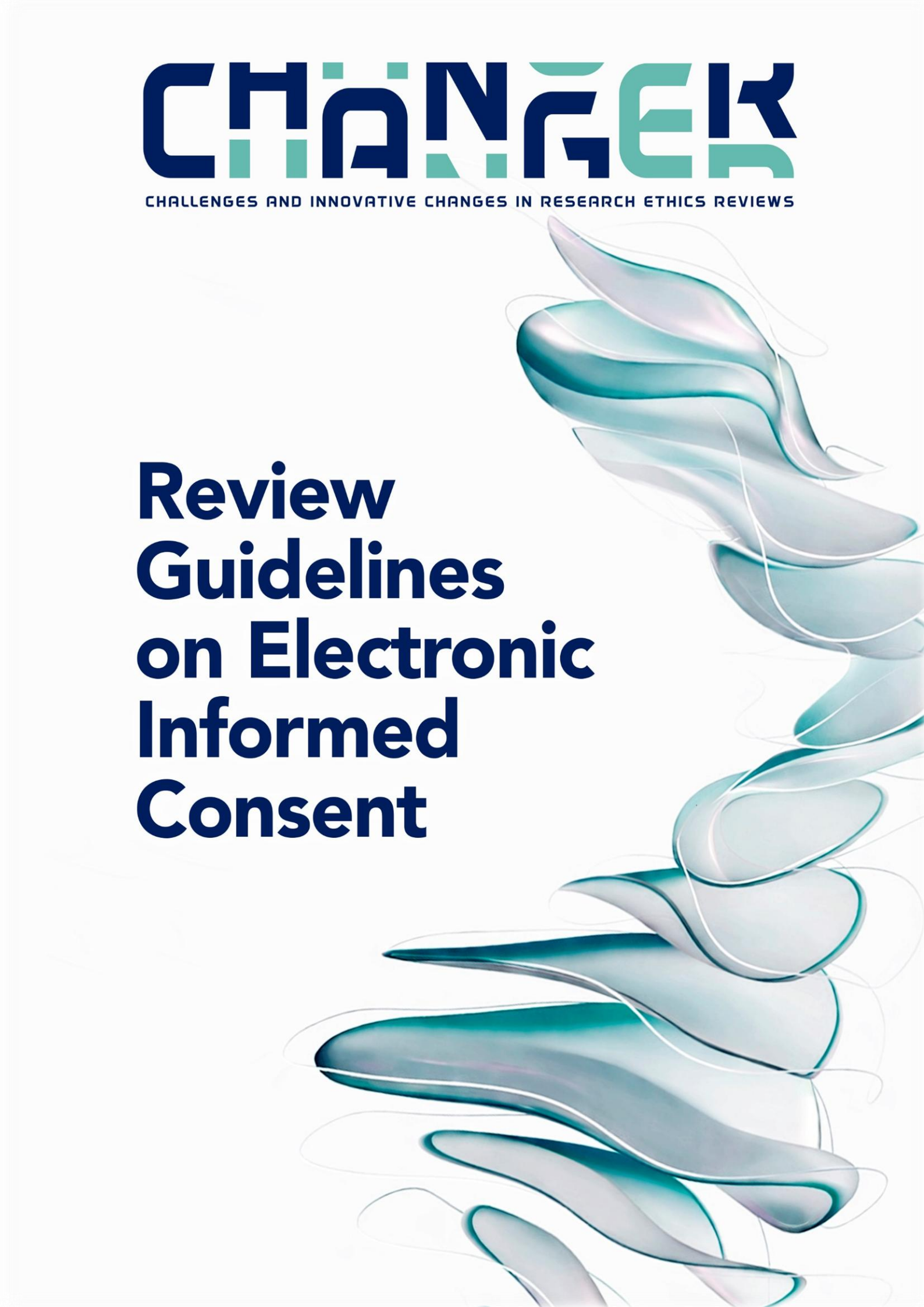
CHANGER

CHALLENGES AND INNOVATIVE CHANGES IN RESEARCH ETHICS REVIEWS



Review Guidelines on Electronic Informed Consent

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Document Revision History *(including peer reviewing & quality control)*

Version	Date	Changes	Contributor(s)
V1.0	23/01/2025	General structure deliverable + electronic informed consent guideline added	Kamiel Verbeke, Pascal Borry, Phaedra Locquet, Margaux Reckelbus, Riya Mohan
V2.0	01/07/2025	Integration of feedback received from WP4 partners on electronic informed consent guideline	*Reviewers:* Jonas Pfister, Marc Florea (RUG), Constantin Vica *Adaptations:* Phaedra Locquet, Pascal Borry
V3.0	02/10/2025	Feedback consortium members received on electronic informed consent	*Reviewers:* Tade Spranger (Sara Dokmanac), Ana Marušić, Jeanne Mifsud Bonnici
V3.1	18/02/2026	Integration of feedback by internal consortium reviewers on the electronic informed consent guideline	*Reviewers:* André Pereira, Vasiliki Mollaki *Adaptations*: Phaedra Locquet

Pending approval from the EC.

