by the site and the study participant can be asked to sign/date with a wet signature as a potential workaround for eSignature. The signed consent would be either uploaded into the system OR the study site would have to document in the system that the study participant signed the consent form.
- Evaluate the regulatory and legal requirements within each country and its impact to operations.
- Some countries (e.g., the UK) require 24 hours between receiving and signing/countersigning the ICF in order for participants to have sufficient time to consider the implications.
- Ensure that eConsent will allow for capturing this information or that there is built-in functionality to only allow signatures after the lag time requirements are met.
- Other methods may be used for documenting consent can also include the fingerprinting, voice recording (maybe in addition to other documentation; consider whether this would be used for the full consenting process or just the actual consent), and a health ID card (e.g., pin code/passcode/username/user ID card). For additional information, please see Operational Considerations in Section 6.3

4.12 Comment Boxes, Free Text Fields, and Study Participant Note Logs

4.12.1 Description of Comment Boxes, Free Text Fields, and Study Participant Note Logs

Comment boxes, free text fields, or logs may be added, allowing the eConsent to become the source document for all elements of the informed consent process. Comment boxes may be implemented for use by the site and/or study participant.

- Site comment box: free text fields for the site to record informed consent documentation
- Study participant comment box: free text fields or a contiguous note space to record notes/clarification about the informed consent or write down any questions.

Example Comment Box
4.12.2 Benefits and Considerations for Comment Boxes

Potential benefits and considerations for comment boxes are described in Table 12.

Table 12 Comment Boxes Benefits and Considerations

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study participant comment box allows study participants to note specific questions within the eConsent content</td>
<td>Study participants, sites, HAs, and sponsors</td>
</tr>
<tr>
<td>Note log provides study participants one location to document notes about the informed consent process</td>
<td>Study participants, sites, HAs, and sponsors</td>
</tr>
<tr>
<td>Site comment box enables remote monitoring</td>
<td>Sites, HAs, and sponsors</td>
</tr>
<tr>
<td>Comments to be readressed during face-to-face discussion can be directly entered when and where these arise, facilitating the discussion</td>
<td>Study participants, sites, and IRBs/IECs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consideration</th>
<th>Stakeholders Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitive personal information may be inadvertently shared or information provided that could unblind the recipient</td>
<td>Study participants, sites, IRBs/IECs, HAs, and sponsors</td>
</tr>
<tr>
<td>Participants with low computer literacy might not be able or willing to use this feature</td>
<td>Study participants and sites</td>
</tr>
</tbody>
</table>

4.12.3 Guidance for Implementation

- Comment boxes can be used to allow free-form text annotation to aspects of the consent that are of interest or points of the consent requiring additional clarification. This in-line notation of specific feedback by the participant can be printed to support the participant’s recall of the answers provided or to reinforce specific content.
- Comment boxes can also be used by the study site staff to annotate anything for reference. It may be useful to have study participant comment boxes be acknowledged by site staff to ensure follow-up was documented.
- Consider whether you want to retain the study participant’s comments. Study participants may not be comfortable with their personal notes becoming part of the study record. This may be more acceptable if the comments are not retained after the study participant signs the consent and only exist as a temporary record.

5 eConsent Pre-Implementation Considerations

eConsent Pre-Implementation considerations should be assessed at different study phases (i.e., startup, execution, and closeout), as these phase-level considerations may have an impact on the overall success of implementation. These include but are not limited to organizational and study team objectives and the scope of vendor services required.

5.1 eConsent Objectives Planning

If an organization is considering piloting/implementing eConsent, it may be useful to document in detail what the organization requires, what it wants to achieve, and any associated impacts. Ideally, this should already align with an organization’s overarching objectives (if not, this may warrant further high-level discussions), and these objectives should be included in the business case (Section 5.3). Companies who do not have internal eConsent experience may consider working with a vendor to develop these objectives.

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The objectives of eConsent must be carefully reviewed and assessed against the needs of both the organization and study team so that both short- and long-term alignment can be attained. Study-specific considerations for planning are covered in Section 6.1, eConsent Study Considerations.

### 5.2 eConsent Impact Analysis

In order to better outline impact, consider the process by which you will operationalize eConsent. By dividing the process into a defined sequence of steps such as planning, development, monitoring, and closeout, it may be easier to identify required tasks, timing, roles, and responsibilities and to ensure all impacts are assessed.

**Illustrative Process for Operationalization of eConsent**

In the sections below, some detailed implementation considerations for assessing impact are provided:

1. eConsent Start-Up Timeline Considerations
2. Privacy/Data Considerations
3. Information Technology Diligence Activities
4. Organizational Impact Analysis
5. Stakeholder Impact Analysis

#### 5.2.1 eConsent Start-Up Timeline Considerations

Ensure full understanding of the timelines for eConsent setup and how this fits into the study timeframe. For initial studies using eConsent, it can take approximately 5-7 months to set up eConsent from vendor.
selection to first participant enrollment, so it is important to determine if eConsent is appropriate as early as possible. Consider the following:

- Vendor selection and final contract execution and the impact on study milestones
- Any changes to the design that would have an impact on timelines to develop the system
- Any translations that need to be made for the study
- IRB/IEC submission documentation and approval process
- Shipment and importation requirements for eConsent devices (country-specific regulations)

Potential vendors should be assessed to determine if they meet the particular sponsor’s policies and requirements, usually through vendor qualification. Ensure that the appropriate department is involved so that this assessment is completed during vendor selection.

The time needed to develop eConsent tools before a study must be considered in the overall study timeline. Figure 2 shows an example timeline, including time for translations if needed, which can be adapted consistent with the sponsor company practices.

### Figure 2  Example eConsent Start-up Timeline

| Week   | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 |
|--------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| RFP and vendor selection |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Contracting and negotiations |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Kick off |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Develop key messages and wireframes |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Iterations |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Review and approve content |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Security risk assessment and data classification |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Internal Study approvals (Reg, Legal, Comp.) |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| System configuration and testing |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Translations (if required) |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Submit to IRB/IEC/Has |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Training Preparation |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Training sites |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Deploy to sites |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |

#### 5.2.2 Privacy and Legal Considerations

In anticipation of the start of an eConsent study, plan for a conversation with internal legal and/or data privacy contacts to ensure the following is being considered:

- Review country-specific regulations or requirements to provide the ICF in electronic or paper format
- Ensure a process for availability of local legal and/or data privacy review, if needed, is in place for the duration of the study.
- Check any company-specific requirements or policies (e.g., SOPs)
- Considerations for eConsent components;
  - Evaluate the multi-media components (Section 4) for privacy, legal, and other processes.
  - Knowledge review: eConsent can provide documentation of knowledge review. Therefore:
    - When a sponsor elects to include a knowledge assessment as part of the eConsent process, the sponsor should discuss the process and confirm the importance of ensuring that the knowledge
assessment is taken prior to the subject signing consent. This information can also be shared with the study participant within the eConsent module (Section 4.6). This will help to ensure that the study participant fully understands the objectives of the research study and is fully informed.

- Are there additional responsibilities for the sponsor to track assessments?
  - Videos: ensure that any video or other supplemental information does not include any unintentional branding/promotion.
  - Be aware of the diversity of the study participants and the impact of the choice of media to be used.
  - Ensure the eSignature method (e.g., ID card, on iPad, thumbprint, secure code, handwritten signature on an electronic device) aligns with local regulations and the study participant demographics (Section 4.11).

- Location of the database and IT administrators: consider any applicable regulations (e.g., EU Safe Harbor regulations)
- Security of the eConsent device and participant-provided/site-provided device: Is there appropriate access control? How does the eConsent technology protect the study participant’s sensitive personal health information (PHI)?
- Security of the database: Is there adequate access control and an audit trail? How does the eConsent protect the study participant’s PHI?
- For remote monitoring with access to the portal from off site: What type of information (e.g., study participant identifiers) can be viewed remotely through the eConsent process? How will confidentiality be ensured?
  - The monitor should only access the system in a secure/private environment.
- Are there additional responsibilities for the sponsor to provide additional tools or guidance for sites, such as requiring a teach-back method, additional review of ICFs prior to signing, or ensuring provision of the paper ICF to study participants prior to signing the consent?

Consult with legal/regulatory experts at your company to determine applicable legal requirements in the relevant jurisdiction and to keep up to date on changes in relevant laws and regulations that may impact the use of eConsent.

5.2.3 Information Technology Diligence Activities

After considering legal and privacy considerations, sponsors should address IT questions regarding system and data security. Depending on the company SOPs or guidelines, different departments may need to be involved (data protection, data sciences/data management, IT, quality assurance [QA], legal, procurement, operations, etc.). These due diligence activities may need to be reviewed regularly to meet evolving regulatory and legal requirements. Some topics to consider include:

- Information classification (i.e., is there identifiable personal information or sponsor confidential information)
- Architecture review:
  - Regulatory risk (whether full validation is required)
  - Project security (includes review of access controls)
  - Mobility standards
  - Plan for application support (including lifecycle management)
- Operational security (security audit logs, software assurance, host architecture, infrastructure, and platform security)
• Identity and access management (authorization, identity provisioning, authentication, key management, encryption, credential compromise or theft, identity and access management)
• Business and continuity management (disaster recovery, backup, incident management, vulnerability testing/malicious software, hardware and software prerequisites, data and service portability)
• Legal requirements
• Privacy review
• Good practice (GxP) compliance

5.2.4 Organizational Impact Analysis

When planning to add a new functionality or capability, an organization should consider the impact across the organization. Because the use of eConsent may bring about new activities or the need for specific skills, an organization’s management may need to redefine roles or consider impacts to the organization and across internal stakeholders. Ensure appropriate awareness and communication to those involved stakeholders as a part of the change management plan. Highlighted below are some potential approaches an organization may consider:

• Creating a new role or group that is responsible for eConsent
  o **Benefits:**
    ▪ Focused understanding of eConsent
    ▪ Potentially skilled on the use of multimedia technologies
    ▪ May reduce timelines
    ▪ May serve as subject matter experts and consultants for additional eConsent studies going forward
    ▪ Increased consistency in implementation of eConsent
  o **Considerations:**
    ▪ Cost (may increase head count)
    ▪ More coordination to add an additional member to the study team

• Adding additional activities to existing study team
  o **Benefits:**
    ▪ Likely no impact to head count
    ▪ Growth opportunity
    ▪ Consistent with industry trends
  o **Considerations:**
    ▪ Bandwidth of resources considering existing responsibilities
    ▪ May limit the consistency in the approach to eConsent at the company level

5.2.5 Stakeholder Impact Analysis

*(Content under development)*

5.3 Business Case

*(Content under development)*
eConsent Feasibility Considerations

Implementation of eConsent in small-scale studies is encouraged as a preliminary step before implementation in large-scale clinical trials and overall organizational implementation. Results from pilot studies will help identify strengths and limitations of eConsent use and operational application within the specific organization. It will signal the need for potential modifications in essential elements or design before eConsent is fully implemented. Demonstrating an overall ease of implementation, use, and stakeholder satisfaction will enhance the probability of successful adoption in subsequent large-scale application. The following considerations are suggested when assessing study-specific feasibility:

1. Review Study Considerations (Section 6.1)
2. Define desired Multimedia Components (Section 6.2, Section 4)
3. Review Operational Considerations (Section 6.3)
   a. Device Management and Technology Availability/Capability
   b. Additional Consent Considerations (e.g., re-consent, optional consent)
4. Consider Data Privacy and Legal Considerations (Section 6.4)
5. Define Stakeholder Roles and Responsibilities (Section 6.5)

As eConsent may be a new way of working or novel technology for the organization, it is important to be flexible and embrace new ways of working.

