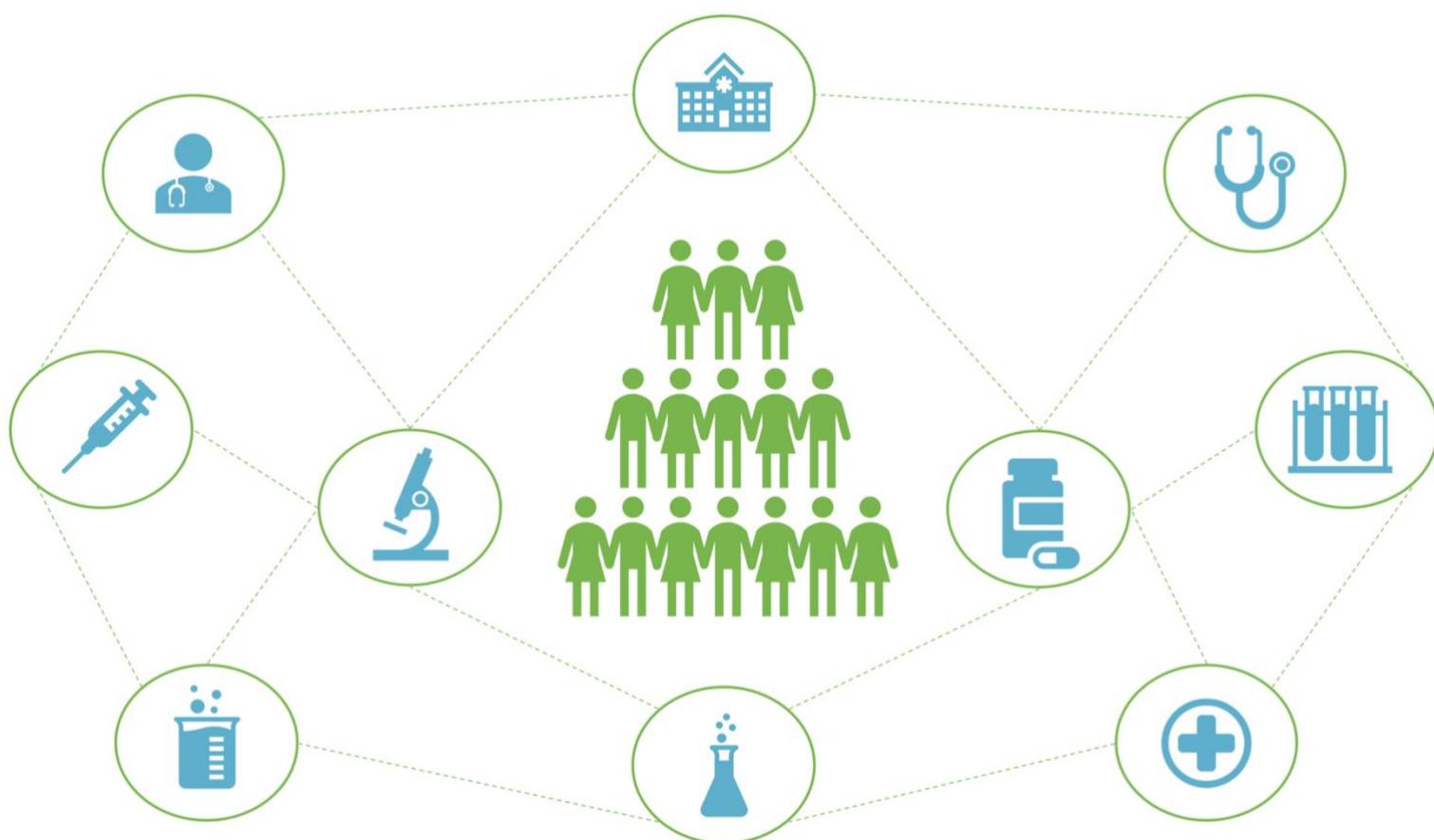


# Electronic Informed Consent Implementation Guide Practical Considerations



A position paper written by a joint task force from the EUCROF New Technologies Working Group and the eClinical Forum

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### *About EUCROF*

The European Contract Research Organisation Federation (EUCROF) consists of members from most European countries and partner members from nearby countries with the aim of promoting clinical research of high quality in Europe in general and in the European Union in particular. EUCROF's objectives include promoting discussions on selected topics with representatives of the pharmaceutical industry to enhance business relations and identify common concerns, supporting more productive discussions with European bodies (EMA/EU Commission), and endeavouring to develop transcontinental relationships with other associations e.g., with ACRO (Association of Clinical Research Organisations) in the USA and JCROA (Japanese Clinical Research Organization) in Japan.

### *About the eClinical Forum*

The eClinical Forum (eCF) is a global, technology independent group representing members of industries engaged in clinical research. The eClinical Forum's mission is to serve these industries by focusing on those systems, processes and roles relevant to electronic capture, handling, and submission of clinical trial data. For further information visit the website at [www.eclinicalforum.org](http://www.eclinicalforum.org). The eClinical Forum has sought out opportunities to promote electronic Clinical Trials since its inception in 2000. The cross-industry forum has a broad view of research with members - Sponsors, Contract Research Organizations (CROs), Technology vendors (both clinical research and healthcare), Academia, and Investigators - and with invited outreach opportunities with global Regulatory representatives.

### *Disclaimer and License*

The information presented in these works draws upon the combined current understanding and knowledge of EUCROF and the eClinical Forum on this topic and is provided as an aid to understanding the environment for electronic clinical research. The opinions of the author(s), EUCROF and the eClinical Forum do not necessarily reflect the position of individual companies. Users should assess the content and opinions in the light of their own knowledge, needs and experience as well as interpretation of relevant guidance and regulations. For additional Disclaimer and License information, see Appendix 1.

## Executive Summary

The aim of this document is to serve as an implementation guide when transitioning to electronic informed consent (eConsent) in clinical trials. The main purpose of the implementation guide is to provide a background of the benefits, processes and nuances of eConsent and offer practical advice to facilitate implementation. The focus of the guidance will be of particular relevance to sponsors and regulators. Although other eConsent guidance documents exist, this paper offers a unique combination of practical considerations from stakeholders, an updated landscape overview of eConsent in today's world, with an outlook on the current regulations and the impact of COVID-19 on demand for eConsent. It is important to stress the significance of ensuring that local regulations, which are often subject to dynamic changes, are followed prior to implementation. The document was created by the EUCROF eConsent group and eClinical Forum, consisting of eConsent experts from the industry. Stakeholders with experience of eConsent from other organisations were also involved in providing their personal accounts of eConsent.