This project has received funding from the European Union's Horizon Europe research and innovation programme, under grant agreement No 101131683.

Table of Contents

1. Guideline electronic informed consent 4
   1.1. Introduction 4
   1.2. Traditional informed consent 5
      Legal and regulatory landscape of informed consent 6
      Research ethics of informed consent 6
      Shortcomings of traditional informed consent 9
      Recommendations* 9
   1.3. Electronic informed consent: Context 10
      Use of electronic informed consent in research 10
      Technical possibilities and constraints of electronic informed consent 10
      Legal and regulatory landscape for electronic informed consent 10
      Recommendations 11
   1.4. Electronic informed consent: Research ethics 12
      The general purposes of the electronic informed consent 12
      The intermediate purposes of the electronic informed consent 12
      Electronic informed consent and participants' realistic levels of control 13
         Participant comprehension 13
         Decision voluntariness 14
         Decision-making competence 14
         Signing and authenticating 15
      Integrating the research ethics assessment 15
      Recommendations 16
   References and further resources 18

1. Guideline electronic informed consent

This guidance document focuses on the use of electronic informed consent (eIC) specifically within the context of clinical research

1.1. Introduction

Informed consent is fundamental to the ethical conduct of clinical research (1). According to Good Clinical Practice (GCP) standards, informed consent is defined 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*" (2). Furthermore, informed consent could function as one of the legal grounds for the processing of participants' personal data, as outlined by the General Data Protection Regulation (GDPR) (3).

The digitalization in science has fostered the use of digital tools not only as research methods, but also as means to optimize the ethical conduct of research. One prominent example is the use of electronic informed consent (eIC). According to the European Medicines Agency (EMA), electronic informed consent refers to "the use of any digital media (e.g. text, graphics, audio, video, podcasts or websites) to firstly convey information related to the clinical trial to the trial participant and secondly document informed consent via an electronic device (e.g. mobile phones, tablets or computers)."(4).

The advent of electronic informed consent could offer several advantages over paper-based informed consent:

- Personalization: the information delivery could be tailored to research participants' needs (5).
- Long-term interaction: ongoing communication between participants and the research team could be facilitated during and in the follow-up of a clinical study. For instance, participants could receive new informed consent versions upon study amendments or study results could be returned (5,6).
- Documentation: documentation issues could be reduced by providing a time-stamped audit trail (7).

Other advantages include the use of audio-visual tools to enhance participant engagement with study materials, as well as short quizzes to assess comprehension and identify any questions that may require clarification prior to consenting (8).

Although an electronic interface for consent procedures provides various and tangible advantages, it is not without its challenges. Given the need the to consider both advantages and challenges, as well as the sheer variation of eIC procedures, the evaluation of study protocols using this digital tool may require additional care from RECs. Therefore, these guidelines offer a practical guide for those confronted with eIC, particularly in assessing its ethical justifiability. Readers interested in detailed

guidance on the technical design aspects of eIC are invited to consult dedicated guidelines on this topic (4,9).

In clinical research, eIC is more than the result of embedding traditional informed consent for research in a digital context. It represents a shift in how consent is obtained and managed, enabling participation beyond the limitations of physical settings. Potential participants can for example be invited to visit a website or navigate an application on a tablet handed to them by the researcher. What traditionally is an in-person conversation and/or written information on a piece of paper now becomes at least partially replaced by digital means of communication. In-person conversations may become video calls, email interactions or chat exchanges, and written text can be displayed on a monitor or made interactive through the use of buttons, links, visuals, sounds, tabs, clicks, tick-boxes, highlighting tools, personalization, scrollable and expandable sections, etc. Once information is taken up by the potential participant, they could be quizzed on their study understanding, asked to explain how the study will go, tick an "I consent" box or sign the informed consent form through a validated electronic signature application. Ongoing access to the eIC platform through their personal devices can allow participants to update their consent decisions, receive information about changes to an ongoing study, or be invited to future studies for which they could be eligible.

eIC would not be a subject matter of a guideline if it did not come with constraints and concerns too. Indeed, participants who navigate through an eIC application will have a different experience than those who consent in a traditional way. The digital realm may well be able to convey information to participants in ways that increase information uptake, it might not account well for all the non-verbal signals and information that normally makes up most of face-to-face communication. Moreover, it also opens up new non-verbal communication, such as through the use of intricate interface design to persuade participants to consent, and ethical challenges can relate to the transfer and storage of consenting information over the internet where this is less of an issue for informed consent forms stored in locked cabinets.