6.1 Study Considerations

In the sections below, study considerations are provided for each of the topic areas:

1. Study design and complexity
2. Region(s)/countries(s)
3. Clinical sites
4. Study size and study participant population
5. Language

These considerations are provided for informational purposes and should be reviewed against company policies, preferences, etc. It is important to note that the detailed considerations provided below are primarily geared towards pilot studies; however, they should also be taken into account and modified for larger or more complex studies. The following could be taken into consideration when determining feasibility of using eConsent in a clinical study.

6.1.1 Study Design and Complexity

- Study phase considerations:
  o Can potentially begin with an small scale study that includes fewer countries/sites
  o Can potentially begin with a late-phase study with a simple, straightforward study design
- Limit the number of different types of consents to be used (e.g., biomarker analysis, bio-banking)
• Consider the feasibility and complexity of the study population (age, awareness of technology, and cognitive ability of study participants) and therapeutic area (e.g., oncology, pediatrics, emergency situations may require additional considerations).

• Consider the possibility that sites may have relatively more limited knowledge and understanding of eConsent if they have more limited exposure to and use of eConsent and eConsent tools, which might occur at sites with lower recruitment.

Consider the pilot design for eConsent, which should be linked to the objectives and metrics for an organization’s pilot. These objectives/metrics may be included in the organization’s business case (Section 5.3).

Several illustrative examples of pilot designs are provided below:

• Pilot design example 1: All study participants receive eConsent

• Pilot design example 2: A percentage of the study participants receive eConsent, and the rest receive paper. This enables comparison of DIFFERENT participant experiences with eConsent versus paper.

• Pilot design example 3: All study participants start with eConsent and later receive a paper-based consent after the first amendment. This enables direct comparison of the SAME participant experiences with eConsent versus paper.

6.1.2 Regions/Countries

• Choose a small number of countries, bearing in mind the requirements needed (may be different for pilot or full-scale implementation), which include:
  o Good technological capabilities, availability, and access to the internet (can be assessed through a feasibility questionnaire)
  o Established process and communication flow with the HA and IRBs or IECs for submission and approvals of consent materials
  o Determine any local requirements, privacy/confidentiality considerations, cultural considerations, and if eSignature is allowed by HAs and IRBs/IECs

• Work with a vendor to assess experience with eConsent submissions/approvals in the countries chosen and IRBs/IECs used

• Balance between central and local IRB/IEC, where possible

• It is an option to use eConsent in some regions/countries/sites and paper consent in others within the same study. This also holds for a country where the IRB/IEC may allow for some sites to use the technology but not others. If such a hybrid approach is used, differences between the countries/sites that are using eConsent and those that are not may be analyzed (using established metrics).

6.1.3 Clinical Sites

• Helpful to know if sites are open to innovation and a change in routine procedures, including a general interest in shaping the future of clinical studies
  o Can be assessed through feasibility questionnaire
  o Staff willing to use eConsent
  o Experience with similar clinical technologies (e.g., electronic patient-reported outcome [ePRO] or electronic clinical outcome assessment [eCOA]) could be an advantage
  o Open to provide feedback in order to improve the technology

• Technology: conduct a feasibility exercise to gauge the following capabilities. If certain capabilities are not available, consider possible alternatives to support the site (e.g., if no internet access, provide the site with a modem).
• Internet access
• Internet bandwidth
• Institutional approvals (e.g., firewall access)
• Availability of device use such as phone, computer, tablet, 3G card, etc.
• Ability to connect with a printer

• Varying levels of review may be needed for processes and procedures

6.1.4 Study Size and Demographics

• The size of the study is an important factor, and this should be taken into account when choosing a study for a pilot.
  o If a larger trial is chosen for the pilot, complexity may be reduced by limiting the number of sites that will use eConsent.
• Determine whether specific eConsent multimedia components would be of benefit to study participants with vulnerabilities or limitations (see Section 10.2).
  o Age (e.g., video, audio, pictures and diagrams)
  o Education level (e.g., dictionary/glossary, video, audio, pictures and diagrams)
  o Culture
  o Economics
  o Disease considerations (e.g., audio, video, signature)
  o Family, spousal support, and caregiver considerations
  o Family and spousal willingness to use technology if signing on behalf of study participant

6.1.5 Language

• If multiple languages are being considered, ensure additional time is allotted - if needed - for translations of eConsent-specific screens/features and voiceovers.
  o Determine if translations will be done locally, outsourced to CRO, or done by a vendor as per the sponsor’s SOPs.

6.2 Considerations for Identifying eConsent Multimedia Components

Consider the following when putting together the multimedia components desired for the study:

• The number and type of multimedia components that are used in the eConsent should be taken into considered, particularly if this is the first time this technology is being used within the company.
• Use the study considerations developed in Section 1 to do a deep dive into the multimedia components (Section 4) and decide what would be nice to have versus needed.
• Involve team members from different functional areas who will have a stake in the end product and therefore have different ideas about functionalities, uses, etc. (reference stakeholder impact assessment [Section 5.2 Error! Reference source not found.] for a detailed description of potentially impacted functional areas.)
• Check with colleagues, who may already have experience with eConsent, to seek advice and to determine if any details have been missed.
• Consider input from sites.
• Create clear criteria that a potential vendor may use to customize their product demonstration.
6.3 Operational Considerations

eConsent is a new technology and thus associated operational considerations should be taken into account when planning its use. Lessons can be learned from similar technology implementations and applied to eConsent. Some examples are provided below.

6.3.1 Device Management (On-Site Consenting)

For on-site eConsent, not remote, devices can be provided in multiple ways, including vendor/sponsor-provided or site-owned devices. (Note: Bring your own device is mentioned in Future State, See Section xx)

When deciding which provisioning option to use, consider potential issues with importing information from the device. Some vendors allow multiple devices with web-based access while others load software onto a single device.

- **Vendor- or sponsor-provided site device**: only 1-2 devices are usually provided per site depending on anticipated recruitment and needs of the site.
  - **Benefits**: ensures that the device has the appropriate operating system to perform eConsent with adequate security management and facilitates helping the site with device management and issues
  - **Considerations**:
    - Sites working on multiple studies with different vendors may have many different devices that they need to store securely.
    - A limited number of available devices may impede adoption of eConsent, especially for high enrolling sites or sites with many satellites, and will necessitate careful planning of study visits to ensure that a device is available.
    - Technology, privacy, and/or system considerations: evaluate the impact of sites using 1-2 devices per study, including connectivity issues due to the sites’ firewalls
- **Site-owned device or site-owned computer with signature pad/consenting option**
  - **Benefits**: limits the number of required devices
  - **Considerations**:
    - Would need to ascertain whether multiple operating systems could be used, how system upgrades would be handled, and whether device availability would be a requirement
    - Evaluate whether a single signature pad may be used for all studies or whether each sponsor would have to provision a signature pad.

Other considerations:

- It is important to establish a device shipment plan that considers restrictions on importation, import license requirements, and potential shipping and custom delays. Refer to Study Considerations in Section 6.1 for region/country-specific considerations.
- Consider a plan in case of system failure and the availability of a paper backup process.
- Consider whether other technologies are in use for other studies (e.g., ePRO/eCOA, eDiary).
  - **Consider the appropriateness of using the same device as used for other assessments in that study (e.g., add eConsent tools to a tablet used for capturing QoL questionnaires).**
Evaluate whether eConsent can be incorporated with other devices. However, some systems may have features that make it difficult to include eConsent and an eCOA or ePRO on the same device. Data plans and the possible impact on cost would also need to be evaluated.

Consider other new technologies that the site is implementing to avoid overwhelming the site with yet another new technology.

6.3.2 Re-consent

Re-consent of study participants may be needed as a result of changes to the study design or risks that require updates to the consent document. eConsent may be especially useful in cases where re-consent is required.

**Benefits:**
- eConsent offers different options for re-consenting to new versions of an ICF and can facilitate this process for both the sites and the study participants. Sponsors must evaluate which option is feasible based on their SOPs and what is deemed acceptable by the IRB/IEC.

**Considerations:**
Re-consent can occur remotely, i.e., outside the study site (see remote consent) or on site. For on-site re-consent, consider the following review options:

- Review the entire new consent, which currently is the most commonly used method for paper consents. The study participant reviews the complete updated eConsent on the device, including sections that were not amended.
- Review summary of changes from the previous signed eConsent: shortens the review time and can increase understanding of the relevant changes

Some IRBs/IECs may object to presenting only a summary of changes. The following approaches may both facilitate study participant understanding of changes and comply with IRB/IEC expectations:

- Review summary of changes with a link back to the entire consent: allows for a targeted review of the relevant changes while providing access to the whole updated consent form so participants may review other sections that are not impacted
- Direct the study participant to specific changes only within the full updated eConsent.

In addition to consent text, other components (e.g., video, glossary terms) may require updating to ensure consistency of the information within the eConsent.

6.3.3 Optional Consent

Some studies include additional optional activities (e.g., optional procedures, notification of primary physician, biobanks) that the study participant does not have to agree to in order to take part in the study. The additional consent may be part of the main consent or a separate addendum ICF. eConsent can facilitate incorporating the optional consent into the main consent.

**Benefits:**
- Ensures that the sections are appropriately completed (e.g., only 1 answer can be selected, yes or no)
- Allows for consent choices to be easily tracked at individual, site, or study level
- Potential to link to other systems such as labs and biobanks (see future state, Section 9)
**Considerations:**

- Ensure the additional activities are appropriately linked to the main consent, e.g., lack of consent to a required additional activity may flag the main consent.

### 6.3.4 Withdrawal of Consent

Regardless of the method of consent, study participants have the right to discontinue participation at any time, and the reasons for withdrawal, if available, must be properly documented by the site staff. Whether the participant chooses to withdraw or the sponsor terminates the study or site, eConsent facilitates documentation and collection of information consistent with the requirements of electronic data capture (EDC). This information includes the following:

- Reason for withdrawal
- Date and time of withdrawal
- Provision of instructions to the study participant by site personnel (e.g., follow-up visits, handling of data, withdrawal from certain activities)

A separate consent option may be used to document withdrawal of consent within eConsent. The site may also choose to track withdrawal of consent for specific participants within the system.

**Benefits**

eConsent can facilitate clearer documentation of the withdrawal status for a study participant and allows for planning and handling of possible participant withdrawals by providing the following:

- Easy, expeditious collection of participant withdrawal information
- Better documentation, depending on components acquired in the system
- Management of data and samples collected and tracking of rationale for withdrawal
- Country- or region-dependent differences (i.e., ensuring regulatory compliance for choices other than withdrawing through site visits)

If a study participant withdraws consent, eConsent may facilitate data reconciliation with other systems (e.g., EDC, lab results).

### 6.3.5 At Home or Remote Consenting

Although consenting is usually done at the site, some country regulations may allow using methods other than a face-to-face interview to obtain informed consent as long as basic informed consent principles are followed.

A meaningful exchange between investigator and participant is critical rather than the method of information exchange. eConsent could provide a first key solution for obtaining consent in:

- Remote studies (observational, pre-screening, or interventional studies); consider increased risk levels in interventional studies where a legal, privacy, or medical assessment may be needed.
- Consent and re-consent process in (ongoing) studies

There are different degrees or levels of at-home or remote consenting:

- The participant is introduced to the study at the site but can review all documentation at home with his/her family and make an informed decision to participate or not at home (partially remote).
- The participant is NOT introduced at the site but becomes aware of the study via another channel (e.g., social media, pharma company website) and can be fully remotely consented. Full remote
consenting might also be a first step towards full virtual trials, where all assessments are occurring at the participant’s home.

