eConsent Initiative

eCONSENT: IMPLEMENTATION GUIDANCE

TransCelerate
BIOPHARMA INC.
ACCELERATING THE DEVELOPMENT OF NEW MEDICINES

Foreword

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

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

eConsent: Implementation Guidance

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2   Abbreviations

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

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 Council 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

QA   quality assurance

SAE   serious adverse event

SOP   standard operating procedure

UAT   user acceptance testing

WHO   World Health Organization

3   Introduction

3.1 Purpose of This Document

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

This guidance provides information on the use of electronic systems and processes that might use electronic media to obtain informed consent. eConsent includes multimedia components (see Section 4), which can be used to develop an interactive and engaging informed consent experience, offering flexibility for diverse learning styles (e.g., auditory, visual).[1] 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.

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.

3.2 Methodology

This document was developed by the TransCelerate eConsent workstream over a 2-year period during which the workstream team compiled information about better practices for implementation.

The eConsent workstream also engaged with patient and site advocacy groups, a CRO forum, and selected health authorities (HAs) and ethic committees to obtain insight on eConsent. Based on those interactions, some features considered important to sites and participants are highlighted in this document:

Icon	Indicator
🏫	Important to sites
👥	Important to participants

After the document was drafted, it was made available for public review and comment. TransCelerate received and incorporated feedback into this document, as appropriate, from the following stakeholder groups: sites, CROs, independent ethics committees (IECs) and institutional review boards (IRBs), eConsent vendors, and patients.

3.3 Introduction to eConsent

The foundation of an effective informed consent process for clinical research studies is to provide study participants with the information that they need to make an informed decision whether 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. As rooted in the Declaration of Helsinki and International Council on Harmonization (ICH) Good Clinical Practice (GCP)[2], 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 the clinical study.

ICF documents have become increasingly complex, technical, and more difficult for study participants to understand.[3] Complicated study designs and specialized study participant populations make clearly conveying the research objectives to the study participants more challenging. Variable 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 that may include multimedia components, as shown in Figure 1 (below).[4] It is important to note that eConsent is not meant to replace the important discussion between the participant and site staff. As with traditional consenting, the site will continue to own the consenting process.**

Ultimately eConsent meets 2 objectives:

- Empowers participants to make informed decisions through the use of interactive multimedia components
- Enables the improved quality and efficiency of clinical studies through insight to the participant experience, improved data quality, and a fully electronic system

Figure 1   Potential Components of eConsent
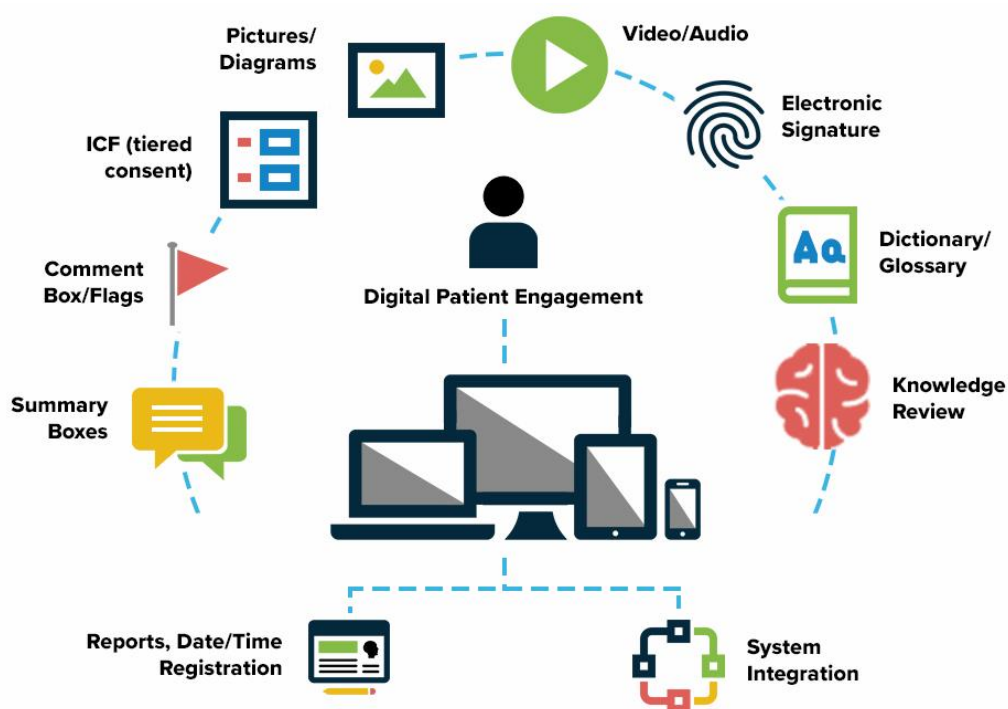
The sponsor must ensure that the eConsent is compliant with all (local) regulatory requirements (see implementation guidance section). In addition to the benefits for potential study participants, eConsent may be advantageous for sponsors, sites, IRBs/IECs, and HAs as described in the section below (Section 3.4).[5]

3.4 Benefits and Considerations for eConsent
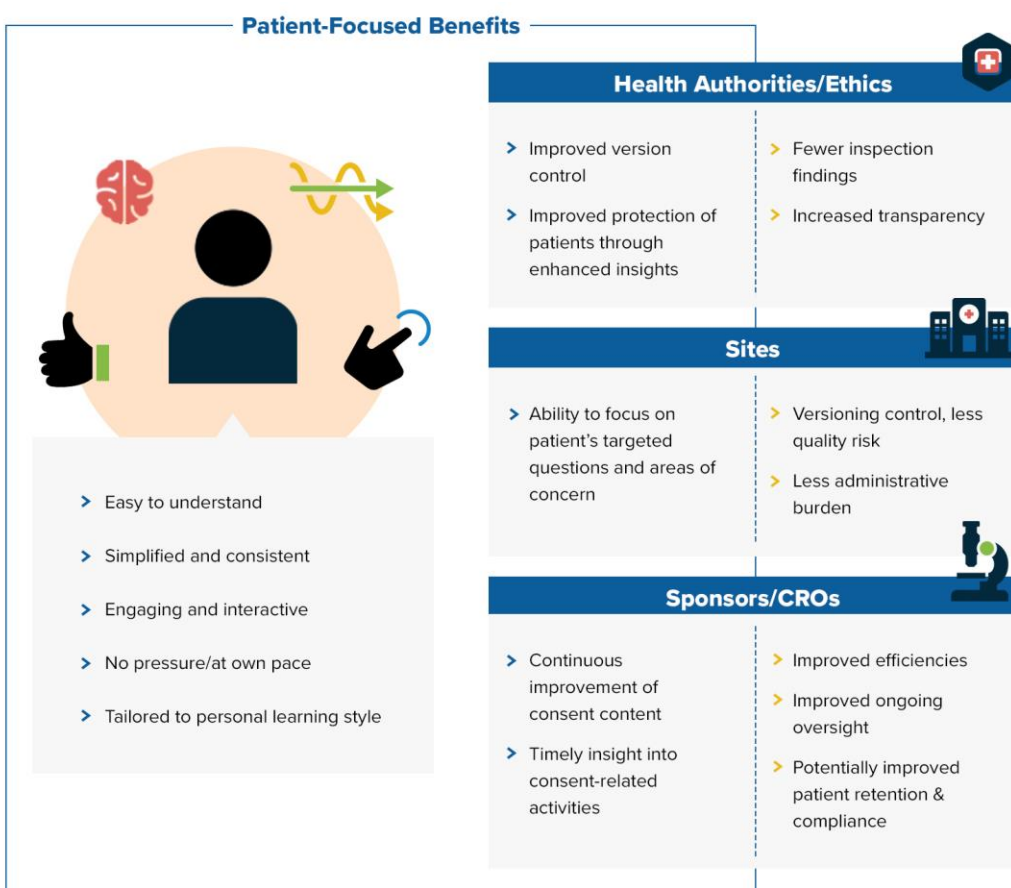
3.4.1   eConsent Benefits

Research has shown that paper-based ICFs do not promote consistent quality dialogue and informed decision-making.[6] eConsent has the potential to improve the consent experience, increase quality, and reduce regulatory inspection

findings.[7] eConsent also complements risk-based monitoring of studies by enabling risk assessment through central and remote monitoring of consent activities.