Sifting through these opportunities and limitations, values and concerns, the current guidelines aim to support those faced with eIC in making the most of this new digital tool. The following sections provide an insight into how traditional informed consent overlaps and differs from eIC in terms of ethics, law and regulations. It aims to facilitate the route of ethics deliberations through the common considerations relevant to eIC, whether ethical, regulatory or legal in kind. The recommendations at the end of each subsection can then assist in the assessment of whether a particular use of eIC is justified.

1.2. Traditional informed consent

Whether consent procedures occur through an electronic or paper-based interface, many of the same general ethical, legal and regulatory principles apply. This section briefly revisits the principles associated with traditional informed consent.

Legal and regulatory landscape of informed consent

Laws and regulations authoritatively determine the general possibilities for and limits of informed consent procedures in research. These laws and regulations can be differentiated into three relevant groups:



The first group of laws and regulations regulates how researchers should ask participants' **consent to participate** in a study. For example, the European Union's (EU) Clinical Trial Regulation and the Good Clinical Practice guidelines require that participants or their legally authorized representatives are well informed about the study, are able to freely and competently decide about their participation, and sign the informed consent form.

The second group of laws and regulations regulates how researchers should ask participants' **consent to the collection and processing of their (personal) data**. The EU's General Data Protection Regulation is a well-known example of a regulation that requires researchers to clarify the legal basis on which they would like to process non-anonymous data, the specific goals of the data processing, the data that is necessary and whether this involves sensitive data, and the measures in place to protect participants' data. Consent is not the only grounds for lawful processing personal data. Depending on the context and the circumstances, other legal bases can be relied on (10).

The third group of laws and regulations can have an **indirect effect** on what is required for consent to participation or data collection and protection. These indirect effects refer to legal and ethical obligations that arise when healthcare data or treatments are used in research contexts, even if consent was originally given for clinical care only. For instance, when an oncologist studies the effectiveness of standard of care treatment for their patients, they will also need to abide by the informed consent provisions for healthcare as stipulated in the applicable patient rights laws.

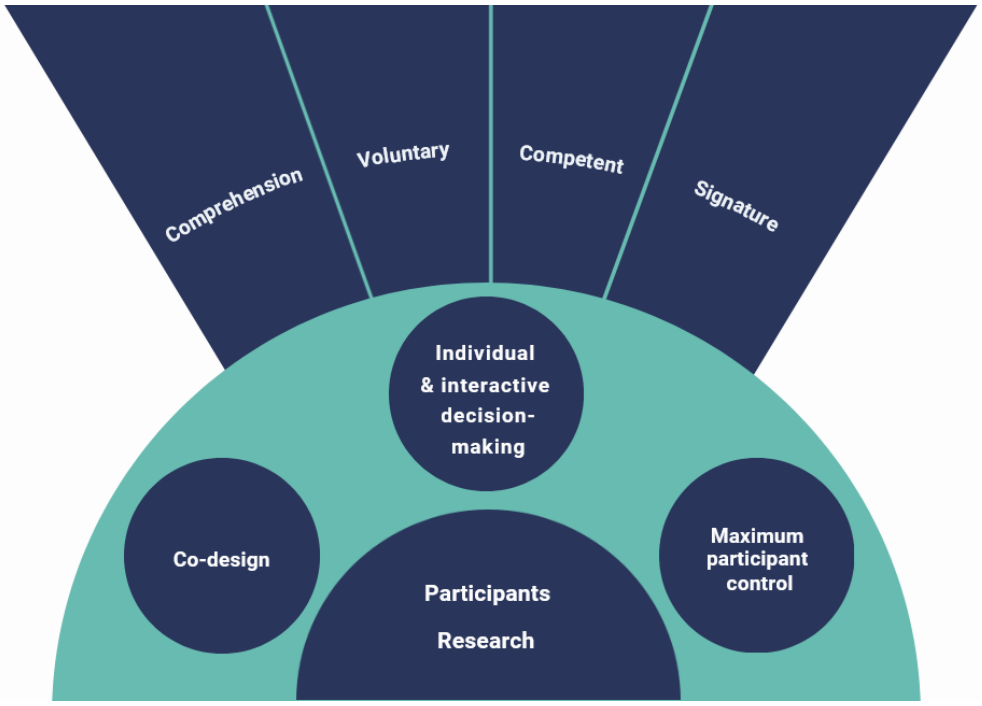
Although these laws have some common requirements, the conditions for obtaining a valid consent differ. For example, pursuant to the GDPR, consent must be free, specific, informed, an unambiguous indication of wishes and the individuals have the right to withdraw consent at any time and without detriment (11).

Research ethics of informed consent

Research ethics frameworks for informed consent can help RECs understand the different ethically relevant characteristics of consent that could be present, and how they relate to the justifiability of

the consent procedure and the overall study. **Figure 4.1** represents a research ethics framework for informed consent, one which will be explained here:

Figure 4.1 – Research ethics framework for informed consent.