**Benefits:**

- Most important: allows for convenient consent (e.g., comfort level, time) at the study participant’s home or elsewhere
- May improve the study participant’s quality of life
- Allows for full remote consenting, without dependence on site-staff. Participants are becoming much more active, want to be involved in deciding the best treatment, and may look for this information on the internet.
- Allows easy sharing of information

**Considerations:**

- The sponsor must make sure that the remote consent is compliant with all (local) regulatory requirements, especially access and privacy regulations, to ensure that the right participant signs the right consent, which can be achieved by using controlled access and password accounts.
- Because informed consent requires information exchange, consider augmenting remote consent or re-consent with telemedicine (e.g., video chat, instant message, phone call, email) with the study site or providing initial consent only after an initial study site visit (e.g., after medical records are provided) or for re-consent, with another on-site visit to re-confirm participation in person. This is especially important for fully remote consenting.
- Telemedicine documentation may need to be retained, depending on applicable requirements.

Overall, remote re-consent allows for quicker provision of new information to the study participant, reducing the risk of missing important safety information and allowing easier access to gain consent, e.g., for follow-up samples or additional study procedures. Remote consenting might kick off a digital pathway for communicating with the participant, with benefits such as re-sending parts of information or video as preparation for a new visit and digital support.

### 6.3.6 Other Methods of Documenting Informed Consent (other than a signature)

eSignature is discussed in Section 4.11. Other methods may be used for documenting consent in some cases:

- Fingerprinting
- Voice Recording (maybe in addition to other documentation): consider whether this would be used for the full consenting process or just the actual consent
- Pincode/passcode/username/user ID card such as Health ID card

**Benefits**

Other methods of documenting consent may be options for typical study participants, those with disabilities (such as missing limbs), or those who cannot write. They may also be used when the signature cannot be witnessed, perhaps during remote consent. These alternate methods may streamline compliance with the additional country-specific mandates.

**Considerations**

Alternative methods of documenting consent may not be allowed in all countries. Determine how evidence of consent would be recorded and stored, and consider whether these other methods would be
used for the initial consent or limited to re-consent. Evaluate the impact to timelines and IRB/IEC approvals.

6.4 Privacy, Legal, and Other Processes

- Other considerations, including privacy, remote monitoring, and fraud are briefly described here. See Section 5.2 Error! Reference source not found. for more information on privacy, legal, and IT considerations.

  6.4.1 Data Privacy/Confidentiality

- Consult with the privacy experts/legal department at your company.
- Consider IT security.
- Consider the capabilities/logistics of the vendor with regard to server location, location of server administrator, access to data, and data storage.

  6.4.2 Remote Monitoring Considerations

- Build protections against potential issues with breach of confidentiality associated with remote monitoring.
- Identify areas of training for remote monitoring and best security practices.
- Consider restricting certain data fields that identify study participants according to local and legal requirements.

  6.4.3 Considerations for Different eConsent Components

- Consider the impact of access to a knowledge assessment, time spent for the informed consent process, and the potential for inspection findings.
- Consider requirements/restrictions for components by the regulatory and data privacy agencies.
- Consider the need for supplemental information (e.g., additional text including glossary).

  6.4.4 Fraud Considerations

- These may include considerations about verification of identity, potential workarounds, and guidance to influence IRBs/HAs.
- Fraud concerns may be more important for at-home use.
- Consider technology that controls user access and ensures patient/participant identity.

6.5 Stakeholder Roles and Responsibilities

Provide clear governance to all internal stakeholders. Below are examples of possible topics to include:

- Review SOPs related to informed consent form to ensure there are no barriers for eConsent use.
- Assess company-specific stakeholders
- Clear goals, objectives, roles, and responsibilities
- Clear guidance and instructions
- Obtain internal stakeholder endorsement
- Forum to drive/lead innovation
- Leadership involvement/sponsorship to set a culture for change
• Financial considerations such as initial cost, return on investment, resource impact
• eConsent enterprise-wide/study strategy
• Champion change management
  o Communication planning to minimize internal stakeholder adoption barriers
  o Internal satisfaction surveys (see Process for Identifying Critical Success Factors in Section 7.3)

7 eConsent Design and Readiness Considerations

7.1 Kickoff Meetings with the Vendor

An important consideration in ensuring the implementation of a successful eConsent process is establishing a good working relationship with the eConsent vendor. A kickoff meeting or meetings between the sponsor and the eConsent vendor should be scheduled as early in the process as possible, to ensure both parties are working toward the same objectives and timelines and to clarify the roles and responsibilities of the team members. Kickoff meeting topics may include general eConsent awareness and study-specific items, such as:

• eConsent components and their IT specifications
  o Creating an interpretation document showing the differences between the paper consent and the electronic version
  o Defining a user access model (what type/level of access for different users)
• User acceptance testing (UAT) plan
  o UAT should occur after validation of the configured eConsent system.
  o UAT scripts can be created.
  o Include people with different (clinical) perspectives for the UAT (e.g., study team, clinical research associate [CRA], local team, eCOA/innovation team) for feedback and buy-in.
  o Keep the end users’ experience in mind when testing the system.
• Adapting the main consent into country-specific ICFs and/or site-specific ICFs
• Translation process/considerations, including:
  o Which elements would need translation (e.g., videos, glossary terms, other components, application screens)
  o Who is responsible for translations (of the main content and other components)
• Training strategy (see Training Strategy for Sites in Section 7.5)
• Document control (e.g., versioning)

7.2 Collaboration and Communication between Sponsor and Vendor

Some items that should be considered throughout the study to ensure a good working relationship between sponsor and vendor are described below.

• Governance planning:
  o Communication plan

DRAFT eConsent Implementation Guidance
- Ensure communication lines are set up; define working relationships
- Identify the main contact person assigned at the vendor
  - Create an issue escalation plan
  - Create a risk identification and contingency plan
- Changing regulatory environment
  - Work collaboratively between the sponsor and vendor to ensure the project remains on track

### 7.3 Setting up Metrics and Critical Success Factors

#### 7.3.1 Process for Identifying & Analyzing Critical Success Factors

Critical success factors (CSFs) allow an organization to define and measure the outcomes of an initiative (e.g., what does success look like). Analysis of CSFs should also provide guidance on how to better manage broader eConsent organizational implementation and assist with more efficient and effective ways of executing work, optimizing resources, and increasing quality through the use of technologies for the betterment of clinical research. CSFs for an eConsent pilot and/or scale-up should demonstrate improved study participant-centric efforts and enhanced integration of the study participant in the overall consent process. It may be useful to consider the following CSFs when planning an eConsent pilot and/or scale-up analysis:

- Audit/inspection reports (e.g., comparative assessment with historical data)
- Quality assessments
- Timing assessment (e.g., study start-up timelines)
- Usage assessment (e.g., patient comprehension/satisfaction, patient engagement)

Surveys and/or interviews may assess the following topics:

#### Table 13 Possible Survey Topics to Assess Critical Success Factors

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<thead>
<tr>
<th>Stakeholder</th>
<th>Survey Topics</th>
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| Study participant, family, legally authorized representative | - Demographics, education  
- Better understanding of consent  
- Ease of use of technology  
- Overall satisfaction with process, willingness to participate in a clinical research study  
- Better/more engagement with process and study staff  
- Ease of asking more informed questions  
- Preferred components, retention, perception (can change over time)  
- Re-consenting process |
| Site (e.g., study coordinators, principal investigators, subinvestigators) | - Ease of technology use  
- Overall satisfaction with process  
- Re-consenting process  
- Administrative burden  
- Workload impact  
- Better/more engagement with study participant and process  
- Changes to study participant retention, training, support |
### Stakeholder Survey Topics

<table>
<thead>
<tr>
<th>Stakeholder (e.g., study team, site monitors, management)</th>
<th>Survey Topics</th>
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<tbody>
<tr>
<td></td>
<td>• Audit/inspection findings, perception (can change over time)</td>
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<td>• Satisfaction with training</td>
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<td>• Ease of technology use</td>
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<td>• Overall satisfaction with process</td>
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<td>• Re-consenting process, version control</td>
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<td>• Better/more engagement with study site</td>
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<td>• Metrics, summary data</td>
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<td>• Improvement in study participant retention, training, support</td>
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<td>• Budget, return of investment (ROI)</td>
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<td>• Process/complexity/time for submission, approval, and implementation (can change over time); consider that these may be different for original and amendments</td>
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<thead>
<tr>
<th>External stakeholder (e.g., IEC/IRB, HA, contract research organization [CRO])</th>
<th>Survey Topics</th>
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<td>• Ease of technology use</td>
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<td>• Overall satisfaction with process</td>
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<td>• Ease of submission</td>
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<td>• Approval and implementation</td>
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<td>• Perception (can change over time)</td>
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### 7.3.2 Metrics

There are generally 3 types of metrics that a sponsors might wish to consider when evaluating eConsent: operational (internal), quality (internal and external), and usage (external). These are in addition to any specialized metrics the sponsor is testing in a specific study. The type of metrics that can be collected and tracked should be established prior to organizational implementation of eConsent.

Sponsor companies should keep in mind that novel technologies and new processes often entail a learning curve before value is realized.

**Potential Operational metrics:**

- **Examples:**
  - Study start-up and recruitment duration metrics (timelines)
  - Implementation burden (e.g., additional time and resource requirements)
  - IRB/IEC approval timelines
  - Time to implement requested changes
  - Amendment processing duration
  - Version control issues
  - Number of consent-related monitoring visits
  - Study team subjective feedback

- **Guidance:** establish baseline operational measures using comparable past studies (i.e., similar scope and disease area)
Potential Quality metrics:

- Examples:
  - Monitoring report findings
  - Deviations and corrective action plans (CAPAs)
  - HA and other formal audit findings related to consent
  - Compliance to the protocol
- Guidance: establish baseline quality measures using comparable past studies (i.e., similar scope, study demographics and complexity, and geography)

Potential Usage metrics:

- Examples:
  - Number and percentage of study participants to fully consent electronically
  - Study dropout rate
  - Section read time
  - Knowledge check (if appropriate) results
  - Number and percentage of video views (if applicable)
  - Observational feedback from site personnel who administered consent (surveys)
- Guidance: engage colleagues who focus on optimizing recruitment review success measures related to study participants; pro-actively identify any potential inspection findings that might occur with collection of usage metrics

7.4 Amendment, Re-consent, CAPA and Audit Strategies

- Plan an amendment strategy and re-consent guidelines prior to going live (e.g., at a kickoff meeting) to ensure system continuity in case of an ICF amendment.
- The IRB/IEC will typically determine the need for re-consenting with updates to the eConsent; however, the vendor and sponsor should develop a plan for submission and re-approval.
  - Develop a plan for documentation and tracking of participants who need to re-consent within the system. This plan is generally not specific to the study, but should be re-visited at the study level.
  - Assess the timing of paper versus electronic ICF approvals and whether SOPs would allow for submission of both paper and electronic or only one ICF type (paper OR electronic). Determine how sites should proceed if there is a delay between paper update approval and electronic update approval.

7.5 Study Oversight

Processes should be put in place to ensure the sponsor has up-to-date access to information from the vendor and can direct or participate in problem solving if issues arise. The sponsor and vendor should jointly address the following:

- Type of reports required
- Identification of risks and how to resolve them
- Solution-based problem solving
- Sharing best practice
7.5.1 Site Capability

Check that sites fulfill the system requirements/prerequisites for using eConsent

7.5.2 Define Processes for Sites

Create guidelines on how eConsent can be incorporated with the normal site procedures:

- When working with sites, ensure that their SOPs allow eConsent; i.e. ensure the site SOPs do not specify paper consent only.
- Ensure that sites can reference eConsent procedures throughout the study (e.g., provide a reference guide).
- Allow for issue resolution (e.g., via helpdesk)

7.5.3 Provide Guidance for Monitors

- Additional training (train-the-trainer) for CRAs (virtual training or at the investigator meeting)
- Add eConsent-specific elements to the monitoring plan (e.g., reports, portal access, source data verification)

7.5.4 Definition of Analytic Data Fields

- See Section 8.2 for possible reports that may be generated from these data fields.
- Identify what analytical data from the eConsent (e.g., date of signature, version signed, summary of unfamiliar terms, time spent on a specific portion of the ICF) should be tracked.
- Develop a data transfer specification document (with names of variables, timelines, instructions to send files, etc.).
- Establish a data transfer schedule throughout life of study.
- If tracking analytical data from the eConsent system, develop a plan for data analysis.