An overview of the benefits of eConsent to different stakeholders is shown in Figure 2.

Figure 2   Overview of eConsent Benefits

Patient-Focused Benefits

> Easy to understand
> Simplified and consistent
> Engaging and interactive
> No pressure/at own pace
> Tailored to personal learning style

Health Authorities/Ethics

> Improved version control
> Improved protection of patients through enhanced insights

> Fewer inspection findings
> Increased transparency

Sites

> Ability to focus on patient's targeted questions and areas of concern

> Versioning control, less quality risk
> Less administrative burden

Sponsors/CROs

> Continuous improvement of consent content
> Timely insight into consent-related activities

> Improved efficiencies
> Improved ongoing oversight
> Potentially improved patient retention & compliance

These potential benefits are shown in greater detail below (Table 1), some of which apply to more than one stakeholder (e.g., sponsor, site). These benefits as well as those listed below for individual eConsent components are based on member company experience, stakeholder input, and hypothesized advantages from using more technologically sophisticated processes. While experience or logic suggests that eConsent can deliver these particular benefits, attaining these specific benefits may vary across companies and across studies and, depending

on the circumstances, some or even all of the specified benefits might not be realized. The degree of benefit will be directly related to the components selected and their fit within a specific context.

Table 1   eConsent Potential Benefits

Potential Benefit	Stakeholders Affected
Increases comprehension and retention of information compared to a lengthy and complex paper document (e.g., complex procedures or study treatments can be shown visually and/or explained out loud)[8]	Study participants
Allows study participants to choose their preferred method of learn	Study participants
Better informed participants are more likely to make an informed decision whether to participate, can better manage their study expectations, and can become active partners	Study participants
Increased understanding leads to better discussions on ICF conten site staff and increased compliance	Study participants
Certain functionalities can be included to help vulnerable populat (e.g., visually impaired, pediatrics)	Study participants
Uses technology that is already regularly used in daily life	Study participants
More engagement with consenting process: empowerment, owne autonomy	Study participants
Reduces audit and inspection findings such as those related to inc versions and missing signatures	Sites, IRBs/IECs, HAs, sponsors
Provides information about study participants' level of understandi during the consent process	Sites
Provides information about study participants' perspectives of the of the informed consent process	Sites
Reduces the need for complex and time-consuming explanations supplementary study explanation tools	Sites
Reduces paperwork and quality risks	Sites
Lowers burden on site staff, allowing a focus on high-value activities, including specific study participant questions and concerns	Sites
Complements risk-based monitoring by providing more information within eConsent (e.g., glossary) to the study participant and enabling some activities to occur remotely	Sites, sponsors
Ensures a consistent and complete explanation is given to all study participants	Sites
Less administration time (e.g., automated reminders for consent amendments, potential for paperless systems, and potential links with other systems)	Sites
Improves management of overall consent tracking (e.g., re-consenting, consent withdrawal)	Sites, sponsors

Potential Benefit	Stakeholders Affected
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)	Sites
Alert messages to site in case of eConsent errors or re-consenting need	Sites
May improve study participant compliance and recruitment, depending on study design/therapeutic area[9]	Sites, sponsors
Improves the review/approval process	IRBs/IECs, HAs
Increases confidence in the informed consent process	IRBs/IECs, HAs
Improves development of a regulatory perspective on informed consent	IRBs/IECs, HAs
Increases retention due to better understanding (reduced dropout rate)	Sponsors
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	Sponsors
Improves timely/immediate identification of consenting issues by the monitor (rather than discovery after the fact)	Sponsors
Increases quality and consistency: Data validity and protection (e.g., access controls and passwords) Quick, easy, remote follow-up on errors Identification and prevention of recurring errors (e.g., version control) Timely re-consent notification linked to protocol amendments and safety updates Fewer transcription errors (e.g., ICF date copied automatically into the electronic data capture [EDC] system)	Sponsors
Improves productivity: May reduce site visit time monitoring ICFs so that clinical research associates (CRAs) can concentrate on other site duties (e.g., safety monitoring) CRAs can check data remotely without visiting the site to check details Central team can review data in core systems/case report form (CRFs) for all sites	Sponsors
Enables possible automated reporting of data in sponsor systems: Partial pre-population of monitoring visit reports prior to the site visit Automated edit checks on completeness of ICF Interdependency with core systems, e.g., interactive voice response system (IVRS), CRF, clinical trial management system (CTMS) Alert messages to sponsor in case of eConsent errors	Sponsors

3.4.2   eConsent Potential Barriers to Implementation

Some potential barriers to eConsent implementation are related to the fact that eConsent is a novel technology and minimal guidance to use this technology currently exists. These may result in both internal and external potential barriers to implementation as shown in Table 2.

Table 2   eConsent Potential Barriers to Implementation

Barriers Related to a New Technology
Some components may not be acceptable in all countries (e.g., eSignature)
Significant initial investment cost and resource needs
Study participants' limited experience and discomfort with the technology
Longer setup time relative to paper
Increased upfront work to tailor eConsent to special subject groups (e.g., pediatric or other vulnerable populations)
Participants opting for paper may limit return on investment
Need for backup system in case of failure and during maintenance periods
Additional cost and time needed for translations
Technical/format limitations, e.g., need to use a particular operating system or device type
Barriers Related to Insufficient Existing Guidance
Inexperience and lack of processes for HAs, IRBs/IECs, sponsors, and investigators in many countries/institutions
Temporarily longer IRB/IEC approval times
Electronic distribution of signed consent form (compliance/IT security/data privacy)
Reluctance of other stakeholders (e.g., IRBs/IECs, HAs) to use the technology

4   eConsent Multimedia Components

Various multimedia components that potentially could be used in eConsent are described below along with a non-exhaustive list of possible benefits and considerations for each.

Note: While experience or logic suggests that the multimedia components can deliver the listed benefits, attaining these specific benefits may vary across companies and across studies and, depending on the circumstances, some or even all of the specified benefits might not be realized.

Sample text or content is provided for illustration only and is not meant to propose or suggest model language. 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. The sponsor must decide whether and how to implement each component during eConsent design.

The choice of a component or format does not automatically exclude others. Any number of components may be used based on the decisions made during implementation. This may also change as eConsent experience grows.

Where possible, it makes sense to develop the components to minimize the need for non-value-added changes. For example, variability around topics such as birth control and genetic risks may create complexity and increase cost by requiring multiple versions of multimedia components (e.g., video) to meet local requirements.

Refer to the eConsent Operational Examples asset to view some publicly available ICF templates developed by the World Health Organization (WHO) and the Clinical Trials Transformation Initiative (CTTI) with examples of how eConsent multimedia components could be incorporated. These will demonstrate some practical application tips that may be considered.

The table below (Table 3) includes a summary of the multimedia components included in the section, as well as a brief definition/purpose.

Table 3   eConsent Multimedia Components

Multimedia Component	Definition/Purpose
Multimedia Tiered Approach	Includes essential elements in a concise main section and more detailed information in later subsections
Video	Provides a visual and potentially auditory overview of the study and promotes participants' better understanding of the selected content
Audio	Voiceover of consent document or other components, voice response elements
Pictures and Diagrams	Visual aids to help explain and reinforce key study components or complex topics
Callout Boxes	Key idea reinforcement highlighted in 1-2 sentences
Knowledge Review	Short set of questions participant asked to answer to highlight key info
Dictionary/Glossary	Glossary is a list of selected terms defined by the sponsor
Content Flags	Allows participant to select words/sections to come back to for questions
Comment Boxes, Free Text Fields, and Study Participant Note Logs	Allows sites or participants to record notes or questions
Chapter/Section or Continuous Content Views	Allows content to be broken into sections or viewed as a single document
Section-based Participant Attestation	Allows participants to acknowledge understanding of specific sections
Electronic Signature	Electronic method of authentication, including fingerprint scan, etc.