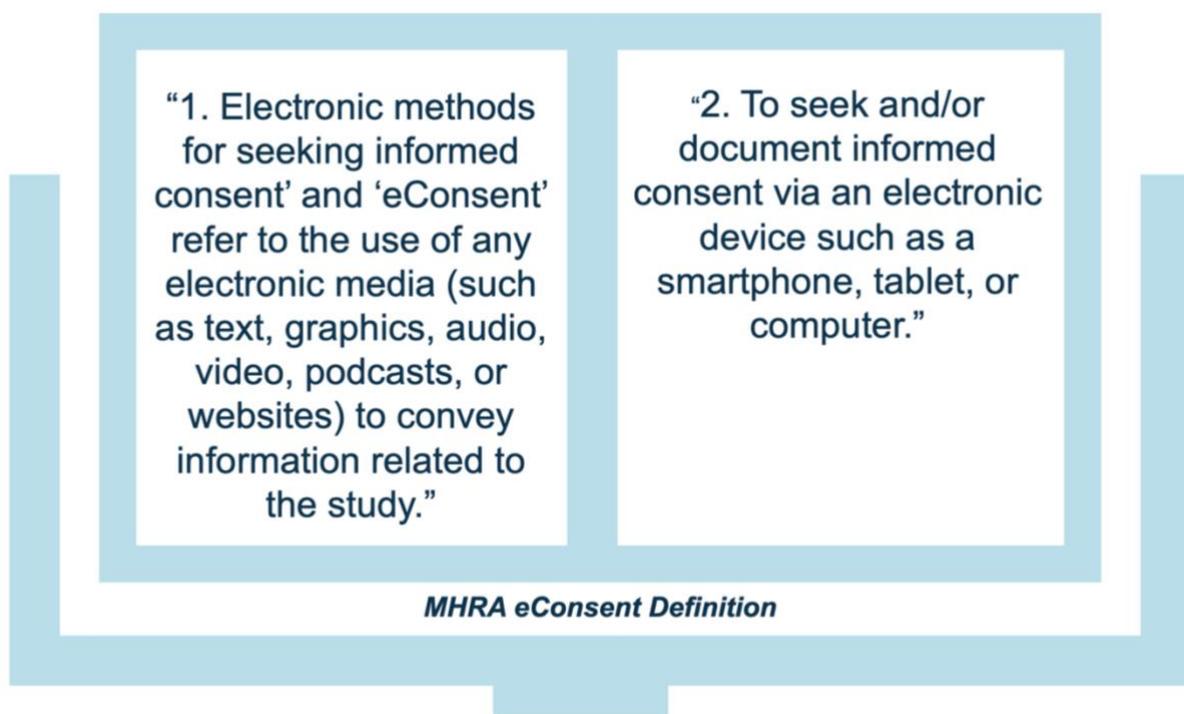
The following implementation guide will take you on the journey that mimics eConsent implementation, starting with an introduction to the process, where you will learn about the possibilities and opportunities that eConsent presents. Then, once you decide that you would like to consider eConsent implementation, you can learn more about the process of the eConsent procedure for the sponsor, site and participant. Afterwards refer to the implementation section for a detailed implementation guide. Lastly, you will be able to understand other stakeholder's experience with eConsent in the stakeholder perspectives section.

## Introduction to eConsent

Informed consent is a pivotal part of clinical trials and is a paramount characteristic of ethical clinical trial conduct. The GCP ICH R2 defines informed consent as “A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject’s decision to participate.” [1]. As the healthcare sector and clinical trial conduct evolves beyond the paper-based systems into electronic alternatives, the healthcare industry is progressing towards a digital clinical trial era in an accelerated manner. eConsent is one of the components of clinical trial virtualisation that the healthcare industry is heading towards [2].

The Medicines and Healthcare products Regulatory Agency (MHRA) and Health Research Authority (HRA) in the UK define the electronic informed consent process as “consisting of two distinct phases of educating and giving consent via a signature” [3].

Electronic consenting is not a new phenomenon but already established and proven and has been in use for around 15 years. As per a survey conducted in 2017, it was indicated that the main drivers for implementation were improved participant satisfaction, reduced regulatory risk, increased participant comprehension and accelerated study and site start-up [4]. Whilst eConsent has been in use for over a decade and there are clear benefits to participants and efficiency gains to be harnessed, there has been slow adoption due to various aspects, such as regulatory barriers, hesitation to change and cultural resistance, to name a few.



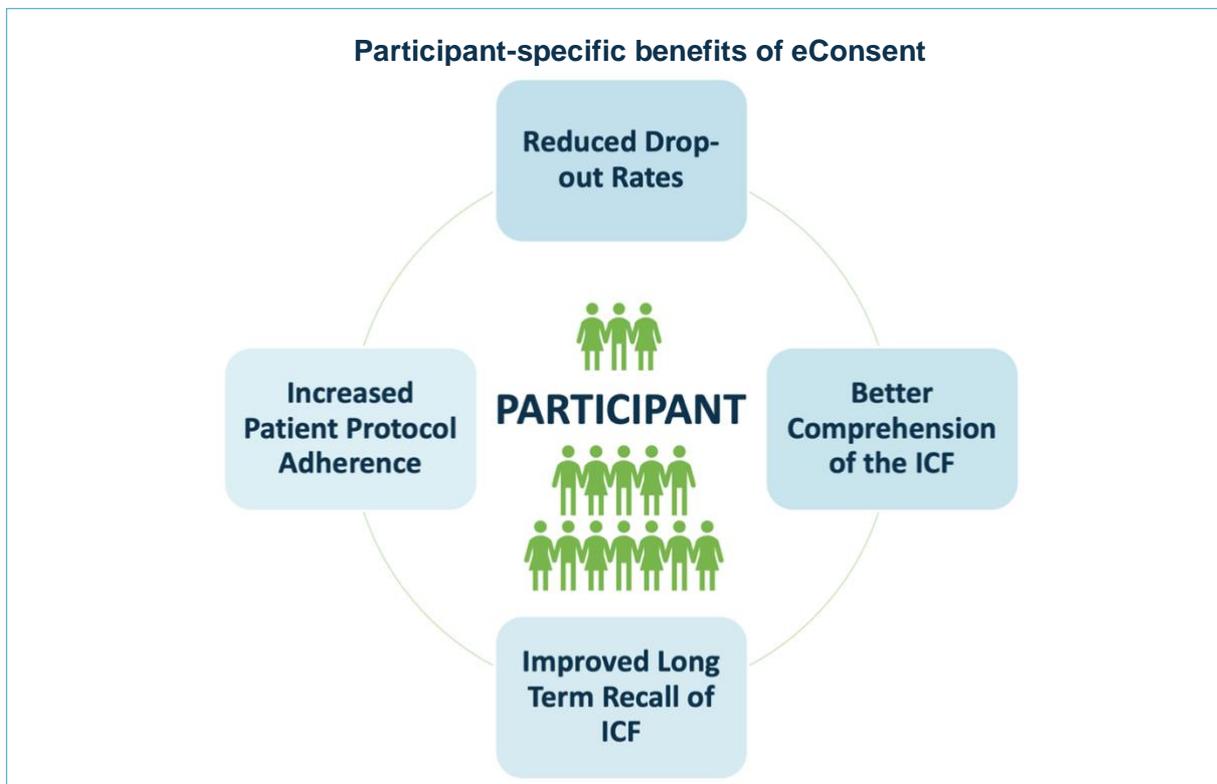
## Improve Participant Experience

The motivation to switch to eConsent does not merely stem from process efficiency and convenience of an electronic procedure over a paper alternative. eConsent provides participants the opportunity to understand and learn information using a variety of more interactive methods. This in turn increases participant comprehension. This was positively demonstrated in a study that compared paper informed consent form (ICF) to eConsent directly [5].