The elements on top relate to the level of autonomous control participants can realistically achieve during an informed consent procedure, as it is determined by whether the procedure facilitates comprehension, voluntary and competent decision-making, and authentic signatures. The three elements in the arch represent the intermediate purposes of informed consent, which are in turn prerequisites for achieving the general purposes.

First, the **general purpose** of the informed consent procedure should be determined. This general purpose can be determined by considering what the informed consent procedure should mean for the interests of participants' and the interests of society which are affected by the outcomes of the study. A REC might assess that a particular informed consent procedure upholds participants' autonomy and well-being to a certain extent, while ensuring that it does not undermine the recruitment and methodological rigor of the study.

The general purpose of an informed consent procedure is significantly affected by the applicable legal, regulatory, practical and scientific **possibilities and constraints**. The laws and regulations outlined in section 4.1 ensure that the interests of research cannot be prioritized to such an extent that the informed consent procedure completely neglects participants' autonomy. Practical

constraints, such as the inability of a legally authorized representative to perfectly know what the participant they represent prefers, can again limit the degree of autonomy that can be ensured. Finally, scientific possibilities, such as the availability of both in-person and online methods to study the same research question, can expand the possibilities for the design of an accompanying informed consent procedure.

Besides possibilities and constraints, the **social context** can affect the preference for a general purpose of an informed consent procedure. When studying participants from societally disadvantaged or marginalized groups, including stigmatized groups, such as certain ethnic minorities, it becomes more important to ensure that their needs and preferences are adequately represented in the informed consent procedure (e.g., in the language used). Similarly, when a researcher simultaneously has another kind of relationship with the participant, such as a physician-patient relationship, the importance of certain interests affected by the informed consent procedure can change (e.g., prioritizing the patient's well-being).

Second, RECs can evaluate whether the informed consent procedure is able to achieve its **intermediate purposes**, which are in turn prerequisites for achieving the general purposes. The framework described here differentiates three groups of intermediate purposes (**Fig.4.1**):

- *The maximal level of autonomous control participants' can achieve over their consent decision under ideal circumstances.*
- *The realistic level of autonomous control participants can achieve under non-ideal circumstances individually and/or in interaction with the researcher.*
- *Co-design of the informed consent procedure with participants to better represent their needs and preferences.*

The **maximal level of autonomous control** participants' can achieve over their consent decision, should they have perfect capabilities to make such a decision, is determined by the control participants get over different decision dimensions. That is, participants can give consent to a broader or more narrow scope of activities, whereby a consent to a broad range of study activities or studies offers less control than a study-specific consent. Furthermore, being able to make sub-decisions about one's participation or what happens to one's data, and the provision of repeated consenting moments throughout a study can also improve the degree of control. In addition, consenting oneself (when possible) or providing an opt-in consent upholds participants' autonomy more than asking a legally authorized representative to consent or allowing for an opt-out consent. Similarly, each of these dimensions can affect the methodological value of a study. For example, opt-out consent procedures may facilitate recruitment, while repeated consent moments require researchers to engage with participants at multiple points in time.

However, decision-making conditions are never perfect. Therefore, researchers can **optimize participants' realistic decision-making capacities** by ensuring that they sufficiently comprehend what their participation involves, are able to make voluntary and competent decisions, and can sign and authenticate their consent forms. A sufficient comprehension requires that all the information

necessary for making a consent decision is disclosed to participants, and that it is disclosed in an intelligible way for the participants. Facilitating voluntary decision-making in turn requires the researchers to exert no unwarranted social influence on the participant so as to steer their consent decision in one way or the other. Competent decision-making should be properly assessed (e.g., through quiz-based assessments). Additionally, providing interactive support (e.g., offering opportunities to ask questions via the platform or scheduling consultations with responsible researchers) can be considered a way of supporting their decision-making competence. Finally, a participants' signature is meant to indicate that they made an agreement with the researcher about the study, which can be audited by authorized third parties to hold the researchers to account in case of irregularities.

Co-designing an informed consent procedure becomes more important when one is uncertain about the needs and preferences of the participants. This could, for instance, be a valuable activity when conducting (participatory) research with disadvantaged communities.

Shortcomings of traditional informed consent

Although paper-based informed consent is widely used in research practices, it has important shortcomings. For example, participants' do not always comprehend what they consent to, those with little physical access to the research site may not be able to consent and participate, the consent procedures are often static and generic instead of dynamic and personalized, and the storage of consent forms may make auditing onerous (9,12).

