Joint statement on seeking consent by electronic methods

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The Health Research Authority is a Non-Departmental Public Body established to promote and protect the interests of patients in health research and to streamline the regulation of research. www.hra.nhs.uk

The Medicines and Healthcare products Regulatory Agency is an executive agency of the Department of Health and is the UK's regulator of medicines, medical devices and blood components for transfusion. www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

Summary

This joint statement, supported and endorsed by the Devolved Administrations, sets out the legal and ethical requirements for seeking and documenting consent using electronic methods. The primary focus is clinical trials of investigational medical products (CTIMPs) but the basic principles can be applied to all research conducted within the United Kingdom.

Electronic methods may be used for seeking, confirming and documenting informed consent in research studies.

Electronic signatures are classified as 'simple,' 'advanced' or 'qualified'. The type of electronic signature that should be used in a study depends on whether the recruitment and consent procedures *taken as a whole* (and considered as part of a proportionate approach) mean that you:

- can trust that the person who signed is who they say they are
- can trust that the consent form they signed hasn't been altered
- can trust when the signature was applied
- can demonstrate that trust if required.

Clinical Trials of Investigational Medicinal Products (CTIMPs)

- Participants must be informed of the nature, significance, implications and risks of the trial in an interview with the investigator, or another member of the investigating team
- The interview should involve two-way communication in real time and allow confirmation of the participant's identity
- Information about the trial does not have to be in writing and can be provided to potential participants using electronic methods. However, special attention should be paid to the information needs of specific patient populations and those of individual participants
- Informed consent must be recorded 'in writing'. Electronic methods for documenting consent can be considered to be in writing
- A copy (physical or electronic) of the signed consent form should be provided to the participant
- For type A trials, which involve risks no higher than that of standard medical care, any simple electronic signature may be used (including typewritten or scanned eSignatures)
- For all type B and C trials including phase I healthy volunteer trials, simple eSignatures that involve tracing the participant's handwritten signature using a finger or a stylus or biometric eSignatures should be used as these allow direct comparison with eSignatures/wet-ink signatures used previously for audit purposes or GCP inspection. Typewritten or scanned images of handwritten signatures should not normally be used
- In clinical trials that are conducted remotely it may not always be possible to verify that the participant is who they say they are. In such circumstances it may be preferable to use an advanced or qualified electronic signature

All other research

- Any form of simple electronic signature will normally be adequate to document consent
- eSignatures traced with a finger or a stylus or biometric eSignatures may be preferable for studies involving more than minimal risk and should be considered in the light of the importance of future audit.

Introduction

For the purposes of this statement, ‘electronic methods for seeking informed consent’ and ‘eConsent’ refer to the use of any electronic media (such as text, graphics, audio, video, podcasts or websites) to convey information related to the study and to seek and/or document informed consent via an electronic device such as a smartphone, tablet or computer.

Where we use ‘must’, we mean there is a specific legal requirement affecting an individual or organisation.

Where we use ‘should’, we mean expectations of minimum good practice, but for which there is no specific legal requirement.

Seeking informed consent is central to the conduct of ethical research and properly respects a person’s right to determine what happens to them. Wherever possible and appropriate, potential research participants should be provided with the information they need to help them decide whether they wish to take part in the research or not. This information is traditionally provided in the form of a paper participant information sheet (PIS) and a face-to-face discussion with one of the investigating team. If the individual agrees to take part, they are usually asked to sign a paper consent form.

However, electronic methods for seeking, confirming and documenting informed consent (often referred to as eConsent) are increasingly being adopted by sponsors and researchers either to supplement the traditional paper-based approach or, where appropriate, as a replacement for it.

There is evidence that multimedia information (for example presented on a tablet) is preferred by potential participants, can test and reinforce participant comprehension and may improve understanding of what taking part in the clinical trial will involve. This can be achieved by the use of self-assessment questions at key points which test participants’ understanding as they work their way through the information. This in turn can be used to highlight areas of uncertainty to the person seeking consent so that they can cover this area in more detail with the participant. It also allows the sponsor to build up a picture of how the information materials could be improved.