7.5.5 eConsent Go-Live Plan

IRB approval:

- Plan should be addressed early in the development process.
- Develop an appropriate package for IRB/IEC submission (see Section 7.6.2).
- Disseminate packet to IRBs and vendor for questions.
- Once approved, activate the site in the system.
- Site access/tablet distribution
  - Ensure timely access to solution ahead of training/go-live
  - Ship to selected sites to meet any agreed timelines
  - Contingency plan for import issues

7.5.6 Contingency Planning

Because of the technical nature of electronic consents, it is important to prepare for the possibility of technical disruptions/failures. Some considerations should include:

- If the site experiences issues with the device (or other electrical means of using eConsent), ensure a replacement device can be provided in a timely manner. Consider the timelines for this replacement and the process for returning the site’s malfunctioning device.
• Using a site-provided device can assist in times where a sponsor provided device has a malfunction. The site could use a computer, cell phone, or another previously identified electronic device to consent the participant.
• Ensure sites have a paper backup option for instances where an electronic backup device is not available or possible. When discussing contingency planning with sites make sure to stress the importance of keeping site visits even if participants need to consent on paper. Sites should never reschedule participants because of technical eConsent issues.
• Ensure a plan is in place to capture data in the system (e.g., date of consent) if the paper backup system is used.

7.5.7 Training Strategy for Sites

• Training for sites can take place in a variety of formats, usually one or both of the following: (1) webinar, or (2) live training on site or during the investigator meeting. The format can be decided at the kickoff meeting.
  o All training should include a live demo using (at minimum) the site’s level of access.
  o Consider a training version of the eConsent prior to go-live to give site staff the opportunity to test the eConsent offline prior to consenting actual participants. Ensure that the offline version cannot be accidentally used to consent participants.
  o If training DOES NOT occur at the investigator meeting, a method of training should be identified.

After training is delivered, ensure the help desk is available at all times and in appropriate languages prior to go-live.

Training for participants may need to be addressed (may be part of the eConsent tools).

7.6 External Processes

When defining the external processes for using eConsent, it is important to note that there are fundamental similarities in the objectives of the core activities between paper ICF and eConsent. The key changes per activity highlighted below are comparable to the types of changes for other eTechnologies (e.g., ePRO). It is important to keep in this in mind when developing processes, defining communication/training, and addressing any implementation impacts.

• Development
  o Key Change: Development and translation of multimedia components
• Submission
  o Key Change: Submission and review of multimedia components
• Execution
  o Key Change: Patient interacts with multi-media components; Site/sponsor receives metadata insight
• Close-Out/Archival
  o Key Change: Archive eConsent data

7.6.1 Site Processes

Site feasibility must be assessed using company SOPs

Engagement with sites should occur early and often throughout the process. Engage sites in the benefits and ease of eConsent and be prepared to discuss perceived barriers.

• Engage sites early in the process to determine willingness to participate and level of interest.
• Try to overcome potential resistance.
• Analyze areas of site resistance (e.g., lack of resources to execute, overburdened by other initiatives, technological constraints, previous bad experience, limited knowledge of study participant/site benefit, institutional restrictions).
• Analyze impacts to the site (e.g., change to SOPs, change to processes) with the site.
• Prepare appropriate materials and communication approaches to address (e.g., generic demonstration or mock study-specific application).
  o TransCelerate tools may be used to support site engagement:
    ▪ Introduction to eConsent for Sites
    ▪ Site FAQ
• If resistance remains, consider using paper consent at that site.

Managing mixed consent formats (paper and electronic) at the site:

• Will be necessary if the electronic informed consent form (eICF) cannot be used for all study participants or at all sites
• Define processes and create instructions for sites (using site SOPs)
  o How will sites file and print eICFs? What country and site filing regulations or SOPs apply? Is filing of the electronic form sufficient or is a paper printout necessary (might be country-specific)? How will eSigned source documents be filed?
  o How will sites archive and print eICFs?

Site system setup and readiness considerations:

• Import licenses may be needed for some countries, and customs clearance may lead to delays.
• Define who will be conducting activities (e.g., vendor or sponsor) and the format (e.g., set up call or on site).
• Site equipment is shipped and access granted by the vendor before readiness assessment begins.
• Will participants use their own devices, and how will this be set up and activated?
• Potential items to consider during setup and readiness are highlighted below (this is not an exhaustive list):
  • Does the internet connection work?
  • Is user access confirmed in the system and test environment (e.g., user names, password)?
  • Will a separate printer be provided to print directly from the device? Does the site have space and is it willing to use it?
  • If the site needs or prefers to use their own printer, can it be connected to the device used for the eConsent or will the site need to access the eConsent from their own computer to print?
    o Instructions need to be provided for both options (possibly in an eConsent manual, see below)

Ensure all site personnel are trained and have the appropriate documentation:

• A training plan must be in place (e.g., online learning courses with certificate at the end, mandatory before system allows access if possible; can be described in an eConsent manual, see below)
• Training may include best practices to integrate eConsent into the consenting process (e.g., eConsent does not replace the important conversation between the site and study participant).
• Training may be conducted via live, online, or device training or at the investigator meeting (which may be virtual).
• Consider using quick reference cards (simplified reference guide with key features)
• Consider how the training will be documented (certification via online learning or face-to-face with certification)

Outline the process for providing the study participant with the copy of the ICF using the following considerations:

• Mechanism by which the study participant will receive the signed copy (e.g., email, paper copy)
• According to the SOPs and local regulations:
  o A signed copy must be provided, or
  o The ICF can be provided to the study participant electronically (e.g., via email or internet link to platform; both password protected)

In case of issues with the device, the site should use their backup process. The following points should be considered:

• The backup process would be the paper consent form.
• Consider how sites will access the paper form in case of system failure (e.g. blank printout available at site).
• The system should have an option to enter/mark study participants as consented in cases where the participant was consented on paper due to system failure
• An eConsent manual for sites may include:
  o Process for user training and certification
  o Process for consent printing
  o Process for archival
  o Helpdesk contact information
  o Backup process in case of system failure or if a study participant chooses not to use eConsent

### 7.6.2 IRB/IEC Processes

Timing of IRB/IEC submissions must be considered to ensure a smooth eConsent process. Before IRB/IEC submissions, consider the timing of approvals, particularly if multiple countries are selected, and the impact this may have on the study timelines.

• Identify the IRB/IEC point of contact and ensure the appropriate sponsor SME is involved in communication.
• If guidance for submission requirements exists, review and understand the requirements.
• If guidance does not exist or if there are questions about existing guidance, set up a meeting with the IRB/IEC to introduce eConsent, discuss submission requirements including multimedia tools, and determine if sponsor assistance is needed.
• Consider providing training to the IRB/IEC to facilitate rapid approval.
• In discussions about or with IRBs, consider the mechanism for negotiating with the IRB/IEC and methods to improve efficiency of IRB/IEC feedback (e.g., integrated authoring tool). Discuss submission package options which provided IRBs/IECs with sufficient information, considering the examples below
Potential interactions with health authorities should be considered in planning.

- Work with the vendor to ensure site-specific requirements are included in the submission (e.g., logos, template features)
- Submit the package to the IRB/IEC and respond to any questions received.
- If significant feedback is received about a specific supplemental eConsent component (e.g., audio, video), consider using a phased release where the supplemental components are included in a later version.
- Notify vendor of all IRB/IEC approvals.

### 7.6.3 Health Authority Process

Potential interactions with health authorities should be considered in planning.

- Involve internal regulatory compliance and legal groups early in the process.
- Reference internal guidance/reaction on existing eConsent regulations.
- Evaluate current regulations to determine if they have any impact.
- Evaluate eSignature requirements and acceptability.
- Where possible, provide proactive comments on draft guidance to align with the company position.
- In countries where there is no established precedent for eConsent, consider a discussion with HAs to define the submission package. The elements of the submission will likely depend on whether the country has IRB/IEC review processes in place and the extent of the health authorities current consent review process. Potential submission scenarios and illustrative packages are described below:

  - **HA Submission and IRB Submission:** In cases of IRB review, documents that might be submitted to the HAs include:
    - Paper ICF content
    - Comment on application form on consent process
  - **No HA Submission; IRB Submission Only:** In cases where only the IRBs review the submission, the following principles may apply for health authorities
    - No ICF submissions
    - Note that data privacy laws still apply to all data storage and processing entities containing information surrounding eConsent
  - **HA Submission Only; No IRB/IEC Submission:** In cases of NO IRB/IEC review or where HAs would require more comprehensive review, the following package options may be considered:
    - Paper submission package: storyboard and/or screenshots, glossary terms, knowledge assessment, eSignature verification form from vendor, data privacy statement from vendor, attestation letter or interpretation document
    - Electronic submission package: link to portal or digitized consent, eSignature verification form from vendor (provides verification that the eSignature complies with local
7.6.4 CRO Processes

Consider the following when considering using CROs to implement eConsent for a study:

- Additional processes and provisions that must be in place
- Initial engagement is as important as continued oversight of and collaboration with the CROs. The initial engagement should precisely and clearly define the expectations for eConsent management and development for the study.
- Involve the CRO as soon as possible in the eConsent development process and determine if the eConsent development process will be led by the CRO or sponsor. The following are areas that sponsors and CROs may wish to address during initial engagement:
  - CRO timelines, roles, responsibilities and planned deliverables of all parties, including expectations for monitoring activities, and any potential metric reporting
  - If the sponsor develops the eConsent, the impact on and expectations of CRO monitoring activities should be considered up front.
  - Risk mitigation and business continuity plans in case of system failure should be established with the CRO, including eConsent-specific considerations. These plans should cover all steps of the eConsent process (before, during and after development and implementation).
  - Quality checks should be put in place at all stages of development and implementation.

7.7 eConsent Archiving

7.7.1 Sponsor Considerations

All versions of the eConsent should be available during the study and following archiving. The exact requirements of what should be archived should be decided by the sponsor and the vendor based on local/regulatory requirements.

When considering archiving of the eConsent documents (approved unsigned and signed versions), the sponsor will need to decide where they want to house the documents and who will have access. During the trial the sponsor may have access to patient data, but after archival the data is de-identified for the sponsor.

eConsent Vendor Considerations:

- Discuss the vendor’s policies for storing and archiving approved documents.
- Discuss who will have access to which files (e.g., only the site should have access to signed consent forms)
- Discuss where files are kept as certain countries have restrictions on where data can be stored
- If deciding to use the vendor as the main storage location, ensure all sponsor approvals of the electronic ICF and its components are still being filed/archived on the sponsor side. The vendor will also need to keep all versions of the approved consents and needs to be able to easily and quickly provide copies when requested.
Sponsor Considerations:
- Sponsors may also house the approved unsigned documents within their own paper or electronic filing system.

Vendor and Sponsor Considerations:
- Sponsors might consider having the electronic ICFs (eICFs) housed with both parties. The vendor can house the actual electronic version of the document, while the sponsor keeps the content of the document filed along with the content of the components. The sponsor should ensure that all sponsor-level approvals for the document and components are filed.

Some additional considerations:
- Ensure the system has the capability for an audit trail. The audit trail will be able to capture any revisions to the eICF, the identity of the person making the changes, the reason for the changes, and the date the changes were made.
- If eICF data are stored on a remote computer, in a data storage center, or on a cloud network, consider any obligations imposed by data privacy laws or regulations.

### 7.7.2 Site Considerations

During and after the trial the site will have access to eConsent data, although the format of that data may change after archival (e.g., CD-ROM).

**Country requirements:**
- Some countries permit filing in an electronic system, while others require printed copies of all documents to be available.