4.1 Multimedia Tiered Approach

4.1.1   Description of Multimedia Tiered Approach

Tiered consent includes essential elements in a concise main section and more detailed information in later subsections (which are optional for the study participant).

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 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 navigate between different sections to learn more about specific items as needed. Enhancements such as hyperlinks can facilitate this and make it easy for the study participant to navigate back to the section of the main consent from anywhere within the tiered part. The tiered consent is structured to ensure all required sections (i.e., main section) are viewed, and the eConsent tool can potentially record time spent in each section.

Tiered content can present information that is more relevant when the study participant approaches a certain study milestone. Just as with paper consent, the eConsent is available throughout the study therefore the investigator can refer participants to a particular section within their eConsent to have the option to re-review when it is more relevant.

Figure 3   Example Tiered Consent

|Illustrative|

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:
    o X-ray
    o 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.

> When the study participant clicks on 'detailed study treatment visit schedule', the full visit schedule appears

	Screening Visit		On the Study Drug (Treatment Phase)								Comments
	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	
Procedures:											
Medical History	X										
Physical Exam	X	X	X	X	X	X	X	X	X	X	May include physical exam, weight, vital signs, pulse, or blood pressure.
Chest x-ray	X										
ECG	X	X					X			X	
Urine collection	X	X				X1		X1		X	
Receive Study drug		X									
Blood collected	X	X	X	X	X	X	X	X	X	X	
Approximate blood draw amount in mL	45	70	10	10	20	10	45	10	10	55	

4.1.2 Potential Benefits and Considerations for Tiered Consent

Potential benefits and considerations for tiered consent are described in Table 4.

Table 4   Tiered Consent Potential Benefits and Considerations

Benefits
Increases readability, comprehension, and ease of use, and allows embedding of other multimedia components
Flexible method of learning that allows participants to choose how they want to use the material
Supports progressive, incremental disclosure
Mitigates against overloading on less relevant information that may mask or fail to convey the importance of more essential information
Considerations
Limited regulatory guidance and experience with the concept in some countries
Participants may not choose to view all information, which may limit understanding of the protocol requirements or willingness to participate

4.1.3 Guidance for Implementation

The informed consent must still contain the required elements of informed consent as per local law/regulation.[10]

Refer to local practices to determine the amount of information that must be included in each tier.

Discussion of informed consent content placement (e.g., main versus sub-sections) should include all relevant sponsor stakeholders (e.g., 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. Some general videos would be reusable across studies. Examples of videos are provided below in the sample "What is a Clinical Trial" and "How to Use eConsent" videos. Other video types may include complex procedures and disease-specific videos.

What is a Clinical Study Video

- Understanding of clinical research
- General concept of risks and benefits to clinical research
- Participation is voluntary
- You can withdraw from the study at any time
- Data are kept confidential

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

Additionally, a video briefly providing a high-level summary of the study may be prepared to introduce participants to the study design.

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 time consuming and design the video to reduce the need for changes. Key topics may include:

- Purpose of the study
- Study design (duration, type of control [e.g., placebo], procedures)
- Reminder that the study has risks (perhaps include a high-level summary)
- Reminder that participation is voluntary and that data are kept confidential

Figure 4   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   Potential Benefits and Considerations for Video Components

Potential benefits and considerations for video components are described in Table 5.

Table 5   Video Components Potential Benefits and Considerations

Benefits
May provide more detailed information on general clinical research and study-related topics without increasing the length of the informed consent document
Study participants may better understand the study and could have more effective and tailored discussions of their questions and concerns with the site staff
Consistent approach to key concepts essential to making an informed decision
Improved understanding on how to use the eConsent device
Standardized content that an organization can use across studies/sites can decrease costs and improve efficiencies
Considerations
Some participants may only pay attention to visual aids and fail to read the full informed consent
Considerable cost/time impact due to site/country variability, protocol amendments, and translations
Visually impaired participants might not be able to use videos
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
Some populations may not be technologically confident and need more direction, or the technology may become more distracting
Consider cultural or ethnic background for videos or visuals; there may be risks for unintended meaning or context

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
- Ensure, if required, that video text can 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. For example, an Indiana University study found that average adults listen effectively for only about 15 to 20 minutes before their minds begins to wander[11]
- Use diagrams and pictures more than text and language
- Voiceovers and animation may be easier to edit and thus less expensive than live action videos
    - Use regionally acceptable practices and tools; for example, a study in Africa might benefit from a song format
    - This example in a different context reflects this: http://www.takeandtell.org/#video
- Consider if previously created video clips may be used (e.g., videos describing a clinical study, the disease, or compound)
- There is variability in how IRB/IECs review video. Work with the IRB/IECs early to plan for submissions. For example, some IRB/IECs want the scripts of the videos and may want screenshots instead of or in addition to the viewing of the video.

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 Potential Benefits and Considerations for Audio Components

Potential benefits and considerations for audio components are described in Table 6.

Table 6   Audio Components Potential Benefits and Considerations

Benefits
Provides alternative access to consent information and increased autonomy for visually impaired, blind, and low literacy study participants
Allows study participants to choose how to receive the information (independent from actual literacy level)
Potentially reduces time spent to ensure comprehension
Considerations
Literate participants who can read quickly may be frustrated by the slow audio pace
Participants may be too embarrassed to use the functionality
Voiceover translations if required may incur additional costs, time, and resources
Additional verification step required to ensure alignment to written consent text
May require additional space (isolated viewing areas) to avoid noise pollution
May impose additional cost for equipment (e.g., headphones)
Hearing impaired participants might not be able to use audio consent and/or can experience problems depending the severity of their condition

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.
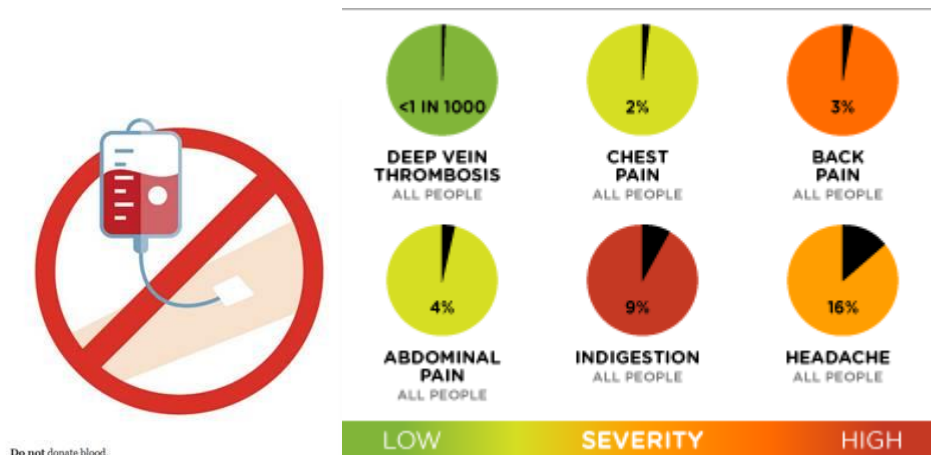
4.4 Pictures and Diagrams

4.4.1   Description of Pictures and Diagrams

Studies have shown that visual aids can help explain and reinforce key study components or complex topics.[12] Example topics include risk percentages, explanation of a serious adverse event (SAE), specific study procedures, and the study schedule.

Figure 5   Example Picture

4.4.2 Potential Benefits and Considerations for Pictures and Diagrams

Potential benefits and considerations for pictures and diagrams are described in Table 7.

Table 7   Pictures and Diagrams Potential Benefits and Considerations

Benefits
Increases understanding of complex information and simplifies ICF information
May support processing of information through different modes
Might facilitate discussion of relevant topics
Considerations
Some information (e.g., risk percentages < 10%) is difficult to show graphically and pictures could be misleading
Some participants might be intimidated or not feel comfortable looking at graphics/schedules
For studies with a wide age range, graphics that are acceptable for all age groups may be difficult to achieve
Some study participants may feel this is too juvenile or not beneficial

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

Figure 6　　　**Example Callout Boxes**

4.5.2　Potential Benefits and Considerations for Callout Boxes

Potential benefits and considerations for callout boxes are described in Table 8.