Better participant comprehension reduces the risk of participant drop out due to a lack of understanding of what they had consented to. This was shown in a study where eConsent was shown to increase participant adherence to the study requirements and retention [6].

A pilot study that was conducted demonstrated that eConsent improves long-term recall of the informed consent elements. This is valuable, as data suggests high rates of participant loss can be traced back to a lack of understanding of paper ICFs, which either leads to less participants enrolling, or increases participant drop-out rates as participants are unaware that they consent to all the aspects and requirements of the clinical trial due to a lack of understanding.

In a survey [7] 35% of prospective participants said that they do not enrol onto a clinical trial due to a lack of understanding of the long paper ICF, clearly indicating that the informed consent process format needs to be improved. eConsent eliminates many of the roadblocks for participants considering participation in a clinical trial and engages them by optimising and clarifying the informed consent content and allowing them to make a more informed and ethical decision.



**Figure 1:** Participant-specific benefits of eConsent showcasing some of the main improvements to the clinical trial.

## The 'Electronic' in Electronic Informed Consent

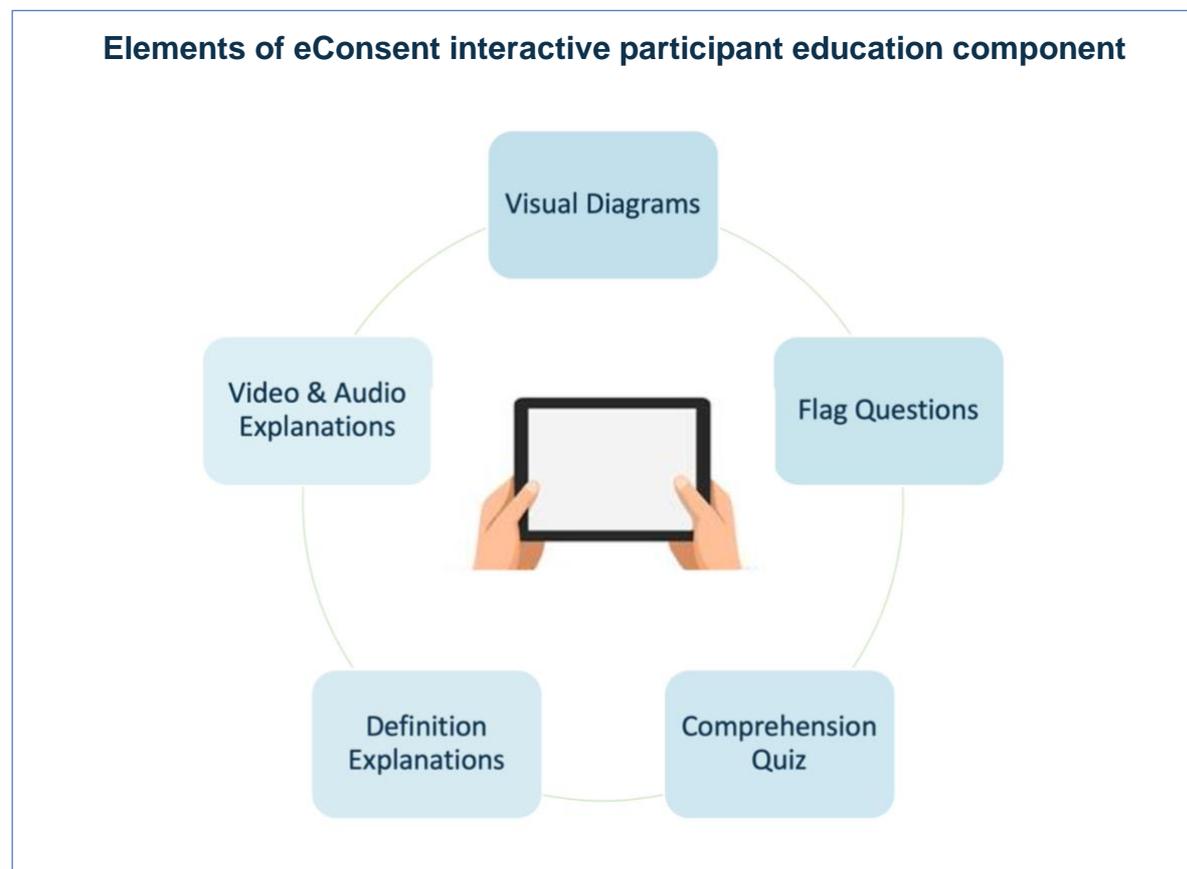
Within this section we will address what exactly does the word 'electronic' refer to in eConsent. The 'electronic aspects of eConsent are highly configurable, with the option to opt in or out of using an electronic interactive participant education component and an electronic signature. Both of these elements of eConsent can serve as substitutes or an addition to the existing paper informed consent processes.

### *Interactive Participant Education Component*

The interactive participant education component could include video, infographics, audio components, as well as a function for looking up definitions and flagging up areas of uncertainty.

This interactive participant education component can be used to augment or substitute traditional paper-based methods of informing the participant. Research has demonstrated that information relayed via multimedia formats are preferred by participants and that overall comprehension is greater [8].

The sponsor and investigator can use additional means to confirm the participant's comprehension through a knowledge check assessment, also referred to as a comprehension quiz, that can highlight areas of uncertainty for the participant and information that should be further emphasised.



**Figure 2:** Examples of Elements of eConsent interactive participant education component that elevate the traditional experience of reading a lengthy paper ICF.

## eSignature

An eConsent platform can be configured to accommodate different signature types, which can be paper or electronic options compliant and in line with the country-specific regulations.