Recommendations*

- Ensure that for clinical trials under the scope of the **CTR**, that the consent procedure aligns with the CTR's consent requirements. Additionally, consider national requirements for consent to participate in research.
- Ensure that the requirements of the **GDPR** and its national implementations and guidelines of data protection authorities are complied with, regarding the legal basis for processing (sensitive) data, conditions for consent, and the information and transparency requirements.
- Ensure that the **indirectly** relevant requirements of other applicable laws and regulations are complied with.
- Ensure that the **general purpose** of the consent is ethically acceptable given the social context, and feasible within the legal, regulatory, technical and scientific constraints.
- Ensure that the **intermediate purposes** of the consent are able to lead to the general purpose through the implementation of their different dimensions.

* These recommendations are presented as those most relevant for the further application of electronic informed consent and are not intended to provide guidance on informed consent itself. For general principles and standards of informed consent, we refer to key references such as the Declaration of Helsinki, the Oviedo Convention, and other internationally recognized guidelines.

1.3. Electronic informed consent: Context

With the broader trend of the digitalization in healthcare, eIC is a relatively new and rapidly growing practice in scientific research. For RECs to effectively assess whether its use is justified, it is important that the context in which eIC is being used is made clear. This context will in turn function as the boundaries within which the ethical evaluation takes place.

Use of electronic informed consent in research

In the context of research, eIC can take on in various shapes, depending on how its constituting criteria are operationalized:

> *"An informed consent process is considered to be an electronic informed consent process if one or multiple elements of the process are set up in a digital way. These elements may include (i) conveying information (e.g. information delivery via digital platforms to facilitate tailoring to the individual's needs), and (ii) obtaining and documenting informed consent (e.g. electronic documentation contributing to efficiency of trial sites)."(13)*

More specifically, eIC is used in research that is either partially or fully digital. In partially digital research, such as in biobanking or clinical trials, eIC can take on a wide range of forms, depending on which part of the informed consent process is digitalized (14,15). In one study, researchers may ask participants to sign the consent form on REDCap after having a video call, and the rest of the study may take place in person (16). Another study may be conducted entirely in a laboratory, with participants signing the consent form on a tablet. Both are instances of eIC. In fully digital research, such as social media research or online surveys, all interactions occur digitally, including the entire informed consent process. Due to the lack of in-person contact, these studies may be particularly at risk of insufficiently autonomous consent decisions (see 5.2).

Technical possibilities and constraints of electronic informed consent

The use of eIC procedures in research requires a **digital infrastructure** in which the informed consent procedure unfolds. These infrastructures or platforms need to manage participant-related and -unrelated information, log the different actions taken along the consent process, provide a user interface for the different user groups (e.g., participants, researchers, sponsors, RECs and auditors), and encode logical procedures for guiding participants through the consent procedure, facilitate authorization, etc. We refer the interested reader to dedicated guidelines for a more in-depth analysis of these technical requirements (4,9).

Various **resources** have been developed for researchers to deploy their eIC. These include platforms such as REDCap, and smartphone apps, among others (16,17).

Legal and regulatory landscape for electronic informed consent

While the same **laws and regulations** for informed consent apply to eIC (see 5.2), additional rules are relevant. Unlike the United States, the EU has no well-integrated regulatory framework for eIC. The

CTR does not specifically address eIC, whereas the GDPR does mention that it allows the use of an electronic interface to request consent. Recent development such as the Data Governance Act (18) that regulates the provision of data intermediation services and a framework for entities which collect and process data for altruistic purposes can or the Regulation for a European Health Data Space, that specifies and complements the rights laid down in Regulation (EU) 2016/679 of natural persons in relation to the primary use and secondary use of their personal electronic health data (19), can have an impact on the requirements for eIC.

Another piece of European legislation that is relevant to eIC is the regulation on electronic identification and trust services for electronic transactions in the internal market (eIDAS Regulation). The eIDAS regulation provides rules for electronic signatures and identification, and some European countries differentiate the rigor of identification depending on the study risk (e.g., simple signature versus more rigorous identity check). Other European countries accept eIC without regulating it, or prohibit using eIC (20). Electronic signatures can be used to sign electronic informed consent forms, and thereby provide proof that the signer acknowledges the information in the consent form. eIC solutions can support one of these signature types provided in the eIDAS Regulation. But there is no general obligation to accept the use of electronic signatures for clinical trials in the EU, the legal acceptance of eIC significantly differs among the Member States.

The legal effect of the electronic signature and the advanced electronic signature is such that it may not be denied legal effect and admissibility as evidence in legal proceedings just because it is in an electronic form or because it does not meet the requirements for qualified electronic signatures. However, this does not automatically mean that a simple electronic signature is always valid. In case the signature is contested in court, it depends on the national legislation and the judicial discretion of the judge to decide whether it should be considered a valid signature. The advantage of a qualified electronic signature is that its legal effect is equivalent to that of a handwritten signature. Furthermore, a qualified electronic signature based on a qualified certificate issued in one Member State shall be recognized as a qualified electronic signature in all other Member States.