Table 8　　　**Callout Boxes Potential Benefits and Considerations**

Benefits
May increase awareness of key concepts essential to making an informed decision
May facilitate finding key information without having to reread whole sections
Supportive tool to drive the discussion with a potential study participant
Considerations
Study participants may not read the other material or access the detailed reference sections
Discussions with the participant might focus only on the highlighted topics
Simplified or interpretive text may require additional review and/or time
Highlighted elements might be regarded as biased
Additional effort required within the study team to identify areas to be highlighted

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.

Figure 7   Example of Knowledge Review

Question 1 of 4

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

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

4.6.2 Potential Benefits and Considerations for Knowledge Review

Potential benefits and considerations for knowledge review are described in Table 9.

Table 9   Knowledge Review Potential Benefits and Considerations

Benefit
Helps to demonstrate that the study participant understands core concepts
Potential for better structured and focused discussion between site staff and study participant based on real participant's needs
Continuous improvement of consent language is easily possible based on real study participant experience and feedback
Helps to reinforce critical information and concepts and encourages the participant to go back to sections that are not clear. Reviewing the questions and answers before signing further reinforces the information.
Can hyperlink related content sections covered by the knowledge review in the consent
Considerations
May create anxiety or cause study participants to have negative opinions/embarrassment
May fear exclusion from the study or judgment by the study staff or third parties
Expectations might arise regarding how to document the rationale to enroll participants who failed the knowledge review
May prevent a detailed discussion with a participant who answered all questions correctly
Increased burden/approval delays due to change requests from individual IRBs

4.6.3 Guidance for Implementation

- 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 and reassure potential participants that knowledge review results do not impact study participation
- Limit the number of questions to approximately 4-5
- 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"
- Questions should focus on key concepts to reinforce, which may include the study purpose, that the study has risks, voluntary nature of the study, 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; provide aids if the study participant answers incorrectly. Provide the answer after a certain number of tries, and retain this information within the metadata.

- If a study participant answers incorrectly, display the relevant source information (e.g., screenshot popup, hyperlink) and allow the study participant to try again, if appropriate
- Use the knowledge check topics to review before signing. Provide instant feedback on the answer to the question with an explanation. Do not quiz study participants as a criterion for study entry.
- 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? Yes or No
  - Very 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 I stop the study at any time? Yes or No
  - 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 my data be kept confidential? Yes or No
  - 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 definitions of words that are maintained independently of the clinical study
- The glossary is a custom set of words/phrases defined by the sponsor and/or vendor

Both dictionary and glossary terms can be made available through standard user interface cues, including hover-over and highlight. The study participant does not navigate away from the primary content; definitions are provided in a pop-up box that may be dismissed by the user.
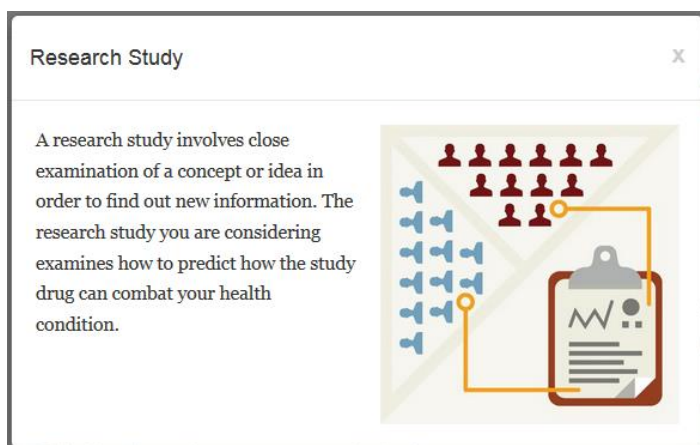
While explanations of complex words and phrases can be provided on paper, this is not as easy to use and lengthens the document.

Consider tracking how often dictionaries or glossaries are used as a measure of health literacy and/or the readability of the consent.

Figure 8   Example Dictionary Component
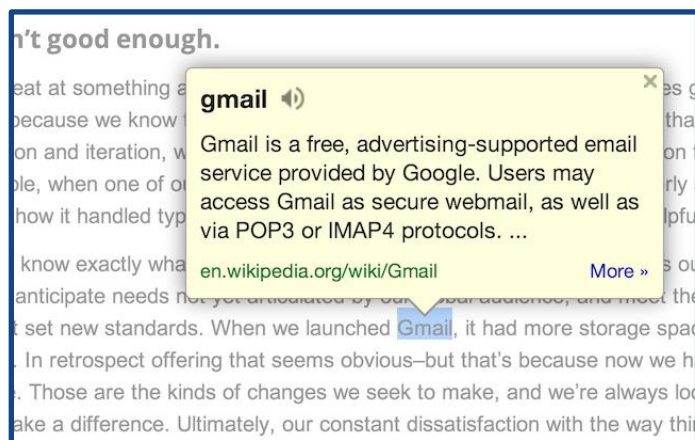
Figure 9   Example Glossary Component

4.7.2   Potential Benefits and Considerations for Dictionaries and Glossaries

Potential benefits and considerations for dictionaries and glossaries are described in Table 10.

Table 10   Dictionary and Glossary Potential Benefits and Considerations

Benefits
Glossary provides definitions for unfamiliar words or phrases
Glossary terms can be tailored to the protocol/population needs
Glossary terms can be defined with graphics, color, video, etc., to provide optimal descriptions
Metadata created from use of the dictionary/glossary may help to improve overall language for future ICFs
Facilitates document understanding and focus on content questions during the face-to-face discussion
Dictionary provides definitions through the operating system
Participants can review words at their own pace, without fear of judgment or intervention from site staff
Considerations
Words or phrases in a dictionary may have a study-inappropriate or no definition
Dictionaries are not available in all languages
Some words or phrases the participant does not understand may not be defined in the glossary
Dictionaries are presented in text only
Creating a glossary is a time- and cost-intensive activity and might require internal discussion to arrive at the right definition

4.7.3   Guidance for Implementation

- Define key words/phrases for clinical studies in the glossary for all studies (e.g., placebo, research study, sponsor, genetics/DNA, study treatment)
- Define key words/phrases for the specific study in the glossary (e.g., disease state, study procedures, drug name)
- Track review of the glossary words, and when possible, dictionary words that are reviewed to look for opportunities to simplify text
- Use videos, icons, or animation in glossaries
- When selecting vendors be mindful of the difference between dictionaries and glossaries and review sources for each
- Keep in mind that dictionary definitions are not always appropriate and may not translate well into other languages

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.

4.8.2 Potential Benefits and Considerations for Content Flags

Potential benefits and considerations for content flags are described in Table 11.

Table 11   Content Flags Potential Benefits and Considerations

Benefits
Creates metadata indicating where questions arose
Allows identification of areas to be covered in depth with the study participant
Some study participants may prefer to flag content as it is easier and less embarrassing for them
Direct feedback from study participants allows areas of focus for continuous improvement of consent
Considerations
Other study participants may not use content flags because they did not understand/remember OR they are embarrassed to flag content that they did not understand

4.8.3 Guidance for Implementation

The site should develop a process for how they will perform the consent process and ensure that all participant questions are answered. Some eConsent systems facilitate this process and documentation; however, if not documented by the system, the site must document this in their files to adhere to regulatory requirements.

If not provided by the vendor, the sponsor may work with the site to identify when content is regularly flagged so that the consent may be improved to increase readability.

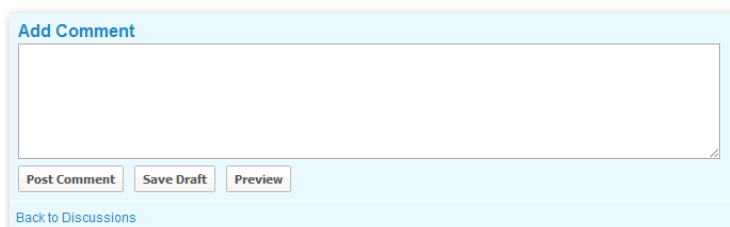## 4.9 Comment Boxes, Free Text Fields, and Study Participant Note Logs

4.9.1 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

Content flags (Section 4.8) may be combined with a comment box in which the study participant can document a specific question.