Whilst it is acceptable to use online text or multimedia material as the primary means of informing potential participants, researchers should be mindful of the possibility that the use of such methods may unintentionally discriminate against people who are not comfortable with or who cannot use such technology. Alternative methods for the provision of information and/or documentation of consent should be available for those unable or unwilling to use electronic methods.

Regardless of whether paper or multimedia formats are used, it is often the face-to-face communication between one or more members of the research team and the potential participant that will be the most effective way of improving potential research participants' understanding of what is involved.

Whilst a consent form provides an important audit trail and assurance that the consent process was conducted appropriately; a signature on a consent form (regardless of whether it is wet-ink or electronic) does not determine that the consent given has been sufficiently informed and is legally valid. Researchers should always assure themselves that the participant (or their legal representative) has actually understood the information provided.

Electronic signatures

What is an electronic signature?

The 'eIDAS' Regulation (EU) No 910/2014 establishes an EU-wide legal framework for electronic signatures. The Regulation, which is supplemented by the UK eIDAS Regulations (SI 2016/696), defines an electronic signature as 'data in electronic form which is attached to or logically associated with other electronic data and which is used by the signatory to sign'.

Electronic signatures can include signatures that are:

- Tickbox plus declarations
- Typewritten
- Scanned
- An electronic representation of a handwritten signature
- A unique representation of characters
- A digital representation of characteristics, for example, fingerprint or retina scan
- A signature created by cryptographic means

Electronic signatures can be divided into three groups:

- Simple electronic signatures – examples are a stylus or finger drawn signature, a typed name, a tick box and declaration, a unique representation of characters and a fingerprint scan.
- Advanced electronic signatures – these are uniquely linked to the signatory, are capable of identifying the signatory, allow the signatory to retain control, and are linked to data within the signature that can detect any changes made.
- Qualified electronic signatures – an advanced electronic signature, uniquely linked to the signatory, that is created by a qualified electronic signature creation device, and which is based on a qualified certificate for electronic signatures.

The use of 'advanced' or 'qualified' electronic signatures provides:

- *Authentication* – the signatory can be linked to the information
- *Integrity* – changes to the information can be detected more easily
- *Non-repudiation* – legal assurance regarding where the electronic signature has come from

Whilst any type of electronic signature is admissible as court evidence by virtue of the 'eIDAS' Regulation, some are more reliable and carry greater evidential weight and assurance than others. For example, 'qualified' electronic signatures are automatically granted the legal effect of a handwritten signature with mutual recognition in EU member states (Art. 24 (2)) but may place a disproportionate burden on both the researcher and the participant and will not always be appropriate.

Legal requirements for seeking consent in CTIMPs

For clinical trials of investigational medicinal products (CTIMPs) the methods used to inform and document the consent of participants need to comply with the requirements of The Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended) (also referred to as the 'Clinical Trials Regulations').

These Regulations implement the EU Clinical Trials Directive (2001/20/EC) in UK law and set out what information should be provided to potential participants and how this should be carried out.

What information must be provided?

Participants must be provided with information on the nature, significance, implications and risks of the trial and the right to withdraw from the trial at any time. A contact point for further information must also be supplied.

How must information be provided?

Participants must be provided information by interview with the investigator or a member of the investigating team.

The purpose of the interview is to provide potential participants with the opportunity to understand the nature, significance, implications and risks of the trial in order that they may make an informed decision about whether to take part or not. Simply providing a potential participant with this information (whether by paper or electronic means) would not be considered to be an interview; this requires an interactive process that allows the participants to ask questions and receive answers from the investigator or a member of the investigating team. In low risk trials, a proportionate approach to the interview and provision of information may be considered.

Where possible, the interview should be conducted in person or, where this can be justified and approved by a research ethics committee, by electronic methods that allow for two-way communication in real time, such as via telephone, video conferencing or VoIP telephony. Whichever method is used, it is important that confidentiality is maintained, and that the communication method is secure.

Research ethics committees will consider proposals to conduct the interview by methods other than audio/audio-visual communication in real time on a case-by-case basis where these can be justified e.g. where the participant/legal representative is unable to communicate using audio/audio-visual methods.