Within Europe, electronic identification and trust services (eIDAS) EU Regulation 910 [9] addresses electronic identification and trust services for electronic transactions specific to the EU region. eIDAS highlights three electronic signature types:

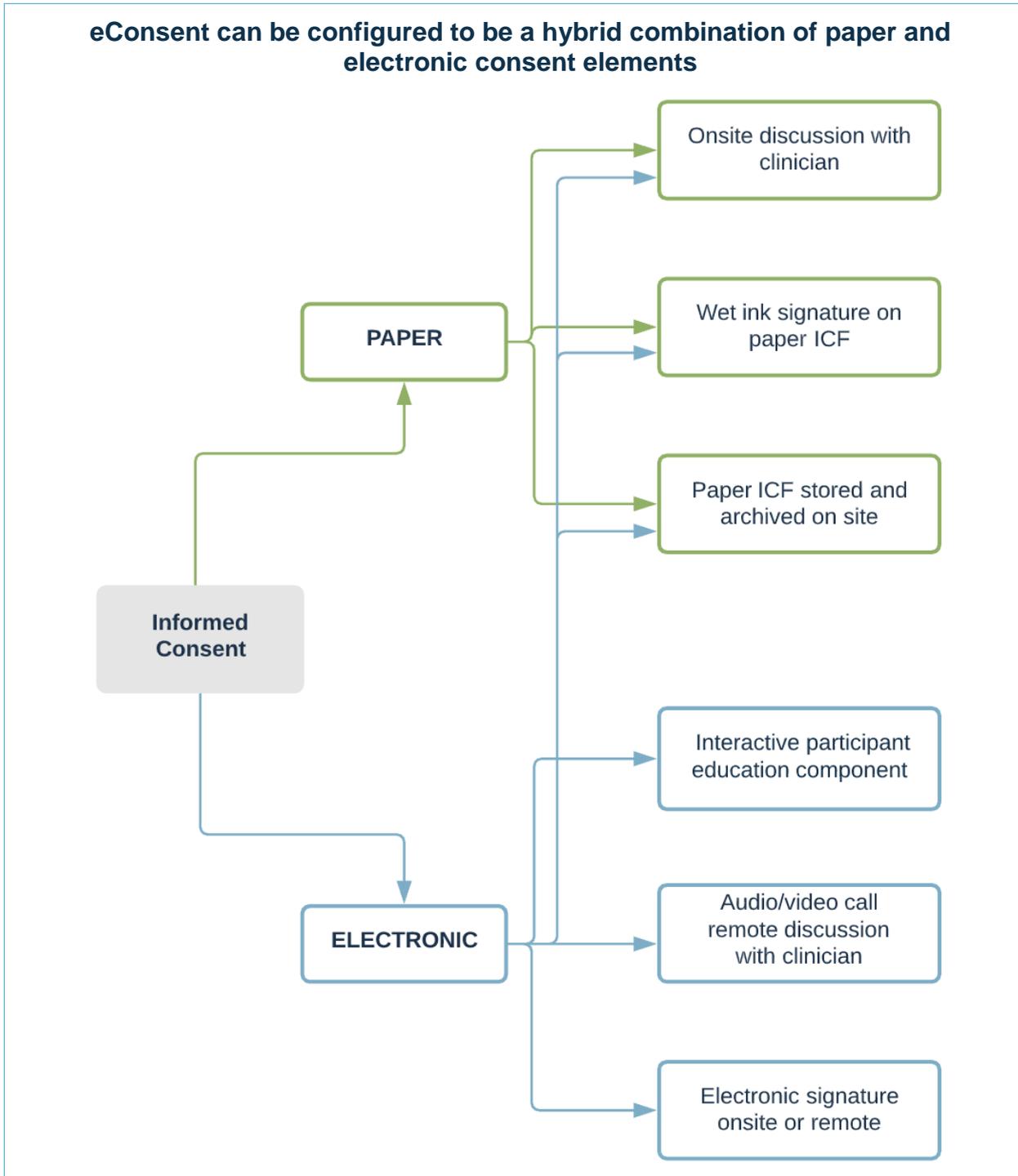
- ✓ Simple electronic signature is defined as data in electronic form that serves a role of authentication. Some examples of simple signatures may include stylus, finger drawn, typed signatures.
- ✓ Advanced electronic signature, which is linked to the signatory in a unique and non-transferable manner as it has verification steps embedded, confirming that the person signing is indeed who he claims to be. An advanced signature is also linked to the document, preventing further modifications post the signing process.
- ✓ Qualified signature is an advanced signature created by an electronic signature device and qualified certification process.

eConsent tools currently support the use of simple and advanced signatures. The laws around electronic signature vary across Europe and some countries do not yet accept it for informed consent purposes mainly due to data protection and privacy aspects. If that is the case, then eConsent can still be implemented with a print-to-sign signature. This print-to-sign option would involve printing the ICF, a wet ink signature from the participant and a wet ink countersignature from the clinician captured. The signed forms can be stored on site like the traditional paper consent process or alternatively can be scanned and uploaded into an electronic system for record keeping.

The FDA also recognises electronic signatures and the criteria under which an electronic signature is considered trustworthy and reliable are outlined in 21 CFR § 11 [10]. All the criteria of 21 CFR § 11 must be fulfilled in order for the electronic signature to be considered equivalent to a wet ink paper signature. A variety of electronic signature methods are recognised by the FDA, however no particular method is mandated.

### Remote and On-Site Options

eConsent is at times viewed as an exclusively remote process. eConsent scenarios may vary as it may be any combination of the remote or on-site interactive participant education component and remote or onsite signature, as is demonstrated in Figure 3.



**Figure 3:** eConsent can be configured to be a hybrid combination of paper and electronic consent elements. The arrows demonstrate how paper consent is enhanced by adding electronic consent elements. Adapted from [11].

For all traditional paper-based trials the whole informed consent process is typically performed on site, with the participant reading the ICF, having a discussion of the ICF with the clinician on site, and finally, signing the paper ICF, which is later stored on site. eConsent offers the chance to substitute or add some electronic alternatives to the existing paper process. These include an electronic interactive participant education component instead of the paper ICF, an online audio or video call to discuss the ICF with the clinician instead of the on-site visit, as well as an electronic signature that can be captured on site or remotely and an electronic database for documentation storage. Implementing eConsent does not necessarily have to involve adopting all the electronic elements of eConsent at once, as any combination could also be value driven.

## COVID-19: The eConsent Catalyst

The current COVID-19 pandemic, although a humanitarian crisis, has served as an exceptional catalyst, allowing nations to shift to more remote strategies for the continuation of current trials and start of new trials during this pandemic.

Unlike the traditional paper consent, eConsent opens a new opportunity of remote access, which is a critical advantage particularly during the current COVID pandemic, as clinical trials worldwide are experiencing enrolment and re-consent issues due to travel restrictions and quarantines.

Some countries have released COVID-specific clinical trials guidelines, with a general trend towards virtualisation of trials to allow for the continuation and start-up of clinical trials. The FDA have responded to the challenge of obtaining informed consent during the pandemic faced by investigators by rolling out the COVID MyStudies application which provides a platform for participants to consent electronically when face-to-face informed consent is impossible or impractical [12].

While the value of eConsent is significantly heightened during a crisis like this, eConsent is not an innovation that would only last as long as the global pandemic. It transforms the traditional paper consent by bringing additional value to the sponsor and investigator, as well as exceptional benefits to the participants. It also supports the ethical mandates of clinical research to have respect for persons, provide beneficence, and meets the standards of justice [13].