Recommendations

- Ensure that the **technical infrastructure** used fulfils the necessary legal and regulatory requirements.
- Ensure that the **eIC is compliant** with the applicable laws and regulations, good clinical practices and the requirements of national regulatory authorities.
- Ensure that eIC platform only processes and stores valid consent signatures that are placed by the intended actors.
    - A valid signature should be unambiguously linked to, at least, the individual that placed the signature, the time of signing, and the exact version of the informed consent form that was signed.

- In a longitudinal e-consent system, the long-term storage of valid signatures must be carefully considered, with particular attention to maintaining integrity in the presence of revocations and/or expirations of certificates and keys.

1.4. Electronic informed consent: Research ethics

While the legal, regulatory, technical and scientific context determine what design choices researchers can make for eIC, RECs and researchers still need to evaluate whether the eventual eIC is ethically justifiable. This is important, as for example the laws and regulations of this new scientific development may not be up to speed with all the relevant concerns that accompany eIC. To conduct a research ethics evaluation of eIC, RECs can start by considering the general and intermediate purposes that researchers aim for with their eIC. This will require knowledge of the practical realities of the eIC procedure, as the concrete design of the eIC will determine whether it will be able to achieve its purposes. This section will therefore provide guidance on where the realities of eIC converge and diverge from the framework for evaluating the justifiability of traditional informed consent (see 5.2).

The general purposes of the electronic informed consent

In 5.2, the **general purposes** of informed consent procedures were defined by the extent to which they address the interests of participants and of society, through rigorous research practices. These general purposes equally apply to eIC. However, one complicating factor for eIC is that due to the decreased in-person interaction between the researcher and the participant, it can make it more difficult for the researcher to know what the **participant interests at stake** exactly are. When having an in-person conversation, various verbal, non-verbal and situational cues can inform the researcher of the participant's needs. In electronic communication, these forms of communication are reduced significantly. Hence, it could become uncertain whether participants' needs are actually met when there is only limited interaction, which becomes especially relevant for populations that are disadvantaged or distrusting of research. In fully digital research, there may be even less interaction, due to which some argue that certain kinds of research become unjustified (e.g., fully digital consent in clinical trials) (13). Increasing **interactivity and co-designing** the eIC with participants may (partly) overcome this shortcoming of eIC.

The intermediate purposes of the electronic informed consent

In 5.2, the intermediate purposes of informed consent procedures were defined as the maximal and realistic levels of control participants can have over their consent decisions, along with the co-design of the informed consent procedure with participants. While these same components apply to eIC, specific challenges and advantages arise here as well.

- *Maximally achievable level of control: Questions regarding the effectiveness of data protection regulations for digital research may require assigning participants a higher*

maximum achievable level of control in privacy-risky research compared to those with lower privacy risks (21). *In general, one can argue that more risky/lower value studies require higher maximal levels of participant control in eIC* (22).

- *Realistically achievable level of control: As the communication between the researcher and the participant is usually reduced in eIC, this can hinder participants' ability to make an informed, voluntary and competent consent decision.*
- *Co-design: The digital context can facilitate the co-design of eIC infrastructures and procedures with participants.*

Electronic informed consent and participants' realistic levels of control

The level of autonomous control participants can realistically achieve during an eIC procedure is determined by whether the procedure facilitates comprehension, voluntary and competent decision-making, and authentic signatures. These criteria are the same as those discussed for traditional informed consent in 5.2. Nonetheless, for eIC, several different ethically relevant considerations come to the fore.

Participant comprehension

The use of eIC highlights a **challenge to participant comprehension** that is less likely to occur in traditional informed consent evaluations, yet it is often overlooked. Besides informing the participant about the study, the verbal, non-verbal interactions, as well as the situated interaction between the participant and the researcher, provides the participant indicators of whether to trust the researcher with safeguarding their interests (e.g., as inferred from the researcher's demeanor or affiliation) (23). Both kinds of information are relevant to the consent decision (24). However, when the communication between researcher and participant is electronically mediated, researchers may not pick up on and act upon subtle signs of a participant's hesitancy or lack of comprehension (25). Additionally, participant may not have access to reliable indicators of the researcher's trustworthiness. In turn, this undermines participants' comprehension of the study.