Whatever method is used it should always facilitate thorough and interactive communication that enables the potential participant to understand what is involved. It should also allow for confirmation of the participant's identity, particularly where the interview and documentation of consent are carried out by electronic methods at a distance.

Does the information provided to participants have to be in writing?

It is not a legal requirement for information about any research study, whether a CTIMP or any other kind of research, conducted in the UK to be provided in writing, whether by hard copy information sheet or by electronic methods.

Nevertheless, potential participants (or, where applicable, their legal representatives) should normally be provided with access to written information about the study for the purpose of seeking their informed consent, either as a physical hard copy or digitally in a form that can also be downloaded. Participants or their representatives can then use this both to help them reach an informed decision initially and to consult later in order to refresh their memory or if they have concerns. They should also be provided with a copy/have access to their signed and dated written consent form (either electronically or on paper).

Where a hard copy of the information provided via an eConsent system is made available, this must contain sufficient information regarding the 'nature, significance, implications and risks' of the trial and explain the right to withdraw from the trial at any time in order to enable the potential participant to reach an informed decision using the paper document alone. However, the hard copy patient information sheet does not need to reproduce multimedia content (such as by the use of storyboards) contained in the eConsent information.

The use of electronic methods to provide information may not be appropriate for everyone. Special attention should be paid to the information needs of specific patient populations and those of individual participants. Wherever possible this should include consideration of the resources which the patient population or individual may need to access this information.

You should use the format best suited to the nature of the information that needs to be provided to potential participants, and which best supports their understanding of it. You could also consider using interactive questioning of potential participants within the consent process to aid their understanding of the information presented and also highlight areas that potential participants could misunderstand without appearing condescending.

How must consent be recorded?

For CTIMPs, the participant's (or, where applicable, the legal representative's) consent must be recorded in writing, dated and signed, or otherwise marked by the participant.

In UK law 'writing' is defined as 'typing, printing, lithography, photography and other modes of representing or reproducing words in a visible form'. Provided that the method used to record consent is able to represent or reproduce words in a visible form (via any media) it will satisfy the requirement for this to be in writing. It does not have to be on paper.

Where the participant has capacity but is unable to indicate their consent by signing (either by wet-ink or electronic signature) or marking a document then their consent may be given orally in the presence of at least one witness and recorded in writing.

For paper documents, a requirement for the document to be 'signed' is usually satisfied by the handwritten addition of the relevant person's name, initials or surname using a pen and ink.

The Medicines for Human Use (Clinical Trials) Regulations 2004 specifically allows for the use of electronic signatures as a method of signing documents referred to in the Regulations. This includes 'simple' electronic signatures. However, the type of electronic signature that should be used will depend upon the specific context of the trial.

All other research

For research which is not a CTIMP, it is not a legal requirement to provide written information or document consent in writing. Nevertheless, for the majority of research it is considered best practice and investigators should document consent unless not doing so can be justified (and approved by a REC).

Participants with capacity who are unable to physically sign a paper or electronic document may provide consent orally or by any other means of communication (such as using augmentative and alternative communication methods).

What type of electronic signature should I use for my study?

The method of authentication of electronic signatures used in a study should be proportionate to:

- the nature and the complexity of the research;
- the risks, burdens and potential benefits (to the participants and/or society);and
- the ethical issues at stake.

In deciding which form of electronic signature is best for your study the key question to ask will be:

Do your recruitment and consent procedures taken as a whole mean that you can:

- trust that the person who signed is who they say they are
- trust that the consent form they signed hasn't been altered
- trust when the signature was applied, and
- adequately demonstrate that trust is justified if required (for example in an inspection, audit or court proceeding)?

The answer to this question (considered as part of a proportionate approach) will help you to decide whether a simple electronic signature may be used and, if so, what type would be appropriate. In rare cases an advanced or qualified eSignature may be more suitable.