## Support Further Use of Biosamples

The value of participant understanding of the consent forms extends even beyond the trial itself. Biosamples that are collected during the trial have the potential to be incredibly useful for research purposes. It is not uncommon for these valuable biological samples obtained from participants to be disposed of due to a laborious paper process. Pharma companies have disposed of hundreds of thousands of participant biosamples that could have been used for research purposes. eConsent addresses this issue, as the consent documents are stored in the electronic system, easily obtainable with minimal risk of data loss and in general a more efficient access to the historical ICFs.

## Compliance Made Easier

eConsent can provide a unified platform from which the individual aspects of informed consent compliance can be managed remotely and effectively.

eConsent has an electronic audit trail, which introduces new data analytics opportunities, as all amendments to the consent documents are recorded on the system, including the precise date and timing, the person performing the amendment, and the reason behind the amendment. This allows sites to easily demonstrate real-time compliance.

Paper-based solutions are more error prone than electronic alternatives when it comes to filling of consent documents. In comparison to hand-written surgical consent forms, a study showed that 44% of paper forms were not completed, signed or dated properly, while the electronic forms indicated no errors [14]. This could be explained by the fact that electronic solutions have multiple additional compliance control elements and are validated, and to the user have such warnings about missing fields in the form, which prevent mistakes which can be a frequent occurrence with paper-based processes [15].

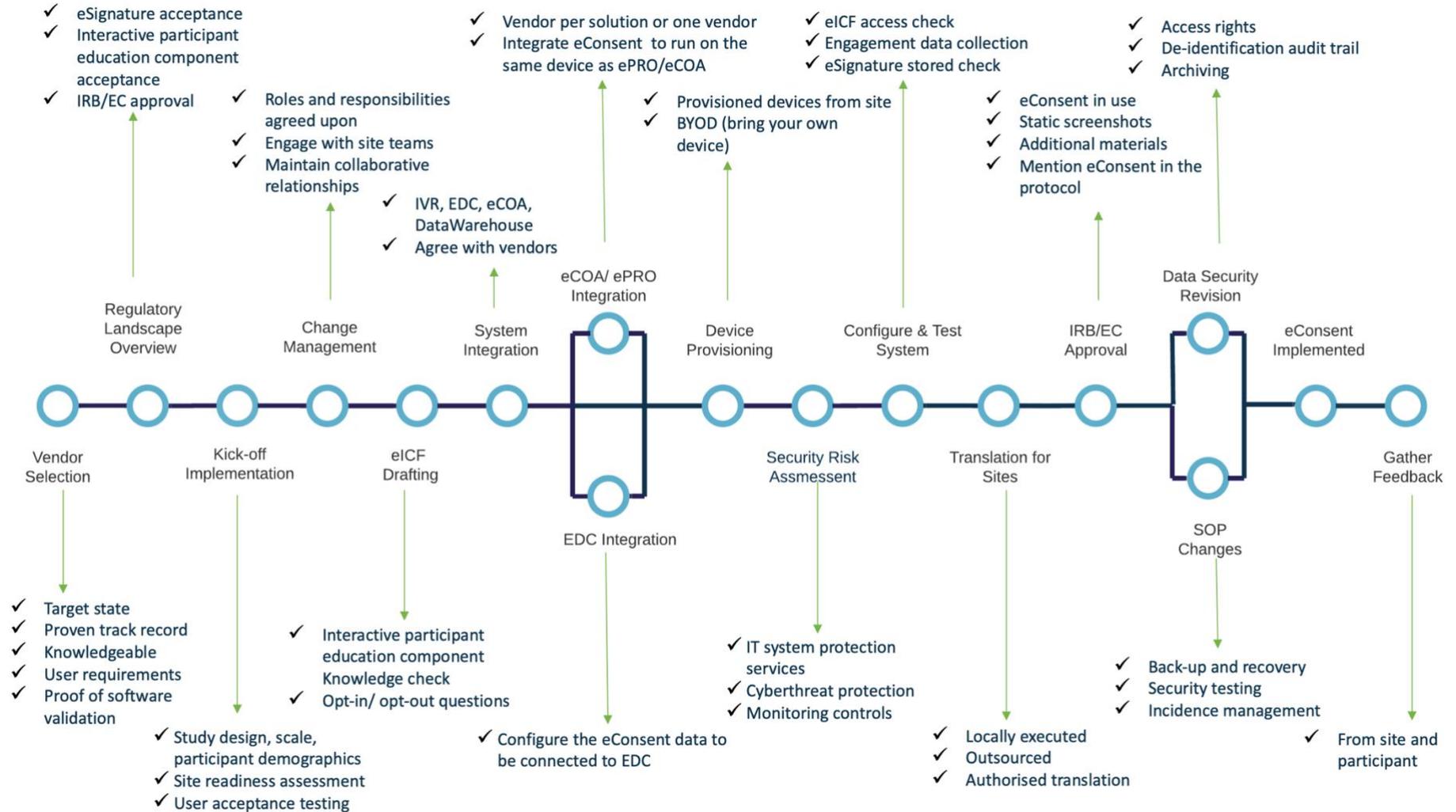
EMA inspection report of ethically relevant issues in clinical trials over 4 years of 2008-2012 outlines that informed consent alone was a source of 11% of the inspection findings during the course of the four years [16]. A quarter of all the informed consent violation findings were caused by signature and ICF date issues. The likelihood of these errors occurring with eConsent is reduced as the missing field or error would be flagged up as a missing or incorrect field, and be rectified at the time, unlike in paper ICF [16].

## eConsent Implementation Guidance

This Section will provide an account of all the points to consider when implementing eConsent, whilst offering some practical advice on how to best approach the transition and make sure that it is smooth and thorough. The eConsent implementation roadmap can guide you through the sequence of events that will occur during implementation, providing an excellent overview of all the necessary points to remember to ensure you are in the best prepared position to kick-start the process.

The Implementation of eConsent is in some ways similar to paper informed consent start-up. As the industry is slowly becoming comfortable with the idea and the transition to eConsent is rapidly expanding, there needs to be a comprehensive guide of all the implementation steps to remember.

## eConsent Implementation Roadmap



**Figure 4: eConsent Implementation Roadmap** - showcases the major steps of eConsent implementation, all of which need to be taken into account prior to eConsent implementation [17], [18].

## Detailed Practical Implementation Guidance

The points below address and expand upon the steps mentioned in the Implementation Roadmap (Figure 4).