**Site SOPs:**
- Some site SOPs might specifically state whether documents need to be physically printed and stored or if they can be maintained in an electronic database.

If eICF data are stored on a remote computer, in a data storage center, or on a cloud network, data privacy laws and regulations that apply to remote storage site(s) may apply and should be considered, in addition to those that apply to the research site.

### 8 eConsent Execution and Closeout Considerations

The eConsent execution phase is critical to a project’s success and entails a significant amount of resource, budget, time and effort. eConsent execution or implementation is when the proposal, tasks and activities that were created in the startup phase are put into action, and where the anticipated outcome is delivery of the expected eConsent results. During eConsent execution, several key factors need to be considered, evaluated, and reviewed against company policies, preferences, etc. to ensure suitability. These factors, discussed in more detail below, include:

- Monitoring methods (Section 8.1)
- Examples of oversight/compliance/management reports to support monitoring activities (Section 8.2)
- Issue management/resolution (escalation, help desk) (Section 8.3)
- Audit/inspection readiness (access to data in eConsent, review, adequacy of processes) (Section 8.4)
8.1 Monitoring Methods

Monitoring is the act of overseeing the progress of a clinical study and ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, ICH GCP guidelines, and any applicable local regulatory requirement(s). This can be done on site, remotely, or via centralized monitoring activities.

- Remote monitoring: electronic case report form (eCRF) completion, SAE notification, ICF review, etc. conducted remotely through electronic systems
- Centralized monitoring: usually performed from the data collected in case report forms (CRFs) through EDC. It enables the identification of outliers or trends that may need attention by the sponsor or CRO to manage and mitigate concerns or issues.

As part of these requirements, sponsor companies are required to train their monitors to review ICFs to ensure that study participants have been consented in accordance with GCP and local regulatory requirements. eConsent allows for informed consent monitoring remotely, centrally, or on site.

Consider how the following ICF monitoring considerations (non-exhaustive list) would be taken into account when using eConsent:

- The amount of time participants had to consider participation in the study
- Were all treatment options discussed and clarified?
- Were procedures and responsibilities discussed and clarified?
- Were all participants’ questions responded to prior to the decision to participate?
- Did participants sign and date the ICF before any of the study procedures were performed?
- Did participants receive a copy of the informed consent form?
- Re-consenting process

8.2 Oversight, Compliance, and Management Reports to Support Monitoring

Some reports to consider for use by monitors or in-house staff include but are not limited to:

- List of all approved ICF versions with dates of implementation
- List of participant numbers with approved ICF versions
- Lists of all study personnel:
  - Trained (with date of training) on eConsent
  - With access to eConsent data
  - With administration rights to the eConsent
- List of comments by the investigator by subject number
- List of participants who agree to have the study site contact their primary physician
- List of consented participants
- List of participants not yet consented
- List of re-consented participants
- List of participants not yet re-consented
8.3 Issue Management and Resolution

eConsent provides the capability of accessing data remotely and centrally. This allows for real-time eConsent review and analysis and therefore quicker identification, resolution, and prevention of issues/concerns. Caution should be taken to ensure that no participant identifiers can be accessed/viewed remotely.

Examples of actions include but are not limited to:

- Check the correct version of signed eConsent (i.e., if different from the global version)
- Check if appropriate study participants signed the correct eConsent/ re-consent (e.g., if only a subset of study participants is affected by re-consent)
- Check the date and time of eConsent signature
- Opportunity to block subject screening/ randomization in real time through an automated system-based process

8.4 Audit/Inspection Readiness

The sponsor’s procedures/policies should be followed to ensure proper audit/inspection readiness.

- Inspector/auditor access to eConsent (system, document, and reports)
- Contingency plan in case of eConsent system failure (business continuity)

8.5 Filing/Archiving

The sponsor’s procedures/policies should be followed to ensure proper management of filing and archiving.

For details on filing/archiving please see Section 7.7.

9 Future State

Technology continues to grow in popularity, expanding and enhancing the experiences of research participants and others. Technological innovation is ongoing and may impact all aspects of clinical studies. eConsent is one of many innovations that are part of the participant experience, and importantly is often the first interaction the participant has with the clinical trial process. As sponsors change their business processes to take advantage of eConsent, they can engage participants through personalized portals where information may be individually tailored. eConsent may serve to support a rich study participant experience throughout the clinical study and beyond.
“There are two areas of focus regarding patient centricity in research: patient centeredness and patient engagement. Patient centeredness is defined as research that is based on outcomes that are important to patients. Patient engagement in research is the active participation of patients throughout the entire research process – the planning, the conduct and the dissemination. Patient engagement is the means to the patient centeredness.” – Sue Sheridan, Director of Patient Engagement, Patient-Centered Outcomes Research Institute (PCORI).

Informed consent is fundamental to patient-centered care. Involving study participants in their care requires that they are fully informed, and electronic, patient-guided technologies will have a significant effect on evidence-based medicine. eConsent is a basic building block in a growing technology environment focused on providing individuals with control over the robust exchange of their health information with health-literate content. Some consumers use portals, including electronic health records (EHRs) supported by medical practitioners and commercial sites provided by insurers, advocacy groups, and patient communities. The future offers an opportunity to create an electronic environment that integrates patient-related information from disparate healthcare providers, thus enhancing the participant’s connection to clinical studies, optimizing information sharing during the consent process, and supporting the participant throughout the study. Ensuring robust security and controlling access allows the sponsor and the site to gain significant efficiencies and reduce effort and cost associated with current consent processes.

The ever-increasing complexity of partners participating in the healthcare of patients, combined with a growing globalization and mobility of our population, is driving the need for an economical and efficient means of bringing information together to facilitate decision-making. Increasing sophistication of data analytics in health information management will enable information mining from consent tools to improve the participant’s experience and save money. Data sharing, which currently entails consents with multiple partners, high cost, and time-consuming efforts, may be simplified, granting increased autonomy to the patient.

9.1.1 Enhancing the Participant Connection to Clinical Trials

In a fully integrated environment that brings together patients’ EHRs and the unique criteria of clinical studies, future studies could involve online prescreening. Once an individual has already participated in an eConsented study, future engagement is possible through a broad use of eConsent within the EHRs that would enable assessment of study enrollment criteria against a prospective participant’s record. This would increase autonomy, allowing proactive seeking out of studies better suited to the individual and/or the choice to share EHRs to see if they may be eligible to participate in studies. This could eventually be fully automated within a shared health IT environment, or partly automated. Integration of health records together with eConsent would also make it easier for investigators to decide whether a specific study is appropriate for a specific patient, and eventually provide an option for study participants to consent on their own, outside of the regular clinical study process. This could be especially beneficial in supporting future-use sample testing where re-consent can often be rate limiting.

Once a prospective participant is linked to one or more clinical studies, the broad-based information technology infrastructure, together with eConsent, can keep prospective participants engaged by first allowing them to review and select the study and the participating clinical site that would be best suited for them. The potential participant could then review the critical elements of the specific informed consent for the study, including the risks, benefits, time commitments, and costs. Such upfront engagement could be at the participant’s convenience and would promote a more robust conversation with the clinician during the formal consent for the study.
9.1.2 Optimizing Information Sharing During the Consent Process

Integration of eConsent with the EHR would also be valuable because a site or sponsor could programmatically confirm that a potential participant is not already enrolled in another concurrent study. Concurrent study participation can easily be missed in today’s siloed technology environment, and when found can be very costly, particularly when procedures and sample analysis have already begun. This integration of eConsent with the EHR can be used to reduce redundant testing by coordinating standard-of-care testing with planned research testing. In addition, potential study participants could gain a better understanding of the costs of participating in a study by integrating insurer information from the EHR as a reference in the eConsent. The better understanding of the time and cost of a particular study would allow a prospective participant to make a better informed choice about participation. Both the principles of informed consent and of patient-centric healthcare would be well served by such a user-centric application to provide more information about the requirements of participation. Improved transparency of clinical trial participation with the patient’s EHR would be another important benefit, leading to a more seamless and coordinated health response involving the primary care physician, a clinical study investigator, and other healthcare practitioners.

9.1.3 Supporting the Participant Throughout the Study

This integrated health information exchange of the future can also support participants’ ability to make real-time choices about their participation and to modify those choices both during and after the study. Participants could also be connected to advocacy and patient groups to allow sharing with other individuals undergoing the same or similar treatment and challenges. However, it is important to note that applicable privacy laws must be considered, including the assurance that the participant has appropriately consented to have their information shared/stored.

A study-participant portal would support broader engagement with the participants, which could include the ability to opt in to access all of their study information, receive payments, be notified of visits through their personal calendars, get alerts, visit reminders, and even access their own study data if agreed in the informed consent. Study participants could be informed about their condition based on study data from a variety of related private or commercial sources that could support them in real time, including providing information about treatment alternatives. A portal can also provide an interface for maintaining contact, outcomes research, and follow-up questions in a structured format designed for analysis, if the participant consents.

Return of research results remains one of the more controversial and debated topics within informed consent, and such portals could help with this issue. Portals could easily be used to deliver standard clinical laboratory results, and further, integrated data portals may allow sending aggregated data to participants who consent, to support exploratory or future research with samples or data collected in clinical studies. If participants have appropriately consented to have their information shared, future research could be robustly supported by exposing potential participants to new proposed research and engaging them in eConsents to participate in these future studies.

Technology development, evolving regulations, and the increasingly complex and matrixed healthcare environment all suggest that the electronic infrastructure will move towards further connecting various healthcare providers for an individual in ways that deliver a custom individualized experience. In the future, eConsent and clinical study offerings could be centralized in an externally hosted location for prospective and active study participants. This could result in a global standard for clinical study information that facilitates the creation of a master list of all approved clinical studies, which when unified
with a global standard eConsent, would support programmatic matching of participants and studies based on information in their EHR or a series of online questions answered by a prospective participant or healthcare provider.

Participation in a clinical study through a centralized database would greatly simplify participant engagement. Industry, academic, and government resources could co-sponsor and fund this centralized matching studies and consents resource, which would eliminate much redundant infrastructure, reduce noncompliance due to multiple study participation, build broader transparency into research, and expose participants and their healthcare practitioners to the best treatment options across research sponsors in industry, academia, and government.

### 9.1.4 Benefits for Sites, IRBs/IECs, and Sponsors

A more streamlined future state would involve fewer different technology interfaces for both study participants and clinical sites, and would allow integration with clinical study operational systems. The current use of multiple electronic systems (e.g., eConsent, eCOA, ePRO) to improve data capture and exchange results in a high degree of complexity in the clinical setting. Multiple devices, varied operating systems, and the increase in data transmissions across networks can be a major disincentive to the use of eConsent and other technology advances.

Moving forward, the importance of using a flexible device approach will become increasingly important. Site-provided devices may not be appropriate for all applications. There may be a future option where a participant may bring his/her own device (bring your own device – BYOD) while giving participants direct access through his/her own device (mobile or desktop) and leading to a sense of greater autonomy and access, does add some complexity to the technology environment. Systems would still require integration behind the scenes while ensuring individual participant access to eConsent.

Another critical consideration is the willingness of companies to mutually recognize tool-based training provided to the site by other sponsors using the same tool. While differences among vendors may still require some study-specific training to ensure that unique differences are identified and incorporated into the site’s training and comprehension, within a single tool it would be highly efficient for some consistent tool-based training that could eliminate redundant activity from sponsor to sponsor and study to study.

The future state also offers opportunities for more efficient informed consent authoring and approval. Technology companies are bringing highly collaborative software and technical environments to encourage sharing ideas and providing feedback, and this could also apply to eConsent. A possible expansion of current functionality might include the ability to collaboratively write and securely approve and version-control standard consent language fluidly between the sponsor and the site/IRB, reducing time and potential for error in the common back-and-forth exchange of documents that occurs today.