Figure 10   Example Comment Box

4.9.2 Potential Benefits and Considerations for Comment Boxes

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

Table 12   Comment Boxes Potential Benefits and Considerations

Benefits
Study participant comment box allows study participants to note specific questions within the eConsent content
Site comment box linked to a participant's consenting process can help support remote monitoring
Comments to be readdressed during face-to-face discussion can be directly entered when and where these arise, facilitating the discussion

Considerations
Sensitive personal information may be inadvertently shared or information provided that could identify the recipient, e.g. name or adverse events
Participants with low computer literacy might not be able or willing to use this feature

4.9.3   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 ask site staff to acknowledge study participant comment boxes 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.

4.10 Chapter/Section or Continuous Content Views

4.10.1 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.

4.10.2 Potential Benefits and Considerations for Chapter/Section or Continuous Content Views

Potential benefits and considerations for chapter/section or continuous content views are described in Table 13.

Table 13   Chapter/Section or Continuous Content Views Potential Benefits and Considerations

Benefits
Shorter sections may facilitate navigation within the document and lessen intimidation due to complex content (chapter/section view)
Supports easier comprehension of material, allows for continuous improvement using metadata, and enables remote monitoring (chapter/section view)
May require less pre-production editing (very useful for amendments), which may affect the cost of changes (continuous content view)
Considerations
Continuous scrolling may not support tiered consent (continuous content view)
May be little value in forcing section breaks and may be more distracting than a continuous flow (chapter/section view)

4.10.3 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
- Sites can use metadata to better frame informed consent discussion when segmented. Sites should be able to demonstrate that they have ensured that study participants understood the content when circumstances might suggest otherwise, for example, the participants 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.
- If sites intend to use metadata as noted above, considerations should be noted in the data protection segment of the consent language

4.11 Section-based Participant Attestation

4.11.1 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.

4.11.2 Potential Benefits and Considerations for Section-based Participant Attestation

Potential benefits and considerations for section-based participant attestation are described in Table 14.

Table 14   Section-based Participant Attestation Potential Benefits and Considerations

Benefits
Decouples information from consent; enables application development, improved education, and a movement toward progressive consent
Metadata indicate which sections raised the most concerns and enables remote monitoring of how long each participant spent per section, allowing queries
Helps to ensure no segment of the consent is missed
Considerations
Requires ongoing interaction from a study participant that may feel redundant or time-consuming
Edits to consent language may be challenging to incorporate, increasing time and cost

4.11.3 Guidance for Implementation

Development and reuse of modular sections supports efficient consent development and reduces redundancy and inconsistencies. Consider using knowledge review as a way of ensuring that the section-based attestation means that the participant has understood the language.
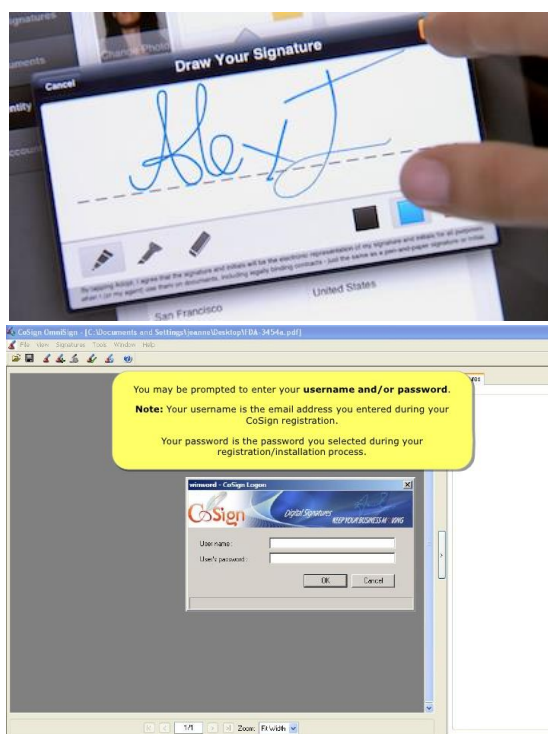
4.12 eSignature

4.12.1 Description of eSignature

Authentication/confirmation of study participant identity by the site is unchanged when using eConsent. 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, which includes evaluation of data

hosting and remote viewing requirements. Current FDA regulatory guidance on eSignature can be found in 21 CFR Part 11 Subpart C.[13] The following are European Union (EU) signature categories (EU Regulation 910/2014)[14]:

- **Electronic signature:** data in electronic form which is attached to or logically associated with other data in electronic form and which is used by the signatory to sign

- **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 electronic signature:** an advanced electronic signature that is created by a qualified electronic creation device, and which is based on a qualified certificate for electronic signatures

Figure 11   Example eSignature

4.12.2 Potential Benefits and Considerations for eSignature

Potential benefits and considerations for eSignature are described in Table 15.

Table 15   eSignature Potential Benefits and Considerations

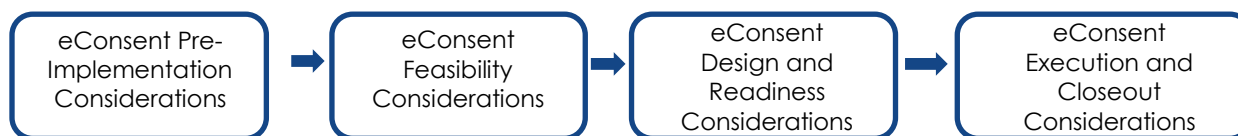| Benefits |
|---|
| Date and time of consent are automatically recorded, reducing the risk of human error and number of audit/inspection findings |
| The signature is embedded in the eConsent process on the device and therefore the consent signature cannot be forgotten |
| Populations with motor skill issues or certain physical impairments can sign electronically more easily |
| The site monitor can remotely monitor the consent process and ensure more quickly that the consents are appropriately signed |
| No need for a pen |
| Potential for remote eSignatures if there are measures in place to prevent fraudulent use of eSignatures |
| eConsent systems ensure the site-based countersignature |
| **Considerations** |
| Electronic signatures are not universally accepted for signing ICFs though often accepted for other legal matters |
| Countries/states/provinces/IRBs/IECs may have varying requirements |
| Participants may have objections to eSignature (lack of trust, privacy concerns) |
| Use of eConsent with remote consent may present a risk for fraudulent eSignature |

4.12.3 Guidance for Implementation

- When considering the implementation of electronic signature, it is important to consider if any patient-identifying information would be stored or accessible outside the site

- Review local regulations, consult with health authorities and/or local privacy offices, and include appropriate references in submission materials (e.g., protocols)

- Potential signature types include handwritten signature on paper, handwritten signature on paper uploaded into the eConsent system, handwritten signature on an electronic device, and eSignature

- 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 several countries based on local requirements. 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 require 24 hours between receiving and signing/countersigning the ICF in order for participants to have sufficient time to consider the implications (e.g., EU will require that adequate time be given to the study participant) or require a second confirmation (e.g., inclusion of an extra "are you sure" question prior to finalizing the signature)
- Ensure that eConsent will allow for capturing this information or that there is built-in functionality to ensure lag-time requirements are met before signatures are allowed
- Other methods for documenting consent can also include 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 5.2.3 and Privacy, Legal, and Other Processes in Section 5.2.4.

5   Planning and Executing eConsent

eConsent considerations over the course of a study are described in the sections below.

| eConsent Pre-Implementation Considerations | → | eConsent Feasibility Considerations | → | eConsent Design and Readiness Considerations | → | eConsent Execution and Closeout Considerations |

5.1   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.