<b>Vendor Selection</b>	<ul style="list-style-type: none"> <li>✓ Consider the target state of the eConsent use and select a vendor that can support your organisational business processes, data storage and document archiving requirements the best</li> <li>✓ Consider systems that allow development and control of eConsent as a self-service if there are existing systems, tools and/or teams already handling consent processes in-house, even if this is a longer-term target state</li> <li>✓ Consider a simple solution if the need is only to collect signatures electronically and just convert the paper ICF documents into digital format</li> <li>✓ Check for a proven track record and knowledge of eConsent regulations, security and data privacy requirements</li> <li>✓ Compare your user requirements to the software capabilities</li> <li>✓ Consider proof of software validation, including performance qualification</li> <li>✓ Ensure robust due diligence practices are performed and system validation documentations is available</li> <li>✓ Select a flexible solution, as multiple institutional review boards (IRB) and Ethics Committees (ECs) involved may have differences in approval requirements</li> </ul>
<b>Regulatory Landscape Overview</b>	<p>Understand the country-specific regulations on the use of eConsent, in particular requirements for:</p> <ul style="list-style-type: none"> <li>✓ Interactive participant education component</li> <li>✓ Electronic signature type or a print-to-sign alternative</li> <li>✓ Participant identity verification</li> <li>✓ Participant-clinician discussion</li> <li>✓ Remote and on-site use acceptance</li> <li>✓ Data storage and document archiving requirements</li> </ul> <p>Engage with IRBs as soon as possible with a gap analysis to identify that the IRB's SOPs can support the electronic process review and approval</p>
<b>Kick-off Implementation</b>	<ul style="list-style-type: none"> <li>✓ Initiated once the contract has been obtained</li> <li>✓ Consider study design, scale and demographics of the participants</li> <li>✓ Assess site readiness for eConsent via a feasibility survey</li> <li>✓ Plan for user acceptance testing (UAT) where it is needed: on global, country and/or site level</li> <li>✓ At the kick-off meeting discuss set-up timelines, timelines for UAT, compatibility for all device types (Apple, Android, etc.) and software versions, timelines for amendments to be implemented, data storage and document archiving expectation and requirements</li> </ul>

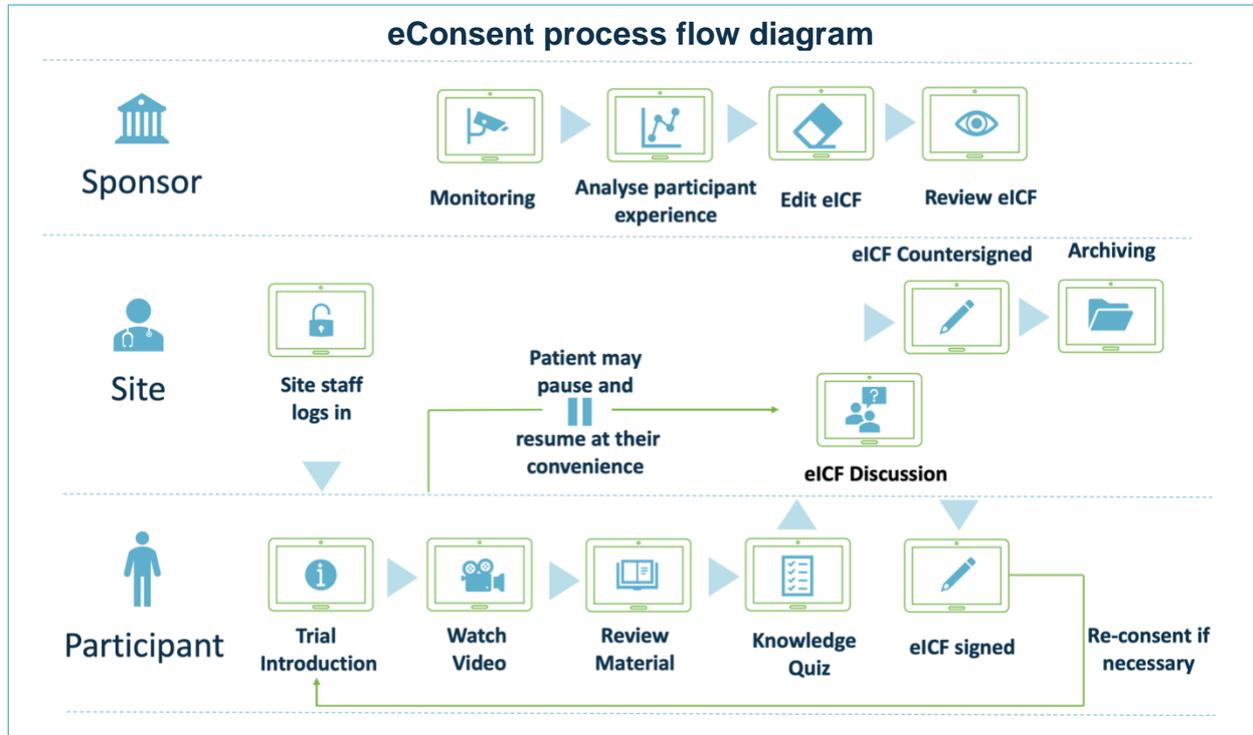
<b>Change Management</b>	<ul style="list-style-type: none"> <li>✓ Plan and agree on roles and responsibilities between stakeholders early on in the process</li> <li>✓ Manage and maintain collaborative relationships with all stakeholders involved</li> <li>✓ Engage with the site teams to ensure a smooth transition from the paper-based consent process to eConsent</li> <li>✓ Support sites throughout eConsent implementation through training and additional helpdesks</li> </ul>
<b>eICF Drafting</b>	<ul style="list-style-type: none"> <li>✓ Consider where to use multimedia, how to structure and create layers for the information, and making some parts of the content optional to read</li> <li>✓ Plan the knowledge check quiz to assess that the participant is truly informed prior to signing the form</li> <li>✓ Identify if there are opt-in/out questions (e.g. on future use of samples) that need to be included</li> <li>✓ Consider country-specific requirements for eICF (e.g. mandatory print-to-sign configuration)</li> <li>✓ Ensure the eICF the paper ICF are equivalent and contain identical information, this guarantees that the participant is fully informed of the clinical trial and you avoid later issues with monitoring and inspections</li> <li>✓ Involve participant feedback in the review and amendment process</li> </ul>
<b>System Integration</b>	<p>eConsent provides the most value as part of the eClinical data flow when you can integrate the consent information with other systems (IVR, EDC, eCOA, DataWarehouse or lab sample management system) and benefits include reduced manual labour, reduced manual errors and real time availability of the data.</p> <ul style="list-style-type: none"> <li>✓ Understand early on what data you would like to integrate and to what systems, data storage and document archiving expectation and requirements</li> <li>✓ Often it is needed to involve vendors for both eConsent and the target system to agree the details of the integration, especially for first integrations</li> </ul>
<b>eCOA/ePRO Integration</b>	<ul style="list-style-type: none"> <li>✓ Select either a vendor per solution, or only one vendor for all solutions</li> <li>✓ Configure the systems to integrate both services to run on a single device, allowing for efficiency gains of integrated systems with no issue of multiple log-ins and system differences</li> <li>✓ Select multiple vendors if you are looking for the best of each product, with an inherent efficiency trade-off, but ensure that the systems are able to fully support participants' GDPR-protected rights to retrieve consent</li> </ul>
<b>EDC Integration</b>	<p>EDC (electronic data capture) is often the central location for collecting the participant data and historically also for consent status.</p> <ul style="list-style-type: none"> <li>✓ Check for SOP requirements</li> <li>✓ Make sure you can configure the eConsent data to be connected to the clinical trial EDC</li> </ul>
<b>Device Provisioning</b>	<p>The devices used for the eConsent process can be either provisional devices from the site, or a BYOD (bring your own device) option may also be implemented, where the participant uses their own personal electronic device to review and sign the eICF. When deciding on the method consider the following points:</p> <ul style="list-style-type: none"> <li>✓ BYOD allows the participant to easily integrate the informed consent process into their life, without the need to familiarise themselves with a new device</li> </ul>