Notwithstanding this challenge, eIC also provides several (**new**) **avenues for improving participants' comprehension**:

- *Initial information provision: the consent information should be concise, clear, easy and highlighted, convey non-misleading trustworthiness indicators (e.g., university logo), and information on eIC personalization and long-term use (e.g., contacting participants for future studies).*
- *Personalized information: the information for participants can be tailored to their specific needs (e.g., disclosing pregnancy risks to women of childbearing age), layered (e.g., hover-over text for more information), customizable (e.g., allow changing font sizes or highlighting) or comprising of multiple formats (e.g., audio, video).*
- *Interaction: the eIC can be guided by the researcher (e.g., parallel video-call) or it can encourage participants to ask questions (e.g., through chat).*

- *Comprehension check: intermediate or final measures could assess participants' comprehension (e.g., quiz, teach-back) and contingently provide support (e.g., schedule a video call) or deny participation under certain levels of understanding (e.g., less than 80% correctly answered quiz questions).*

Decision voluntariness

The most well-known instances of research conduct that **reduce the voluntariness of consent**, such as coercion or offering clearly excessive financial incentives, are arguably similar between traditional informed consent and eIC. Instead, some more subtle forms of influencing participants' consent decisions during eIC appear more bespoke to the digital context. For example, researchers could use persuasive designs to attract participants' attention to a study, device or software on which the eIC is provided (e.g., through push notifications, repeated emails). Moreover, they may contain misleading trustworthiness indicators which participants may be unable to scrutinize in an electronic context. Researchers may also employ attractive colors or pre-ticked "I consent" checkboxes to nudge participants to consent.

Several traditional and digitally enabled design choices can be made to **support participants' voluntary decision-making** during an eIC procedure:

- *Reduce persuasion, manipulation, nudging and related techniques: researchers can remove persuasive or otherwise influencing elements that are not strictly necessary, indicate to participants that these techniques will be used, and/or allow participants to switch them off (e.g., change colors, notification frequency).*
- *Future studies: Researchers can allow participants to set their preferences for being contacted through the eIC interface about future studies.*

Decision-making competence

eIC also poses particular **challenges to assessing and improving participants' decision-making competence** when it comes to consent decisions. Due to the potential difficulties associated with authenticating a participant's true identity, it can be difficult to assess whether that participant can be presumed to have decision-making competence (e.g., is a child impersonating an adult?). Furthermore, decision-making competence is a dynamic ability, which can be affected by emotional or other affective states (e.g., feeling apathetic or overwhelmed with fear) as well as social support (26). In eIC, the decreased interaction between the researcher and the participant makes it more challenging for researchers to identify whether participants require more support related to study comprehension, emotional reassurance, or acquiring the necessary skills and resources to use digital means necessary for eIC (e.g., a stable internet connection, access to a computer). This becomes even more pronounced when certain digitally less-educated populations would otherwise risk not being included in research (27).

To **support participants' decision-making competence** when going through the eIC process, the following approaches can be taken:

- *Assessment: researchers can have a more interactive and humane encounter with participants (e.g., a video call), during which they can pick up on more subtle cues that indicate the need for support.*
- *Support: researchers can provide participants with the necessary digital tools and infrastructure, educate them on using these tools, or allow them to fill out a paper-based informed consent form instead.*

Signing and authenticating

As for traditional informed consent, participants can sign eIC forms and thereby indicate their identity. Researchers are then tasked with protecting these digital traces of participants' identities from unauthorized access. However, eIC poses particular **challenges to signing and authentication**. In the absence of face-to-face interaction when a participant signs the eIC form, it becomes more difficult to assess whether it was actually the participant who signed the form. Additionally, it raises challenges in determining whether the signer is a human or an AI system. Additionally, when consent forms are stored on servers and transmitted over the internet, there is a risk of unauthorized parties accessing the consent forms digitally. This becomes even more damaging when the consent form links an individual participant to a study on a sensitive topic (e.g., on their experiences as illicit drug users).