5.1.1   eConsent Objectives Planning
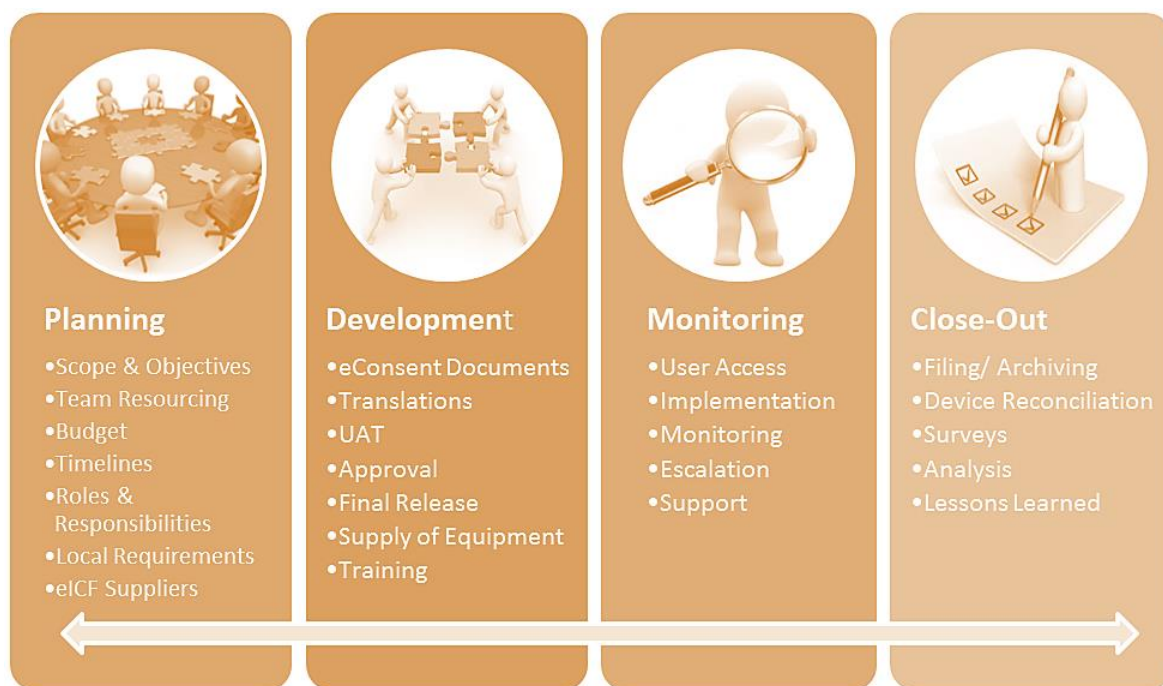
When considering piloting/implementing eConsent, document in detail what the organization requires, what it wants to achieve, and any associated impacts. Ideally, this should align with an organization's overarching objectives (if not, this may warrant further high-level discussions). Companies with no internal eConsent experience may consider working with a vendor to develop these objectives.

Review and assess eConsent objectives against the needs of the organization and study team to ensure short- and long-term alignment. Study-specific considerations for planning are covered in Section 5.2.1, eConsent Study Considerations.

5.1.2   eConsent Impact Analysis

By dividing the eConsent operationalization 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.

Figure 12   Illustrative Process for Operationalization of eConsent

Planning
- Scope & Objectives
- Team Resourcing
- Budget
- Timelines
- Roles & Responsibilities
- Local Requirements
- eICF Suppliers

Development
- eConsent Documents
- Translations
- UAT
- Approval
- Final Release
- Supply of Equipment
- Training

Monitoring
- User Access
- Implementation
- Monitoring
- Escalation
- Support

Close-Out
- Filing/ Archiving
- Device Reconciliation
- Surveys
- Analysis
- Lessons Learned

Detailed implementation considerations for assessing impact are provided below:

1. eConsent Start-Up Timeline Considerations
2. Privacy/Data Considerations
3. Information Technology Diligence Activities
4. Organizational Impact Analysis
5. Stakeholder Impact Analysis
6. Critical Success Factors (see Section 5.3.4)

5.1.2.1   eConsent Start-Up Timeline Considerations

For initial studies using eConsent, it can take several 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, training, 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)

Assess potential vendors to determine if they meet the sponsor's policies and requirements. 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 shows a sample timeline, including time for translations if needed.

Figure 13   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
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 IRBs/IECs/ HAs																									█	█	█	█	█	█	█	█
Training preparation																									█	█	█	█				
Training sites																													█	█	█	█
Deploy to sites																														█	█	█

5.1.2.2   Privacy and Legal Considerations

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
- When considering the implementation of electronic signature and collection of any other patient-identifying information (e.g., patient name, patient signature), it is important to consider if that information would be stored or accessible outside the site. Review local regulations, consult with health authorities and/or local privacy offices, and include appropriate references in submission materials (e.g., protocols).
- 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:
  o Evaluate the multimedia components (Section 4) for privacy, legal, and other processes
  o Knowledge review: eConsent can provide documentation of knowledge review. Therefore:
    ▪ When including a knowledge assessment, discuss the process and confirm the importance of ensuring that the knowledge assessment is taken prior to the participant signing consent. This information can 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?
  o Ensure that any video or other supplemental information does not include any unintentional branding/promotion
  o Be aware of the diversity of the study participants and the impact of the choice of media
  o 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 4.12)
- Location of the database and IT administrators: consider any applicable regulations (e.g., EU data protection (EU) 2016/679 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 information?
- Security of the database: Is there adequate access control and an audit trail? How does the eConsent protect the study participant's sensitive personal information (such as name)?
- 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?

- o 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.

5.1.2.3 Information Technology Diligence Activities

Depending on the company SOPs or guidelines, different departments may need to be involved in discussions on system and data security (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:
  - o Regulatory risk (whether full validation is required)
  - o Project security (includes review of access controls)
  - o Mobility standards
  - o 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

5.1.2.4 Organizational Impact Analysis

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 Potential 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 staff/resources)
    - More coordination to add an additional member to the study team
- Adding additional activities to existing study team
  - o Potential 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 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, and potential modifications needed 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 5.2.1)
2. Define desired multimedia components (Section 5.2.2, Section 4)
3. Review Operational Considerations (Section 5.2.3)

      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 5.2.4)
5. Define stakeholder roles and responsibilities (Section 5.2.5)

5.2.1 Study Considerations

Study considerations provided for each of the topic areas are primarily for pilot studies but can be adapted for larger studies:

1. Study design, duration, 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.

5.2.1.1 Study Design, Duration, and Complexity

Consider a pilot study with relatively few variables. Some considerations include:

- Can potentially begin with a small-scale study with few countries/sites
- Can potentially begin with a late-phase study with a simple, straightforward study design
- Consider a short-term study unlikely to be amended
- Consider the feasibility and complexity of the study population (age, awareness of technology, and cognitive ability of study participants), study design (study site location, interventional versus observational, use of other technology), and therapeutic area (e.g., oncology, pediatrics, emergency situations may require additional considerations)
- Limit the number of different types of consents to be used in the pilot (e.g., assents, biomarker analysis, bio-banking)
- Consider that sites with low recruitment rates may have less experience with eConsent

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.

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.

5.2.1.2   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 IRBs/IECs, where possible
- eConsent may be used in some regions/countries/sites and paper consent in others within the same study. This would allow for analysis of differences between the countries/sites that are using eConsent and those that are not (using sponsor-established metrics).

5.2.1.3   Clinical Sites

- Assess whether 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 and assist with troubleshooting as needed.
  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
- Assess 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).
  o Internet access
  o Internet bandwidth

- o Institutional approvals (e.g., firewall access)
- o Availability of device use such as phone, computer, tablet, 3G card, etc.
- o Ability to connect with a printer
- Varying levels of review may be needed for processes and procedures

5.2.1.4 Study Size and Demographics

- The size of the study is an important factor that should be considered when choosing a pilot study
  - o If a larger study is chosen, consider 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 (refer to the eConsent Vulnerable Populations guidance)
  - 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

5.2.1.5 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 or outsourced as per the sponsor's SOPs

5.2.2 Considerations for Identifying eConsent Multimedia Components

Consider the following:

- Number and type of multimedia components, particularly if this is the first time this technology is being used within the company
- Study considerations (Section 5.2.1) will help determine which multimedia components (Section 4) are needed versus nice to have
- Involve team members from different functional areas who will have different ideas about functionalities, uses, etc.