	<ul style="list-style-type: none"> <li>✓ For the site, implementing BYOD eConsent prevents some costs and storage burden that may be associated with managing and storing many devices on site</li> <li>✓ BYOD avoids shipping delays and allows the trial to commence efficiently</li> <li>✓ Some participants may require provisional devices if their personal device does not support eConsent</li> <li>✓ eConsent and other eClinical applications, such as ePRO, should ideally be run on the same device to allow the participant to control all the clinical trial elements with ease whether a provisional device or BYOD is used</li> <li>✓ Ensure devices can be configured for site staff with a local language keyboard</li> </ul>
<b>Security Risk Assessment</b>	<ul style="list-style-type: none"> <li>✓ Consider the security systems in place that are provided by the vendor, including their IT system protection services, such as cyberthreat protection</li> <li>✓ Pay attention to remote monitoring controls being in place</li> </ul>
<b>Configure &amp; Test the System</b>	<ul style="list-style-type: none"> <li>✓ Complete test runs to check that the eICF can be accessed via the chosen mechanism, such as a web page or app, the flag feature is functioning,</li> <li>✓ Check that all data points about participant engagement are collected, data and eSignatures are stored securely on the system with an immutable and transparent audit trail</li> </ul>
<b>Translation</b>	<p>If multiple languages are needed for different sites, the eICF should be translated.</p> <ul style="list-style-type: none"> <li>✓ Determine if translations will be executed locally or outsourced through a third-party provider and if any translation process automation is available</li> <li>✓ Preferable method is an authorised translation that some vendors provide</li> </ul>
<b>Obtain IRB/EC approval of the eConsent</b>	<ul style="list-style-type: none"> <li>✓ eConsent used needs to be specifically explained in the trial protocol presented for approval</li> <li>✓ Ideally the IRB/EC would be able to review the eConsent in action but will often accept static screenshots for review.</li> <li>✓ Both a paper and eConsent should be submitted, as this also allows the paper version to be used if there is an issue with eConsent</li> <li>✓ Some IRBs require paper printouts for archival purposes, check whether this is the case for your sites</li> <li>✓ Consider all information that is participant facing, such as privacy statements, user instructions for provisioned devices etc.</li> <li>✓ Additional materials or formats may be required by specific IRB/EC so it is worth enquiring prior to submissions where possible</li> </ul>
<b>Data Security Revision</b>	<ul style="list-style-type: none"> <li>✓ Consider data storage, access rights levels and protection, access to personally identifiable information (PII), archiving process decided upon by the sponsor and vendor according to the local laws</li> <li>✓ Ensure the vendor has the capabilities to store all the eICFs versions, including re-consent and consent withdrawal information</li> <li>✓ Ensure system capabilities for an electronic audit trail that captures all amendments made to the consent documents, including the nature of the change, the person executing it and the date and time of execution</li> </ul>

	<ul style="list-style-type: none"> <li>✓ Assess vendor mechanisms to pseudo anonymise PII (to block sponsor from accessing PII) and securely storing identifiable information on site only</li> <li>✓ Vendor and site should agree on a role-based access plan for PII depending on how crucial it is for the specific staff member</li> </ul>
<b>SOP Changes and Staff Training</b>	<ul style="list-style-type: none"> <li>✓ Consider regulatory risk, security protection pathways, operational changes to system management, including access and authentication</li> <li>✓ Back-up and recovery processes, security testing and incident management</li> <li>✓ Device management if provisional devices are used instead of BYOD options</li> <li>✓ Plan out re-consent options, align them with the country specific regulations</li> <li>✓ Outline and update roles and responsibility as needed if any changes are expected, such as data protection responsibility of investigator, sponsor and the vendor</li> </ul>
<b>eConsent Implemented</b>	<ul style="list-style-type: none"> <li>✓ Participants begin the informed consent process and subsequent enrolment</li> <li>✓ Assess the progress through dashboards and reports</li> <li>✓ Make sure CRAs can access the informed consent data</li> <li>✓ Remote monitoring will generate many benefits as problems can be identified faster and in a more accurate manner</li> </ul>
<b>Gather Feedback</b>	From the site and the participant on the eConsent process, adapt the eICF according to the participant requirements based on the time spent per section data, the number of flagged items and the knowledge checks to improve the informed consent process.

## eConsent Advances the Informed Consent Process

This section will help you understand the typical process of the eConsent procedure that will occur following the implementation of eConsent.



**Figure 5:** eConsent Process Flow Diagram – summarises what the eConsent process looks like to the participant, site and sponsor, including the specific roles and activities within the eConsent process.

### *The Sponsor:*

As per Figure 5, the sponsor is involved in implementing the eConsent solution, but in the process of carrying out the informed consent, the sponsor's main function is monitoring or data gathering. eConsent allows for the collection and analysis of data points that were not previously available to sponsors, such as information about the way participants interact with the eConsent, how long do they spend reviewing each section, which sections lead to questions, etc. These data points allow the sponsor to improve their eICF based on participant experience, which is a novel opportunity exclusive to eConsent.

### *The Site and Participant:*

The site sends the participant a link or login details to access the eICF. As the participant is progressing through the eICF, any areas of uncertainty can be flagged up and later addressed during the audio or video call discussion. eConsent facilitates the discussion between the participant and site personnel, bringing the focus on any remaining questions that need to be clarified and ensuring the participant is well-informed of the trial requirements, main principles and risks. Participant's understanding is confirmed by a knowledge check quiz. After the participant decides to sign the eICF, the site countersigns it. Regardless of the tool used, paper or electronic, the responsibility of storing participant consent information in a secure manner and safely securing any participant identifiable information is still the site's responsibility. The site archives the data and securely stores it in the system.

Re-consent may be required in certain cases, where the original informed consent provided by the participant is no longer valid due to changes in the protocol or the participant's condition. Some examples of such scenarios include changes in procedures, risks, potential benefits, or the worsening of the participant's condition. Re-consent aims to ensure that the trial participation remains consistent with the participant's interests. Re-consent principles and requirements are not dependent on the consent format, paper or electronic, thus standard procedures may be followed. An updated version of the eICF containing all the amendments is sent to the participant again, and the consent process is repeated (Figure 5) in an identical manner with the updated information. If the participant chooses to consent to and sign the updated eICF, the site countersigns and the trial participation continues.

## Stakeholder Perspectives

This section showcases some of the thoughts on eConsent that stakeholders have expressed following their personal experience with the implementation and use of eConsent.