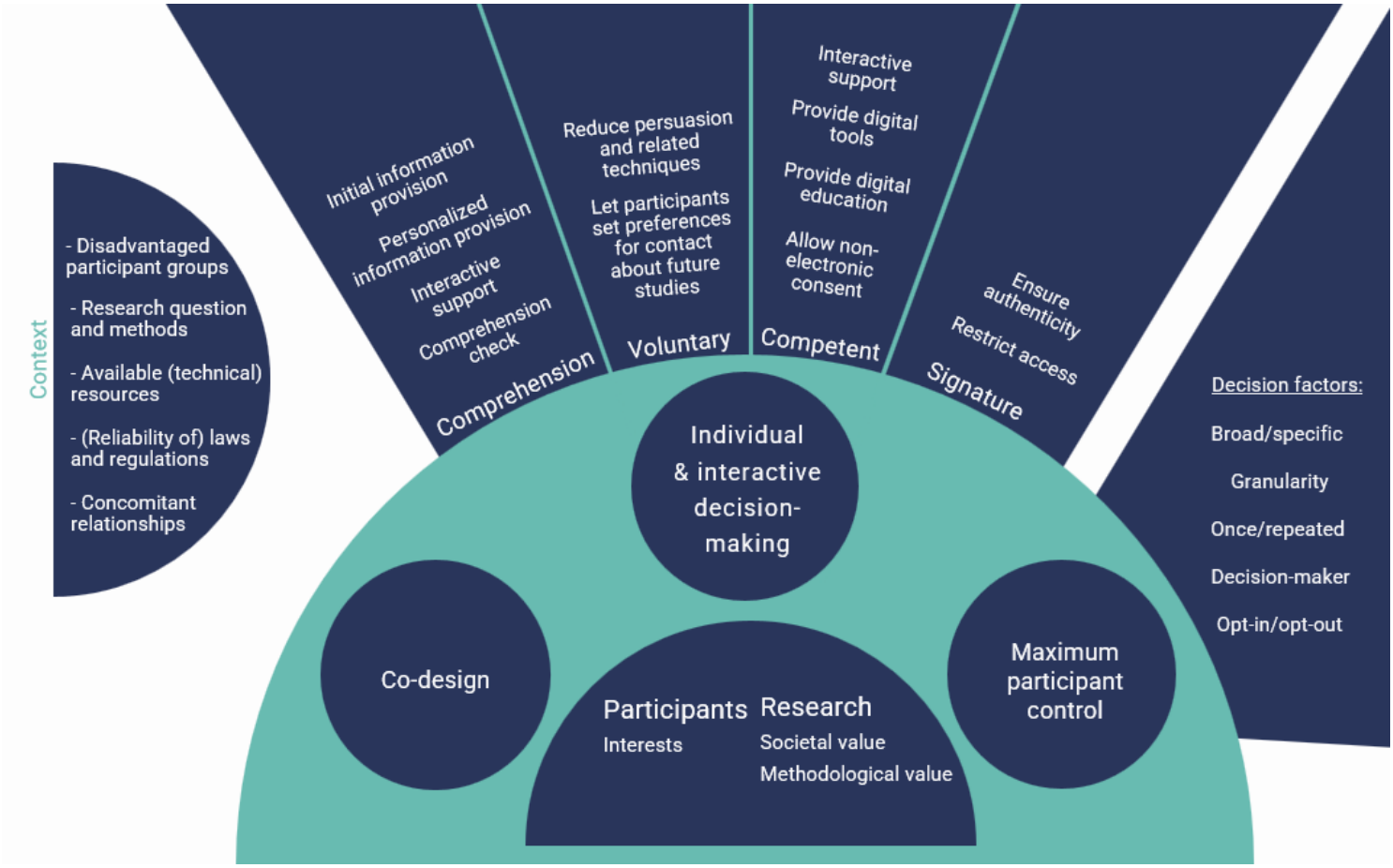
Researchers can take several approaches to **ensure that signing and authentication is both effective and safe**:

- *Ensure signature authenticity: researchers can ensure that the signature contains various identifiers (e.g., person, time, document version), and they can have an in-person interaction with the participant when the eIC is being signed (e.g., a video call).*
- *Protect signed documents from unauthorized access: researchers can provide unidentifiable data to certain parties (e.g., auditors, sponsors, RECs), assess whether unauthorized parties have access (e.g., eIC infrastructure providers), protect the data (e.g., limit and deidentify the collected consent data), the consent document (e.g., secure long-term storage, read-only documents) and the electronic infrastructure (e.g., the participants' device and their browser history, the eIC platform), and update protection measures.*

Integrating the research ethics assessment

RECs are tasked with evaluating the justifiability of eIC forms and the studies in which they occur. Based on the above recommendations and considerations, RECs can determine whether the general purpose of the eIC is justified, whether the intermediate purposes align with this general purpose, and if these intermediate purposes are realistically achievable given the eIC design or require further optimization. The following figure integrates these different considerations:

Figure 4.2 – Research ethics framework for electronic informed consent.



Recommendations

- Ensure that the **general purpose** of the eIC procedure is made clear, and that an electronic interface is appropriate given the usually reduced degree of researcher-participant interaction.
- Ensure that the **intermediate purposes** of the eIC procedure are clear and able to fulfill the general purpose, and that the protocol accounts for the impact of digital interactions on participants' realistic levels of control and the co-design of consent, as well as the impact of the novelty of eIC on the reliability of applicable laws and regulations.
- Ensure that **participants' study comprehension** is optimized with regards to the initial information provided, the personalized information, the interactive support and the comprehension check.
- Ensure that **participants' decision voluntariness** is optimized by reducing social influence techniques to a minimum and allowing participants to set their preferences for being recontacted about future studies.

- Ensure that **participants' decision-making competence** is assessed as adequately as feasible and necessary, while also providing support for their digital and comprehension-related decision-making needs.
- Ensure that **participants' signatures are authentic and protected** by verifying their identity and implementing adequate cybersecurity measures.

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This project has received funding from the European Commission Horizon WIDERA under Grant Agreement No 101131683