As other healthcare information becomes more available to sponsors, sponsors may realize significant cost reductions and reduced re-work through improved sharing of relevant data. As soon as the study participant has signed his eConsent, data with his ID, birth date (if allowed), and gender could be accessed by the central laboratory, IVRS, EDC, servers, etc. Connecting eConsent with IVRS will decrease transcription errors and reduce the burden to site staff to capture the same data in different systems at different times. This would ensure that appropriate consent is obtained before any participant is enrolled, data collected, or study treatment dispensed, enhancing patient protection. Integrating eConsent with central laboratory or biorepository systems would result in tighter control over chain of custody for samples and ensure appropriate consent prior to any test execution. This vision demands a more rigorous harmonization of metadata across the integrated infrastructure, agreements on data...
exchange principles and privacy, authoritative source alignment, and assessment and mitigation of global regulatory and legal considerations. While that may sound complex, the increased benefit gained by improvements in accuracy, elimination of manual error, and improvements in speed to information are well worth the investment.

9.1.5 Closing Thoughts

Some of these future considerations may be realized soon, and may require significant advancement in both technology and change readiness across all participants in the healthcare IT infrastructure. These future potential changes may provide opportunities that include but extend beyond eConsent. TransCelerate can participate in future activities in ways including the following:

- Patient portals connecting eConsent, study information, training, results, study information, and other interactive participant engagement technologies
- Harmonized metadata for studies and consents that would promote global access to treatment options
- Common clinical study research result portal to deliver aggregate results of exploratory research, clinical study outcomes, and future research consented through both traditional and electronic means

Imagining a future for eConsent inspires a broader array of digital engagement that demands a more holistic adoption of health literacy approaches and alignment across platforms, and suggests an opportunity for an integrated approach to participant engagement.

10 Appendices

10.1 Example Templates

Two publicly available templates were selected to demonstrate how ICF content might be incorporated into eConsent multimedia components. These examples are intended to demonstrate what could be done and should not be interpreted as a requirement or endorsement to use these particular templates. The concepts can be applied to any ICF.


(This template is for either clinical trials or clinical research)
(language used throughout form should be at the level of a local student of class 6th/8th)

Notes to Researchers:

1. Please note that this is a template developed by the WHO ERC to assist the Principal Investigator in the design of their informed consent forms (ICF). It is important that Principal Investigators adapt their own ICFs to the outline and requirements of their particular study. The logo of the Institution must be used on the ICF and not the WHO logo.

2. The informed consent form consists of two parts: the information sheet and the consent certificate.

3. Do not be concerned by the length of this template. It is long only because it contains guidance and explanations which are for you and which you will not include in the informed consent forms that you develop and provide to participants in your research.

4. This template includes examples of key questions that may be asked at the end of each section, that could ensure the understanding of the information being provided, especially if the research study is complex. These are just examples, and suggestions, and the investigators will have to modify the questions depending upon their study.

5. In this template:
   - square brackets indicate where specific information is to be inserted
   - bold lettering indicates sections or wording which should be included
   - standard lettering is used for explanations to researchers only and must not be included in your consent forms. The explanation is provided in black, and examples are provided in red in italics. Suggested questions to elucidate understanding are given in black in italics.

TEMPLATE ON FOLLOWING PAGE
[Informed Consent form for ________________]

Name the group of individuals for whom this informed consent form is written. Because research for a single project is often carried out with a number of different groups of individuals - for example healthcare workers, patients, and parents of patients - it is important that you identify which group this particular consent is for.

(Example: This Informed Consent Form is for men and women who attend clinic Z, and who we are inviting to participate in research on X. The title of our research project is "___________________".)

You may provide the following information either as a running paragraph or under headings as shown below.

[Name of Principal Investigator]
[Name of Organization]
[Name of Sponsor]
[Name of Proposal and version]

This Informed Consent Form has two parts:

- Information Sheet (to share information about the research with you)
- Certificate of Consent (for signatures if you agree to take part)

You will be given a copy of the full Informed Consent Form

PART I: Information Sheet

Introduction
Briefly state who you are and explain that you are inviting them to participate in the research you are doing. Inform them that they may talk to anyone they feel comfortable talking with about the research and that they can take time to reflect on whether they want to participate. Assure the participant that if they do not understand some of the words or concepts, that you will take time to explain them as you go along and that they can ask questions now or later.

(Example: I am X, working for the Y Research Institute. We are doing research on Z disease, which is very common in this country. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.)
Purpose of the research

Explain in lay terms why you are doing the research. The language used should clarify rather than confuse. Use local and simplified terms for a disease, e.g. local name of disease instead of malaria, mosquito instead of anopheles, “mosquitoes help in spreading the disease” instead of “mosquitoes are the vectors”. Avoid using terms like pathogenesis, indicators, determinants, etc. There are guides on the internet to help you find substitutes for words which are overly scientific or are professional jargon.

(Example: Malaria is one of the most common and dangerous diseases in this region. The drugs that are currently used to help people with malaria are not as good as we would like them to be. In fact, only 40 out of every 100 people given the malaria drug XYZ are completely cured. There is a new drug which may work better. The reason we are doing this research is to find out if the new drug ABX is better than drug XYZ which is currently being used.)

Type of Research Intervention

Briefly state the type of intervention that will be undertaken. This will be expanded upon in the procedures section but it may be helpful and less confusing to tell people from the very beginning whether, for example, the research involves a vaccine, an interview, a biopsy or a series of finger pricks.

(Example: This research will involve a single injection in your arm as well as four follow-up visits to the clinic.)

Participant selection

State why this participant has been chosen for this research. People often wonder why they have been chosen to participate and may be fearful, confused or concerned.

(Example: We are inviting all adults with malaria who attend clinic Z to participate in the research on the new malaria drug.)

► Example of question to elucidate understanding: Do you know why we are asking you to take part in this study? Do you know what the study is about?

Voluntary Participation

Utilize a summary box to highlight the concept of voluntary participation. Indicate clearly that they can choose to participate or not. State, what the alternative - in terms of the treatment offered by the clinic - will be, if they decide not to participate. State, only if it is applicable, that they will still receive all the services they usually do whether they choose to participate or not. This can be repeated and expanded upon later in the form as well, but it is important to point out clearly at the beginning of the form that participation is voluntary so that the other information can be heard in this context.

(Example: Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose not to participate in this research project, you will offered the treatment that is routinely offered in this clinic/hospital for disease Z, and we will tell you more about it later. You may change your mind later and stop participating even if you agreed earlier.)

► Examples of question to elucidate understanding: If you decide not to take part in this research study, do you know what your options are? Do you know that you do not have to take part in this research study, if you do not wish to? Do you have any questions?
Include the following section only if the protocol is for a clinical trial:

**Information on the Trial Drug [Name of Drug]**

1) give the phase of the trial and explain what that means. Explain to the participant why you are comparing or testing the drugs.
2) provide as much information as is appropriate and understandable about the drug such as its manufacturer or location of manufacture and the reason for its development.
3) explain the known experience with this drug.
4) explain comprehensively all the known side-effects/toxicity of this drug, as well as the adverse effects of all the other medicines that are being used in the trial.

(Example: The drug we are testing in this research is called ABX. It has been tested before with people who do not have malaria but who live in areas where malaria is common. We now want to test the drug on people who have malaria. This second research is called a “phase 2” trial.

The drug ABX is made by Company C. You should know that it has a few side effects. One of the side effects, or problems, is that you may feel tired for the first day after being given the drug. Also, 20% of the people who tried the drug in previous research experienced temporary swelling where the injection entered the skin. We know of no other problem or risks.

Some participants in the research will not be given the drug which we are testing. Instead, they will be given the drug XYZ, the drug which is most commonly used in this region to treat malaria. There is no risk associated with that drug and no known problems. It does not, however, cure malaria as often as we would like.)

**Procedures and Protocol**

Describe or explain the exact procedures that will be followed on a step-by-step basis, the tests that will be done, and any drugs that will be given. Explain from the outset what some of the more unfamiliar procedures involve (placebo, randomization, biopsy, etc.) Indicate which procedures are routine and which are experimental or research. Participants should know what to expect and what is expected of them. Use active, rather than conditional, language. Write "we will ask you to…" instead of "we would like to ask you to…".

In this template, this section has been divided into two: firstly, an explanation of unfamiliar procedures and, secondly, a description of process.

**A. Unfamiliar Procedures**

This section should be included if there may be procedures which are not familiar to the participant.

If the protocol is for a clinical trial:

1) involving randomization or blinding, the participants should be told what that means and what chance they have of getting which drug (i.e. one in four chances of getting the test drug).

(Example: Because we do not know if the new malaria drug is better than the currently available drug for treating malaria, we will compare the two. To do this, we will put people taking part in this research into two groups. The groups are selected by chance, as if by tossing a coin. Participants in one group will be given the test drug while participants in the other group will be given the drug that is currently being used for malaria. It is important that neither you nor we know which of
the two drugs you are given. This information will be in our files, but we will not look at these files until after the research is finished. This is the best way we have for testing without being influenced by what we think or hope might happen. We will then compare which of the two has the best results.

The healthcare workers will be looking after you and the other participants very carefully during the study. If we are concerned about what the drug is doing, we will find out which drug you are getting and make changes. If there is anything you are concerned about or that is bothering you about the research please talk to me or one of the other researchers.

2) involving an inactive drug or placebo, it is important to explain to the participants what is meant by a placebo or inactive drug.

(Example: A placebo or inactive medicine looks like real medicine but it is not. It is a dummy or pretend medicine. It has no effect on a person because it has no real medicine in it. Sometimes when we want to know whether a new medicine is good, we give some people the new medicine and some people the pretend or dummy medicine. For the research to be good, it is important that you do not know whether you have been given the real medicine or the pretend or dummy medicine. This is one of the best ways we have for knowing what the medicine we are testing really does.)

3) which may necessitate a rescue medicine, then provide information about the rescue medicine or treatment such as what it is and the criterion for its use. For example, if the drug does not control pain, then intravenous morphine may be used as a rescue medicine.

(Example: If we find that the medicine that is being used does not have the desired effect, or not to the extent that we wish it to have, we will use what is called a “rescue medicine.” The medicine that we will use is called QRS and it has been proven to control pain. If you find that the drug we are testing does not stop your pain and it is very uncomfortable for you, we can use the rescue medicine to make you more comfortable.)

If the protocol is for clinical research:
Firstly, explain that there are standards/guidelines that will be followed for the treatment of their condition. Secondly, if as part of the research a biopsy will be taken, then explain whether it will be under local anesthesia, sedation or general anesthesia, and what symptoms and side effects the participant should expect under each category.

(Example: You will receive the treatment of your condition according to national guidelines. This means that you will be (explain the treatment). To confirm the cause of your swelling, a small sample of your skin will be taken. The guidelines say that the sample must be taken using a local anesthesia which means that we will give you an injection close to the area where we will take the sample from. This will make the area numb so that you will not feel any pain when we take the sample.)

For any clinical study (if relevant):
If blood samples are to be taken explain how many times and how much in a language that the person understands. It may, for example, be inappropriate to tell a tribal villager that blood equal to a wine-glass full will be taken but it may be very appropriate to use pictures or other props to illustrate the procedure if it is unfamiliar.

If the samples are to be used only for this research then explicitly mention here that the biological samples obtained during this research procedure will be used only for the research purpose and will be destroyed after ____ years, when the research is completed. If the tissue/blood samples or any other human biological material will be stored for a duration longer than the research purpose, or is likely to be used...
for a purpose other than mentioned in the research proposal, then provide information about this and obtain consent specifically for such storage and use in addition to consent for participation in the study - (see last section)

(Example: We will take blood from your arm using a syringe and needle. Each time we will take about this much blood (show a spoon, vial or other small container with a small amount of water in it. In total, we will take about ..........this much blood in x number of weeks/months. At the end of the research, in 1 year, any left over blood sample will be destroyed.)