PARTICIPANT	SPONSOR	SITE	MONITOR	ETHICS COMMITTEE
<p>“Technology has become the norm, and participants expect to be able to benefit from a similar level of convenience in the clinical trial informed consent process with a life-like and easily digestible information presentation.”</p>	<p>“Participants enrolled are more informed and qualified to participate in the trial, increasing participant retention rates and participant compliance, and hence data quality. The ability to access real time data analytics and incorporate amendments make for a dynamic system, empowering the sponsor to improve its processes and better adapt them to the participant’s needs.”</p>	<p>“eConsent creates transparency, the ability to track consent and systematically update eICF versions, which results in reduced site burden and improved participant retention. eConsent supports the site in inspection readiness and a consequent reduction in the risk of non-compliance and increased quality overall.”</p>	<p>“The electronic audit trail of eConsent facilitates the process of compliance monitoring of the informed consent process, allowing for more time to be spent on valuable monitor work, such as engaging with the site staff to understand how the informed consent process is performed and perceived.”</p>	<p>Motivation to publish a position statement was the fact that the tools and possibilities for electronic informed consent already exist, but the use is limited due to a lack of clear regulatory guidance. A bioethics professor says that “there is no ethical opposition to eConsent” and “authorities should be finding ways to enable technology to move clinical trials forward.”</p>
<ul style="list-style-type: none"> <li>✓ Technology expectations</li> <li>✓ Life-like format</li> <li>✓ Easy comprehension</li> </ul>	<ul style="list-style-type: none"> <li>✓ Improved data quality</li> <li>✓ Access real time data</li> <li>✓ Adapt to participant needs</li> </ul>	<ul style="list-style-type: none"> <li>✓ Transparency</li> <li>✓ Reduced burden</li> <li>✓ Inspection readiness</li> <li>✓ Reduced risk of non-compliance</li> </ul>	<ul style="list-style-type: none"> <li>✓ Electronic audit trail facilitates process</li> <li>✓ Allows to spend more time with site staff</li> </ul>	<ul style="list-style-type: none"> <li>✓ Technology exists with a lack of regulatory guidance</li> <li>✓ Participant-site interaction preserved</li> </ul>

## Regulatory Acceptance

### *Data Security and Laws*

Informed consent forms contain personally identifiable information (PII), such as name, date of birth, signature and age. Europe has a complex plethora of regulations, directives and national laws around data privacy. For more details on the specific regulations to be aware of when implementing eConsent, refer to the following document [19].

Verifying participant identity using eConsent does not have to differ from the traditional paper consent process, as the face-to-face verification can be carried out on site as normal. eConsent can simply be used to facilitate the explanation of the clinical trial aspects to the prospective participant using the interactive participant education component. The electronic signature of the eICF, or the wet ink signature of the print-to-sign option can be obtained on site. In the case of remote eConsent, participants can be identified using real time audio and visual methods, such as an audio or video call with the site clinician. An advanced signature might be used where acceptable by the regulatory authorities. eConsent platforms will have a security system in place that ensures that signed documents cannot be altered. An electronic audit trail keeps a bulletproof record of all activities related to the informed consent process performed by the participant or on their behalf, as required by 21 CFR § 11 and ICH/GCP. These activities will include the date and time when the participant accessed the eICF, the record of the eSignature if applicable, as well as any record of further viewing, printing and email of the ICF documents. The informed consent records are only stored transiently on the eConsent device and are transmitted to a secure remote server and all the data is subsequently removed from the device.

To ensure data security the design of the eConsent should follow some recommendations and study team should take a proactive approach to data protection like ensuring that updated anti-virus and anti-malware software is in place, and sponsors should prefer the use of eConsent platforms with embedded end-to-end encryption security.

## Acceptance in Countries

Before clinical research is initiated, it is the responsibility of relevant competent institutional review boards or independent ethics committees to review the research protocol and informed consent documentation to ensure adequate electronic or paper informed consent procedures are established and implemented in an ethical way without endangering the rights, safety and well-being of the participants. Informed consent is governed by clear global and local regulations and guidelines, beginning with the Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects adopted by the World Medical Association as amended in 2013 and more fully developed through international and regional standards [20].

It is very typical for pharmaceutical companies to conduct multi-site and multi-country clinical trials. Markets can have their own in-country laws which can add inefficiencies and delays to the drug development process. International Council for Harmonization, ICH, acts to standardise and harmonise guidelines for international use, allowing for clinical trial reporting and marketing applications to be submitted to regulatory agencies around the world in a consistent manner, avoiding duplicative processing and testing.

eConsent regulations still remain country-specific due to a lack of a unified position. In 2018, the UK MHRA and HRA published a joint statement [21] that sets out the legal and ethical requirements for seeking and documenting consent using electronic methods. This was the first official statement and position by a European country. Belgium has since also released an official regulatory guidance [22] on the use of eConsent in interventional clinical trials, outlining regulatory acceptance of eConsent. The

FDA allows the use of eConsent and further details can be found in their guidance [23]. Singapore's HSA has recently released an updated guidance [24] on clinical trial conduct in response to the COVID-19 pandemic, where eConsent has been mentioned as an acceptable procedure. More countries are following this example, and official regulations are becoming clearer, allowing for eConsent implementation. It is vital to follow the country-specific regulations, which are subject to change. For the latest updates on the regulatory positions, refer to [18] or contact [info@eucrof.eu](mailto:info@eucrof.eu).

In light of the COVID-19 pandemic, the EMA has released guidance [25] on the management of clinical trials, where informed consent is addressed. The EMA outlines that in the case where a participant is unable to consent in person when in isolation, an alternative method of obtaining informed consent should be considered, such as oral consent in the presence of an impartial witness, who can sign the ICF on behalf of the participant. For re-consent purposes, the EMA proposes an oral re-consent with a supplemented confirmation via email. Importantly, the EMA confirms that any valid electronic methods of obtaining informed consent can still be used throughout the pandemic as long as they are permitted by the individual country legislation. eConsent brings the unique advantage of audit ability and immutability that alternatives do not provide.

## In Summary

In order to ensure that eConsent is able to make a change in the compliance monitoring activities, it is vital to ensure that regulatory authorities around the world set out clear guidance on the regulations surrounding the use of eConsent in clinical trials performed in their respective countries. This aim needs to become a priority of regulatory bodies to ensure that trials running in their nations can implement eConsent, and hence eliminate many inspection findings that arise due to the informed consent process non-compliance. ICH (E6) R3 is set out to address eConsent as “Patient involvement, openness to eConsent, decentralised trials and the need for consent to be informative” should be incorporated into the new revision, which will be a great step forward towards global eConsent adoption [26]. eConsent provides an unprecedented opportunity to adapt to the changing times in an effective manner, without compromise to the trial process and efficiency. A unified approach to addressing novel technologies will allow nations to implement value-driving improvements to clinical trials, and ultimately improve the participant experience and facilitate healthcare progress.

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