- Check with colleagues who 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

5.2.3 Operational Considerations

Consider lessons learned from similar technology implementations. Some examples are provided below.

5.2.3.1 Device Management (On-Site Consenting Option)

For on-site eConsent, devices can be vendor/sponsor-provided or site-owned (bring your own device is mentioned in the eConsent Emerging Trends and Future Considerations guidance).

When deciding how to provide the device, consider potential issues with importing information from the device. Some vendors load software onto a single device, while others allow eConsent to be accessed through a secure website from any device.

Vendor- or sponsor-provided device:

Potential 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

- How many devices should be provided to the site and the impact on recruitment and other site activities (potential for eConsent activities to interfere with or limit access to eCOA/ePRO activities)
- 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
  - o Sites working on multiple studies with different vendors may have many different devices that they need to store securely
  - o 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:

Potential Benefits

- Limits the number of required devices

Considerations

- 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

- Establish a device shipment plan that considers impact to importation, import license requirements, potential shipping and custom delays, and other regional differences (such as power requirements). Refer to Study Considerations in Section 5.2.1 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)
  - o 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 quality of life questionnaires)
  - o 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.
  - o Consider other new technologies that the site is implementing to avoid overwhelming the site with yet another new technology

5.2.3.2 Re-consent

eConsent may be especially useful when re-consent is required.

Potential Benefits

- eConsent offers different options for re-consenting to new versions of an ICF and can facilitate this process. Sponsors must evaluate which option is feasible based on their SOPs and what is deemed acceptable by the IRB/IEC.
- Easier to operationally track when participants have been re-consented or need to be re-consented

Considerations

Re-consent can occur remotely, i.e., outside the study site (see Section 5.2.3.5) or on site. For on-site re-consent, consider the following review options:

- Review the entire new consent, including sections that were not amended, which currently is the most commonly used method for paper consents
- 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: targeted review of the changes while allowing review of 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 for consistency. Re-consent guidance will need to be established for eConsent because of the need to update the system.

5.2.3.3 Optional Consent

Some studies include additional optional activities (e.g., optional procedures, notification of primary physician, biobanks) that are not required for study participation. The additional consent may be part of the main consent or a separate addendum. eConsent can facilitate incorporating the optional consent into the main consent.

Potential 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 (refer to Emerging Trends and Future Considerations guidance)

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

5.2.3.4   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. 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 (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 track withdrawal of consent for specific participants within the system.

Potential 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).

5.2.3.5   At Home or Remote Consenting

Although consenting is usually done at the site, some country regulations may allow 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:

- Participants are introduced to the study at the site but can review all documentation at home with their families and make an informed decision to participate or not at home (partially remote)
- Participants become 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 studies, where all assessments are occurring at the participant's home.

Potential 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
- Reduced shipping costs

Considerations

- 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, providing initial consent only after an initial study site visit (e.g., after medical records are provided), or remote consent only 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 the ability to re-send parts of information or video as preparation for a new visit and digital support.

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

eSignature is discussed in Section 4.12. Other methods may be used for documenting consent, depending on the local jurisdiction's requirements. Below are a few examples:

- Digital 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

Potential 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.

5.2.4   Privacy, Legal, and Other Processes

- Other considerations, including privacy, remote monitoring, and fraud are briefly described here. See Section 5.1.2 for more information on privacy, legal, and IT considerations

5.2.4.1   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, administrator location, access to data, and data storage

5.2.4.2   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

5.2.4.3   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)

5.2.4.4 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

5.2.5 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 and obtain their endorsements
- Clear goals, objectives, roles, responsibilities, guidance, and instructions
- 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 5.3.4)

5.3 eConsent Design and Readiness Considerations

5.3.1 Kickoff Meetings with the Vendor

Establishing a good working relationship with the eConsent vendor is important in ensuring a successful eConsent process. 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 could 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 (including use of multimedia components)
- 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 5.3.5)
- Required material for submission to the IRB/IEC; include discussions regarding storage/archival
- Document control (e.g., versioning)

5.3.2 Collaboration and Communication between Sponsor and Vendor

Consider the following throughout the study to ensure a good working relationship between sponsor and vendor:

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

5.3.3 eConsent Data Access and Archiving

5.3.3.1 Sponsor Considerations

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

The sponsor will need to decide where they want to house the documents and who will have access. During the study the sponsor may have access to participant data, but after archival the data is de-identified for the sponsor.

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 the vendor will be 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 be able to readily 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:

- Consider storing the electronic ICFs 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.

IRB Considerations

- Some IRBs may require paper-based versions of the eConsent documents for IRB/IEC archival purposes

Some additional considerations:

- Ensure the system has the capability for an audit trail. The audit trail will be able to capture any revisions, the person making the changes, the reason for the changes, and the date the changes were made.

- If 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

5.3.3.2 Site Considerations

During and after the study 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 specify whether documents need to be physically printed and stored or can be maintained in an electronic database

5.3.4 Setting up Metrics and Critical Success Factors

For examples of site and patient surveys, please refer to the Site Survey Template and Patient Survey Template guidance.

5.3.4.1 Process for Identifying and 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. 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., participant comprehension/satisfaction, participant engagement)

Surveys and/or interviews may assess the following topics:

Table 16   Possible Survey Topics to Assess Critical Success Factors

Stakeholder	Survey Topics
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, sub-investigators)	• 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 • Audit/inspection findings, perception (can change over time) • Satisfaction with training
Internal stakeholder (e.g., study team, site monitors, management)	• Ease of technology use • Overall satisfaction with process • Re-consenting process, version control • Workload • Time spent on monitoring ICF activities • Better/more engagement with study site • Metrics, summary data • Improvement in study participant retention, training, support • Budget, return of investment • Audit/inspection findings • Process/complexity/time for submission, approval, and implementation (can change over time); consider that these may be different for original and amendments

Stakeholder	Survey Topics
External stakeholder (e.g., IEC/IRB, HA, contract research organization [CRO])	- Ease of technology use - Overall satisfaction with process - Ease of submission - Approval and implementation - Perception (can change over time)

5.3.4.2   Metrics

There are generally 3 types of metrics to consider when evaluating eConsent: operational (internal), quality (internal and external), and usage (external), along with any sponsor- or study-specific metrics. 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 findings
  - 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 with 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:
  - o Number and percentage of study participants to fully consent electronically
  - o Study dropout rate
  - o Section read time
  - o Knowledge check (if appropriate) results
  - o Number and percentage of video views (if applicable)
  - o Observational feedback from site personnel who administered consent (surveys)
- Guidance: engage colleagues who focus on optimizing recruitment review success measures; proactively identify potential inspection findings that might occur with collection of usage metrics

5.3.5   Study Oversight

Develop processes 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. Consider the following:

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

5.3.5.1   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)

5.3.5.2   Definition of Analytic Data Fields

- See Section 5.4.2 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

5.3.5.3   eConsent Go-Live Plan

IRB approval:

- Develop a go-live plan early
- Develop an appropriate package for IRB/IEC submission (see Section 5.3.6.2)
- Disseminate packet to IRBs and vendor for questions
- Once approved, activate the site in the system
- Site access/tablet distribution
    o   Ensure timely access to solution ahead of training/go-live
    o   Ship to selected sites to meet any agreed timelines
    o   Contingency plan for import issues

5.3.5.4   Contingency Planning

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

5.3.5.5   Training for Sites

Training for sites can take place in a variety of formats, usually one or both of the following: (1) virtual, (2) electronic training upon initial system access or (3) live training on site or during the investigator meeting. The format can be decided at the kickoff meeting.

- Training may include a live demo using (at minimum) the site's level of access
- 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 training version cannot be confused with the live eConsent that is used to consent study participants. For instance, create a training eConsent where sites can practice using the device in a fictitious, nonclinical related study.
- If training DOES NOT occur at the investigator meeting, a method of training should be identified
- Include guidance or "best practices" to incorporate eConsent into the consenting process

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).