B. Description of the Process
Describe to the participant what will happen on a step-by-step basis. It may be helpful to the participant if you use drawings or props to better illustrate the procedures. A small vial or container with a little water in it is one way of showing how much blood will be withdrawn.

(Example: During the research you make five visits to the clinic.)

- In the first visit, a small amount of blood, equal to about a teaspoon, will be taken from your arm with a syringe. Tests will be performed of the blood to determine the presence of substances that help your body fight infection. You will also be asked questions about your general health and measure how tall you are and how much you weigh.
- At the next visit, which will be two weeks later, you will again be asked some questions about your health and then you will be given either the test drug or the placebo/pretend drug for malaria. As explained before, neither you nor we will know whether you have received the test or the dummy/pretend drug.
- After one week, you will come back to the clinic for a blood test. This will involve...

Duration
Include a statement about the time commitments of the research for the participant including both the duration of the research and follow-up, if relevant.

(Example: The research takes place over ___ (number of) days/ or ___ (number of) months in total. During that time, it will be necessary for you to come to the clinic/hospital/health facility ______(number of) days , for ____ (number of) hours each day. We would like to meet with you three months after your last clinic visit for a final check-up.

In total, you will be asked to come 5 times to the clinic in 6 months. At the end of six months, the research will be finished.)

- Examples of question to elucidate understanding: Can you tell me if you remember the number of times that we are asking you to come to the hospital to complete the treatment? The research project? How many injections will you be given? How many tablets? How much blood will be taken from your veins, using a syringe and needle? Over how many weeks? Etc. Do you have any other questions? Do you want me to go through the procedures again?

Side Effects
Potential participants should be told if there are any known or anticipated side effects and what will happen in the event of an unexpected event.

(Example: As already mentioned, this test drug can have some unwanted effects. It can make you tired and it can cause some temporary swelling around the place where the injection goes into your arm. It is...
possible that it may also cause some problems that we are not aware of. However, we will follow you closely and keep track of any unwanted effects or problems. We may use some other medicines to decrease the symptoms of the side effects or reactions. Or we may stop the use of one or more drugs. If this is necessary we will discuss it together with you and you will always be consulted before we move to the next step.

Risks
Explain and describe any possible or anticipated risks that will be available in the event that harm does occur, who thought of as being the possibility that harm may that the participant can make an informed decision. (Example: By participating in this research it is possible that you will be at greater risk than you would otherwise be. There is a risk that your disease will not get better and that the new medicine doesn't work as well. If, however, the medicine is not working and your fever does not go down in 48 hours, we will give you quinine injections which will bring your fever down and make you more comfortable. While the possibility of this happening is very low, you should still be aware of the possibility. We will try to decrease the chances of this event occurring, but if something unexpected happens, we will provide you with______.)

Examples of question to elucidate understanding: Do you understand that, while the research study is on-going, no-one may know which medicine you’re receiving? Do you know that the medicine that we are testing is a new medicine, and we do not know everything about it? Do you understand that you may have some unwanted side-effects from the medicines? Do you understand that these side-effects can happen whether or not you are in the research study? Etc. Do you have any other questions?

Benefits
Mention only those activities that will be actual benefits and not those to which they are entitled regardless of participation. Benefits may be divided into benefits to the individual, benefits to the community in which the individual resides, and benefits to society as a whole as a result of finding an answer to the research question.

(Example: If you participate in this research, you will have the following benefits: any interim illnesses will be treated at no charge to you. If your child falls sick during this period he/she will be treated free of charge. There may not be any benefit for you but your participation is likely to help us find the answer to the research question. There may not be any benefit to the society at this stage of the research, but future generations are likely to benefit.)

Reimbursements
State clearly what you will provide the participants with as a result of their participation. WHO does not encourage incentives. However, it recommends that reimbursements for expenses incurred as a result of participation in the research be provided. These may include, for example, travel costs and money for wages lost due to visits to health facilities. The amount should be determined within the host country context.
We will give you [amount of money] to pay for your travel to the clinic/parking and we will give you [amount] for lost work time. You will not be given any other money or gifts to take part in this research.

**Examples of question to elucidate understanding:** Can you tell me if you have understood correctly the benefits that you will have if you take part in the study? Do you know if the study will pay for your travel costs and time lost, and do you know how much you will be re-imbursed? Do you have any other questions?

Confidentiality

Explain how the research team will maintain the confidentiality of data, especially with respect to the information about the participant which would otherwise be known only to the physician but would now be available to the entire research team. Note that because something out of the ordinary is being done through research, any individual taking part in the research is likely to be more easily identified by members of the community and is therefore more likely to be stigmatized.

**Example:** With this research, something out of the ordinary is being done in your community. It is possible that if others in the community are aware that you are participating, they may ask you questions. We will not be sharing the identity of those participating in the research.

The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [name who will have access to the information, such as research sponsors, DSMB board, your clinician, etc.]

**Example of question to elucidate understanding:** Did you understand the procedures that we will be using to make sure that any information that we as researchers collect about you will remain confidential? Do you have any questions about them?

Sharing the Results

Where it is relevant, your plan for sharing the information with the participants should be provided. If you have a plan and a timeline for the sharing of information, include the details. You should also inform the participant that the research findings will be shared more broadly, for example, through publications and conferences.

**Example:** The knowledge that we get from doing this research will be shared with you through community meetings before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced. After these meetings, we will publish the results in order that other interested people may learn from our research.

Right to Refuse or Withdraw

This is a reconfirmation that participation is voluntary and includes the right to withdraw. Tailor this section to ensure that it fits for the group for whom you are seeking consent. The example here is for a patient at a clinic.

**Example:** You do not have to take part in this research if you do not wish to do so and refusing to participate will not affect your treatment at this clinic in any way. You will still have all the benefits that you would otherwise have at this clinic. You may stop participating in the research at any time that you...
wish without losing any of your rights as a patient here. Your treatment at this clinic will not be affected in any way.)

OR
(Example: You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected.)

Alternatives to Participating
Include this section only if the study involves administration of investigational drugs or use of new therapeutic procedures. It is important to explain and describe the established standard treatment. (Example: If you do not wish to take part in the research, you will be provided with the established standard treatment available at the centre/institute/hospital. People who have malaria are given….)

Who to Contact
Provide the name and contact information of someone who is involved, informed and accessible (a local person who can actually be contacted. State also that the proposal has been approved and how.

(Example: If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: [name, address/telephone number/e-mail])

This proposal has been reviewed and approved by [name of the local IRB], which is a committee whose task it is to make sure that research participants are protected. If you wish to find out more about the IRB, contact [name, address, telephone number]. It has also been reviewed by the Ethics Review Committee of the World Health Organization (WHO), which is funding/sponsoring/supporting the study.

- Example of question to elucidate understanding: Do you know that you do not have to take part in this study if you do not wish to? You can say No if you wish to? Do you know that you can ask me questions later, if you wish to? Do you know that I have given the contact details of the person who can give you more information about the study? Etc.

You can ask me any more questions about any part of the research. Do you have any questions?

PART II: Certificate of Consent
This section should be written in the first person and have a statement similar to the one in bold below. If the participant is illiterate but gives oral consent, a witness must sign. A researcher or the person going over the informed consent must sign each consent. The certificate of consent should avoid statements that have "I understand…" phrases. The understanding should perhaps be better tested through targeted questions during the reading of the information sheet (some examples of questions are given above), or through the questions being asked at the end of the reading of the information sheet, if the potential participant is reading the information sheet him/herself.

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.
CTTI: Samples Tiered Informed Consent Model

The following text is intended as an example of the Tiered Informed Consent Model structure. It is intended to be an informed consent document template. We encourage flexibility in individual informed consent document language, dependent upon the nature of the study. The third tier as described above is not described in this example.

[tiered informed consent details]

The basics

- The consent form explains the study and what happens if you decide to join.
- Take as much time as you need to make a decision about joining the study.
- Feel free to ask any questions at any time.
- Your condition may or may not improve if you join the study. But, the information from this study might help other patients with the same condition in the future.
- If you join the study, you can leave at any time. Leaving will not affect your care.
- If you choose to leave the study, please let us know as soon as possible.
- If you don’t join the study, you will continue to receive care for your [condition]. [briefly describe]

Why do we want to talk to you about joining the study?

- You have [condition].
- We are doing this study to learn more about [experimental drug/device/procedure].
- Some parts of this study are experimental which means [define, “they have not been tested yet, fully tested”, etc].
- The untested parts of the study are [description of which parts of research are experimental].
- About [number] [people/women/men] will take part in this study.

What will happen if you join the study?

- You will be in the study for [length of time].
- [if RCT] You will be randomly assigned a study treatment.
- “Randomly assigned” means that whatever treatment you get will be by chance, like flipping a coin or drawing names out of a hat.
- You will have to [describe number and type of procedures, such as “you will have 10 visits that will last between 1 and 3 hours”]
- To read more about this, turn to [refer to additional procedures information provided in the Detailed Reference Section]

What are the risks of joining the study?

- [Medications/procedures/other] that are part of this study may have side effects.
- The most common or serious side effects of this [treatment/medicine] are:
- It is possible that some patients could have side effects that we do not know about.

Consider using a glossary term and graphics or video to define “randomization”
• If you have severe side effects from the [treatment/medicine], the study doctor may ask you not to continue in the study.
• To read more about the other risks turn to [refer to additional risk information provided in the Detailed Reference Section]
• [insert brief statement about reproductive risks, if applicable]

Could something change while you are in the study?
• Things may happen in the study that could make you change your mind about continuing to take part.
• If something changes, we will tell you as soon as possible.
• You can choose to leave the study at any time.
• The study doctor can also choose to take you out if they believe that it is best for you.

What will happen to your information if you join the study?
• We will protect your privacy and work to ensure that your information is kept confidential.
• Other people who look at study data and study quality may see your study information (like the study sponsor, US FDA or Institutional Review Board).
• We may share your study information with other researchers in the future.
• To read more about how your study information will be used turn to [refer to additional confidentiality and data sharing information in the Detailed Reference Section].

Will you get paid for joining the study?
• No/Yes, you [will/will not] be paid to be in this research study.
• [If yes, provide amount]

What do you have to pay if you join the study?
• [as applicable] Some of the tests that will be done in this study will be billed to your insurance.
  o If you have health insurance, you will be responsible for any copays or deductibles.
• Treatments/drugs you receive only as part of the study will not be billed to your insurance.

What happens if you are harmed or injured during the study?
• If it is an emergency, call 911 right away or go to the emergency room.
• Contact your study doctor as soon as you can.
• For other medical problems, contact your study doctor right away. They will treat you or contact another doctor.
• The costs for care you need because of an injury or illness during the study will be billed to you or your insurance.
Who can answer any questions you have?

Remember, there are no stupid questions! Feel free to ask at ANY TIME! It is your right to be fully informed before deciding to take part in this study.

Investigator
Address:
Phone:
E-mail address:

Study Coordinator
Address:
Phone:
E-mail address:

A description of this study will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time, using the following study number: [xxxx].

Detailed Reference Section

Chapter 1     Detailed Study Treatment Schedules
[INSERT TABLE(S)]

Chapter 2     Complete List of Risks and Side Effects
[INSERT TABLE(S)]

Chapter 3     HIPAA/Protected Health Information

Chapter 4     Additional Financial Information

Chapter 5     [additional information as necessary]

Chapter 6     [additional information as necessary]

[Note that the signature block may be appropriately placed prior to or following the detailed reference section, and its placement may vary based on the contents of the informed consent document (i.e., inclusion and placement of all elements required by federal regulation) and study complexity. Additional consideration of the signature block placement, and factors affecting it, should be undertaken.]
Print Name of Participant__________________
Signature of Participant__________________
Date __________________________
    Day/month/year

If illiterate
A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness______________________    AND    Thumb print of participant
Signature of witness______________________
Date __________________________
    Day/month/year

Statement by the researcher/person taking consent
I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:
1. 
2. 
3. 
I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent__________________

Signature of Researcher/person taking the consent__________________
Date __________________________
    Day/month/year
10.2 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

There are several definitions available for the term vulnerable population, which refers to a subset of the community that may have additional considerations impacting their ability to make a voluntary and informed decision. Therefore, these populations require extra care and special considerations for their protection in clinical research.

Vulnerable populations considered here include:

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

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

eConsent may help improve understanding during consent for some vulnerable populations, in a way that is more difficult with paper consent, e.g., by:

- Enhancing the environment for asking questions
- Using web links within the consent that allow study participants to view 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.

10.2.1 Better Practices

The following are some suggested best practices that a sponsors might wish to consider when assessing how to use eConsent with vulnerable populations:

- Weigh benefits of multimedia components and new technology against population characteristics. Consider age, education, health literacy, the health problem being addressed, cultural values, and health beliefs to judge whether to use alternate formats for informed consent information.
• Ensure people involved (e.g., site staff) understand how to use metadata, which may be more useful to address possible challenges that may occur with vulnerable populations, such as how to encourage participant questions.

10.2.2 Considerations for Specific Vulnerable Populations

eConsent considerations applicable to certain specific vulnerable populations are described in the following sections.

Pediatric Populations

The pediatric population is vulnerable for multiple reasons, including parental pressure, low literacy, brain development, and incomplete physical development (including varying ability to clear drug or increased exposure issues due to larger skin surface to body volume). The pediatric population 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 considerations with the use of eConsent in pediatric populations include:

• The legally acceptable representative (LAR) actually 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. The electronic environment enables easy tracking of the signatures on these important documents, and can facilitate linking the assent to the consent.

• There is a great deal of interest in how children learn and what they retain from multimedia presentation of information. Many children are very accustomed to multimedia content on a variety of mobile devices, for both entertainment and educational purposes. Multimedia content may include audio, visual, textual, 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.

• Another concern is that the 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.

• 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

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V0.1
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

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. Poor translations may cause the failure of the study participant to act as instructed, disparities in prescription and administration of the study treatment, and reduced 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.

10.2.2.1.1 Translation, Interpretation and Localization

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

Translation is often confused with interpretation. While both involve adapting from one language to another, there are important differences:

- Interpretation occurs in real time and is spoken versus written, in person, on the phone, or through a television/video service.
- 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 is more like cultural adaptation than translation, as it 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.

Consider:

- Outsourcing to 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, and the language may not be immediately available in eConsent.
  - Consider using paper ICFs for initial consent instead of delaying the participant’s entry (to await translated consent content and multimedia components).
  - In the US (or other locations where allowed), consider using generic pre-translated paper short forms. Evaluate if the short forms will be digitized and made available within eConsent, noting that the multimedia components will need to be translated in order to be used in these instances.

10.2.2.1.2 Language Access vs Language Assistance

Language access is achieved when non-native speaking participants can communicate effectively with study staff and effectively 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.

Low-literacy Population in Typical Research

Multimedia approaches to improve informed consent in both treatment and research settings have been studied in recent years, but findings on the effectiveness of these methods have been mixed for low health literacy individuals.

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.

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

- Considerations:
  - Age dependent
  - Dependent on education level
  - Computer experience needed
  - Low health literacy
  - 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, including video and audio, beyond verbal and written communications have been effective. The effectiveness of these alternative formats depends on education level, age, and computer experience.

Some researchers have suggested that in the absence of consistent findings, the consent format could depend on the level of risk in the study. Observational studies may be better suited to consent using only multimedia components or other less well studied methods. Interventional studies may use a combination of multimedia components and a written portion.

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.
- Allowing an electronic link to the eConsent to be shared makes it easy for the study participant to review information about the study with friends and family. Some participants feel more comfortable if they are able to share information about possible study participation.
- 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 appendix on health literacy (Section 10.2).

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 may reduce the vulnerability of these study participants. Multimedia components may increase autonomy, while alternative documentation options may decrease the likelihood of coercion.

Consider using certain multimedia components that may increase autonomy 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 (see Section 4.11):
  - 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. See Section 4 for more information on the multimedia components and Section 6.3 for operational considerations.

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 to the partner 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 outcomes (requirements may vary based on local regulations). Partner involvement may occur 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 (e.g., physically unable to attend the study visit), 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 best be told how to protect themselves during the study and any safety follow-up period.

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 them 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.

Legally Authorized Representatives

Some vulnerable population study participants may be unable to consent, such as pediatric participants (see Section 10.2). 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 Section 4) may increase the ease of obtaining and comprehending this information.

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.

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 trials, 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.

See Section 4 for more information on multimedia components, See Section 6.3 for operational considerations, and Section 10.2 for considerations related to vulnerable populations.

### 10.3 Health Literacy Considerations, Best Practices, and Tools

Health literacy is strongly related to study participant understanding of informed consent, and research supports the links between plain language, clear communication, and informed consent. Both the complex nature of medical research and the limited literacy skills of many potential participants can make obtaining consent challenging. Studies suggest that study participants frequently may not understand the information presented during the informed consent procedure.

Informed consent forms should be designed to inform potential study participants about the research, use, and sharing of their health information in terms that they can understand. The process is an educational activity in which potential study participants are the learners. Researchers have a responsibility to ensure that potential participants understand the information provided. eConsent and its multimedia components provides a unique opportunity to educate potential study participants in a health-literate way.

#### 10.3.1 Why Does Health Literacy Matter?

Health literacy is defined as the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions (Institute of Medicine and Healthy People 2020).

Only a small percentage of adults globally have proficient health literacy skills (Figure 3, Figure 4). Given the spectrum of health literacy skills, it is important to consider impacts for individuals with limited skills who are less likely to understand terminology, risks, and benefits as described in traditional informed consent documents.
Figure 3  Overall Health Literacy by Country and for the Total Sample

![Health Literacy by Country and for the Total Sample](image)


Figure 4  US Health Literacy Map

![US Health Literacy Map](image)

Low Health Literacy affects more adult Americans than Obesity, Diabetes, HIV/AIDS & Breast Cancer combined

Health Literacy levels:
- Proficient: 12%
- Intermediate: 53%
- Basic: 22%
- Below Basic: 13%

77 million American adults have basic or below basic literacy skills
10.3.2 Health-literate Communication Principles

Health literacy principles can also be applied to eConsent. Incorporating evidence-based health literacy best practices into eConsent can make the content readable, understandable, and actionable. The principles described here are not all inclusive, none are required, nor is any one recommended over the other.

Critical principles for presenting information effectively include using simple, short sentences, avoiding medical jargon, and presenting complex concepts in an understandable way. Breaking apart information into small sections with subheadings also improves readability.

- Be clear and concise.
- Keep the objective of the consent in mind.
- Chunk content: break apart information into small sections using subheadings to provide context
- Clear hierarchy, of header, subheading and body copy: use distinct type sizes and styles to distinguish headers, subheadings, and body copy
- Callouts: use to segment content, isolate and highlight numbers, or draw attention to key information. Keep these short and try to use an icon or infographic to support the information.
- Large font sizes: body copy should be a minimum of 14 points
- Sans serif fonts: use for headers and subheadings to help improve readability
- Serif fonts: reserved for longer paragraphs of body copy
- Emphasize short text passages (e.g., headings, subheadings, important statistics) using bold rather than italic font, which is harder to read
- Avoid all capital letters; use title or sentence case for headings and subheadings
- Adequate contrast for all type, graphics, and icons: use dark type on a white background and white type on a dark background
- Use ample white space: keep layouts clean and simple
- Supporting images: photos, graphics, icons, and infographics to support the content
10.3.3 eConsent Content Considerations

The goal of the content is to help participants understand what to do with the information provided and find the confidence to make informed decisions about their clinical research options.

Active Voice and You-Language

- Use active voice to clearly outline who is doing what.
- Use second person (you/your) whenever possible to make the content personal and friendly. This many change based on local cultural considerations. For example, in France, it is not polite to use the second person unless a friendship exists.

Length

- Keep content focused and succinct, including need-to-know but not nice-to-know information.
- Include only relevant and meaningful information for the intended audience.
- If content within a section becomes long, consider breaking it into smaller components.
- If the content is used online, consider including a hyperlink to a pop-up glossary for complex terms.

Headings

- Create headings that are relevant, meaningful, and engaging.
- Be mindful of the consumer audience and create a heading that piques interest.
- Keep headings short and free of industry terminology (such as disclosure).

Literacy Demand

- Ensure people with various degrees of health literacy can read and understand the content.
- Consider using a readability calculator but be sure to understand its limitations.
- Avoid using jargon, abstract words, technical terms, statistics, and abbreviations and acronyms that are not properly explained.

Use of Numbers

- Ensure that understanding the numbers presented does not require addition, subtraction, multiplication, or division.
- Consider presenting numbers in graphs or images.
- Use whole numbers when possible (e.g., 1 in 1000 instead of 0.001).
- Express risks as frequencies (e.g., 1 out of 10 instead of 10%).

Cultural Sensitivity

- Recognize and address the unique cultures, languages, and health literacy needs of diverse target populations, which may affect the choice of eConsent components.

http://www.transceleratebiopharmainc.com/assets/clinical-trial-diversification-4/

Health Literacy Resources

Some available health literacy resources are provided below, including general guidance, tools, and readability assessments. This is not an all-inclusive list of guidance or resources that are available. The use of these guidelines are not required nor is any one recommended over the other.

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<td>WHO Health Literacy: The Solid Facts</td>
<td>This site identifies practical and effective ways public health and other advocates can take action to strengthen health literacy in a variety of settings. Specific evidence is presented for educational settings, workplaces, marketplaces, health systems, new and traditional media and political arenas. <a href="http://www.euro.who.int/__data/assets/pdf_file/0008/190655/e96854.pdf">http://www.euro.who.int/__data/assets/pdf_file/0008/190655/e96854.pdf</a></td>
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<td>Health Literacy Europe</td>
<td>This site is a network for researchers and professionals involved in promoting health literacy in research, policy and practice. <a href="http://www.healthliteracyeurope.net/">http://www.healthliteracyeurope.net/</a></td>
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<td>CDC Health Literacy Website</td>
<td>This site aims to bring new and timely information about the CDC’s work to improve health literacy and highlight the work of others who are implementing the goals and strategies of the National Action Plan to Improve Health Literacy. <a href="http://www.cdc.gov/healthliteracy/">www.cdc.gov/healthliteracy/</a></td>
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<td>Health Literacy Principles Checklist</td>
<td>This site provides guidance for making information understandable, useful, and navigable. <a href="http://www.centerforhealthguidance.org/health-literacy-principles-checklist.pdf">www.centerforhealthguidance.org/health-literacy-principles-checklist.pdf</a></td>
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<td>Health Literacy Lab</td>
<td>This site is a library of easy and entertaining lessons and tips for health and safety communicators on how to create clear and effective communications for a lay audience. <a href="http://www.healthliteracylab.com">www.healthliteracylab.com</a></td>
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<td>The Plain Language Thesaurus</td>
<td>This site offers plain language equivalents to medical terms, phrases, and references</td>
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<td>This site contains examples of tested graphic displays of health information. <a href="http://www.vizhealth.org">www.vizhealth.org</a></td>
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<td><strong>Readability Assessments</strong></td>
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<td>Readability Calculations Software</td>
<td>This site provides software used to calculate readability scores according to the most widely-used classic readability formulas. <a href="http://www.micropowerandlight.com/rd.html">www.micropowerandlight.com/rd.html</a></td>
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11 References

Note to Reviewers: The references section is still under development.

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https://pbrn.ahrq.gov/sites/default/files/docs/Kass%202014.pdf

### Revision History

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