5.3.6   External Processes

There are fundamental similarities in the objectives of the core activities between paper ICF and eConsent. The key changes per activity noted below are comparable to the types of changes for other eTechnologies (e.g., ePRO). Keep these in mind when developing processes, defining communication/training, and addressing any implementation impacts.

- **Design**
  - o   Key change: development and translation of multimedia components
- **Readiness**
  - o   Key change: submission and review of multimedia components
- **Execution**
  - o   Key change: participant interacts with multimedia components and might not receive a paper copy of the eConsent but a link to the eConsent or a copy emailed to them; Site/sponsor receives metadata insight
- **Closeout/Archival**
  - o   Key change: archive eConsent data

5.3.6.1   Site Processes

Work with sites to determine the site's capabilities to use eConsent. Create guidelines on how eConsent can be aligned with the normal site procedures:

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.

- It is a good idea to include a link to a sample eConsent when asking for sites' participation
- 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) and try to overcome them
- 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 (Introduction to eConsent for Sites, Site FAQ) may be used to support site engagement
- If resistance remains, consider using paper consent at that site

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

- Will be necessary if eConsent cannot be used for all study participants or at all sites
- Define processes and create instructions for sites (using site SOPs)
- 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. Determine how sites should proceed if there is a delay between paper and electronic update approval.
  - o How will sites file and archive eConsents? 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)?

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., setup 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):
  - o Does the internet connection work?

- o Is user access confirmed in the system and test environment (e.g., user names, password)?
- o Will a separate printer be provided to print directly from the device? Does the site have space and is it willing to use it?
- o 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? 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

5.3.6.2 IRB/IEC Processes

Timing of IRB/IEC submissions must be considered to ensure a smooth eConsent process. Before 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 subject matter expert 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 that each IRB/IEC may have differing expectations/requirements on what needs to be reviewed/approved
- 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). Ensure that the submission package allows the specific IRB/IEC to edit/comment on the eConsent using a format that is readily available. Discuss submission package options which provided IRBs/IECs with sufficient information, considering the examples below (Table 17).

Table 17   Potential IRB/IEC Submission Package Types

Type of Package	Possible Contents
Paper	Storyboard and/or screenshots, glossary terms, knowledge assessment, eSignature verification form from vendor, and data privacy statement from vendor, attestation letter or interpretation document
Electronic	Link to portal or digitized consent, eSignature verification form from vendor (this document provides verification that the eSignature is compliant with local regulations; will be used as appropriate), and data privacy statement from vendor, attestation letter or interpretation document
Paper and electronic	Combination of the elements above
Initial (one-time only)	Demonstration in addition to one of the package options above

- Work with the vendor to ensure site-specific requirements are included in the submission (e.g., logos, template features)
- Study teams should be aware of the additional time needed to address specific requirements from local IRBs/IECs (especially in pediatric studies)
- 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

5.3.6.3   Health Authority Processes

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 (Only Informed):** In cases of NO IRB/IEC review or where HAs would require more comprehensive review, the package options shown in Table 17 may be considered.
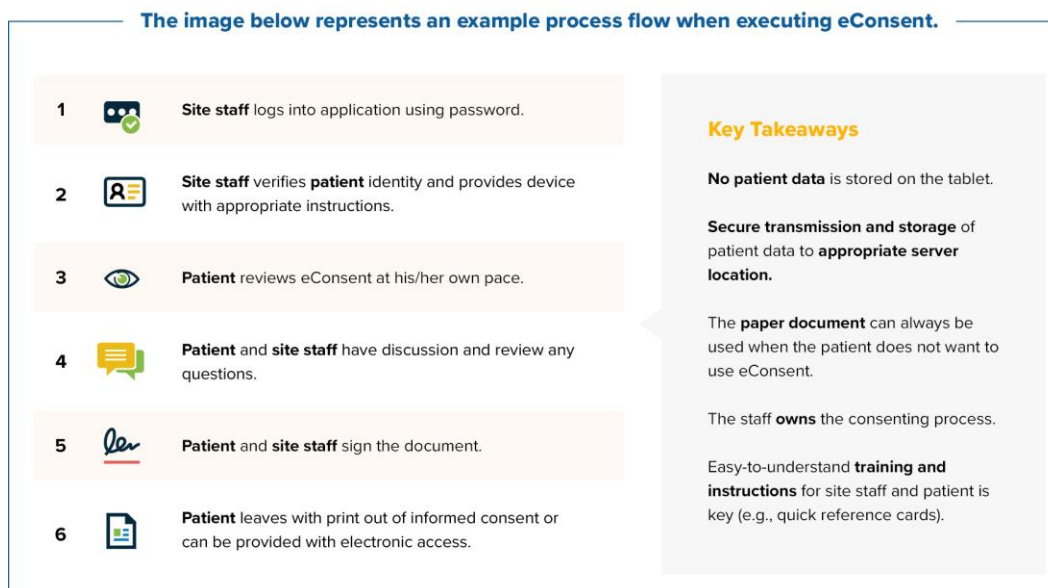
5.3.6.4   CRO Processes

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. Determine if the eConsent development process will be led by the CRO or sponsor. The following are possible areas to address during initial engagement:
  - o CRO timelines, roles, responsibilities and planned deliverables of all parties, including expectations for monitoring activities, and any potential metric reporting
  - o If the sponsor develops the eConsent, the impact on and expectations of CRO monitoring activities should be considered up front
  - o 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).
  - o Quality checks should be put in place at all stages of development and implementation

5.4   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. The execution phase is when the proposal, tasks, and activities that were created in the startup phase are put into action and where the anticipated outcome of the expected eConsent results is delivered.

Figure 14   eConsent Execution Potential Process Flow

The image below represents an example process flow when executing eConsent.

1. **Site staff** logs into application using password.
2. **Site staff** verifies **patient** identity and provides device with appropriate instructions.
3. **Patient** reviews eConsent at his/her own pace.
4. **Patient** and **site staff** have discussion and review any questions.
5. **Patient** and **site staff** sign the document.
6. **Patient** leaves with print out of informed consent or can be provided with electronic access.

Key Takeaways

No patient data is stored on the tablet.

Secure transmission and storage of patient data to **appropriate server location**.

The **paper document** can always be used when the patient does not want to use eConsent.

The staff **owns** the consenting process.

Easy-to-understand **training and instructions** for site staff and patient is key (e.g., quick reference cards).

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 5.4.1)
- Examples of oversight /compliance/management reports to support monitoring activities (Section 5.4.2)
- Issue management/resolution (escalation, help desk) (Section 5.4.3)
- Audit/inspection readiness (access to data in eConsent, review, adequacy of processes) (Section 5.4.4)
- Filing and archiving (Section 5.4.5)

5.4.1   Monitoring Methods

Monitoring is the act of overseeing 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 as indicated in the monitoring plan.

- 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 regulatory 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

5.4.2 Oversight, Compliance, and Management Reports to Support Monitoring

Some reports to consider for use by monitors or in-house staff, depending on role, 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:
  o Trained (with date of training) on eConsent
  o With access to eConsent data
  o 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
- List of participants who consented through a legally acceptable representative (LAR)
- List of participants signature date and time

- List of ICF sections that required clarification
- Withdrawal of consent for use of samples or data
- Time participants spent with each ICF section
- Total time participants spent consenting
- Result of the knowledge review, if used
- Automated alert reports to investigator/sponsor

Reports should be appropriate to the individual's role (e.g., in house staff, laboratories, or training staff would see coded aggregate data) and contain specific restrictions/protections to prevent sharing data inappropriately or unnecessarily.

5.4.3 Issue Management and Resolution

eConsent provides the capability of accessing data remotely and centrally, allowing for real-time eConsent review and analysis and thus quicker identification, resolution, and prevention of issues/concerns. Ensure that no participant identifiers can be accessed/viewed remotely.

- 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

5.4.4 Audit/Inspection Readiness

The sponsor's procedures/policies should be followed to ensure proper audit/inspection readiness, including:

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

5.4.5 Filing/Archiving

The sponsor's procedures/policies should be followed to ensure proper management of filing and archiving. For details on filing/archiving at the site please see Section 5.3.6.1.

6   Background Resources

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