CTIMPs

For most CTIMPS, and other research involving more than minimal risk, burden or intrusion, simple eSignatures that involve the participant tracing their handwritten signature using a finger or a stylus or biometric eSignatures should normally be used as they allow for direct comparison with eSignatures and/or wet-ink signatures previously used by the participant for the purpose of audit or where the consent is contested.

Where the CTIMP involves risks no higher than that of standard medical care (categorised as "type A" under the MHRA's risk-adapted approaches to the Management of CTIMPs) then any simple electronic signature may be used (including typewritten or scanned signatures)

For CTIMPs involving risks somewhat higher (Type B trials) or markedly higher (Type C trials including Phase I studies) than that of standard medical care typewritten or scanned images of handwritten signatures should not normally be used.

Where sites hold electronic files of scanned signatures of participants from previous trials, this introduces the risk that these could potentially be used without the knowledge of the participant.

A specific situation or type of trial may require the use of 'advanced' or 'qualified' electronic signatures in order to provide greater assurance that the documentary evidence does indeed

represent the consent of the specific participant it purports to for example where the trial is to be conducted entirely remotely and face-to-face verification will not be possible.

Studies other than CTIMPs

For the majority of non-CTIMP research involving only negligible or minimal risk (for example, face-to-face surveys or non-sensitive qualitative research) any simple electronic signature is normally adequate where it is appropriate to seek consent.

Where the research involves more than minimal risk, burden or intrusion simple eSignatures that involve the participant tracing their handwritten signature using a finger or a stylus or biometric eSignatures should be considered as they allow for direct comparison with eSignatures and/or wet-ink signatures previously used by the participant for the purpose of audit or where the consent is contested.

For postal/online surveys or self-administered questionnaire-based research where identifiable personal data are collected, and 'consent' used as the legal basis for the purposes of compliance with the General Data Protection Regulation (GDPR), then the participant must be able to actively signify their consent. This can be achieved by providing an explicit consent statement and a tickbox within the survey/questionnaire that the participant can complete if they are in agreement. A handwritten or biometric eSignature is not required.

Specific consent scenarios

CTIMP (Type B or C) where the consent process takes place in person at a research site (including phase I trials)

Where the eConsent process takes place at a research site, verification of the participant's identity should be no more burdensome than it would be for a traditional hard copy consent process.

eSignatures that involve the participant tracing their handwritten signature using a finger or a stylus or biometric eSignatures can be used to document consent where the clinical trial (including clinical trials of devices or surgery, and interventional studies) involves:

- participants already identified on the clinical system; or
- the person seeking consent from the participant is also their treating healthcare professional; or
- the participant is known to the person recruiting them.

For CTIMPs employing an eConsent process where the participant is not known to the team seeking consent, there should be an auditable trail which makes it is possible to demonstrate that the person making the electronic 'signature' was indeed the participant. Whilst 'advanced' or 'qualified' electronic signatures are also permissible (and indeed offer greater certainty) they may be unnecessarily burdensome for both researchers and participants where the identity of the signatory is not in question.

Handwritten or biometric eSignatures may also be used for healthy volunteer phase I trials as participants are normally required to show official photo identification such as a driving licence or a passport for verification at every visit. This is also a requirement for registration with The Over-Volunteering Prevention System (TOPs).

CTIMP where the patient is remote at the time of consent

In some rare circumstances, face-to-face verification will not be possible, for example where the trial is to be conducted entirely remotely. The conduct of a CTIMP remotely would need to be approved by both the MHRA and a recognised REC. In such trials the participant's identity may be verified visually via a video link or other means. It may also be possible to utilise general practices or other NHS sites local to the participant in order to verify their identity.

Where consent is given remotely and the participant is required at some point to visit a study site for the purposes of the trial then verification can be done in person using information from official photo ID. Where such face-to-face verification is possible, and can be completed prior to the participant receiving any research intervention, a simple electronic signature (such as a handwritten signature using a finger/stylus or biometric eSignature) will normally be acceptable to document consent.

Where it is not possible to verify that the participant is who they say they are, for example by checking official photo ID, it may be preferable (though not legally required) to use an advanced or qualified electronic signature that uniquely identifies the individual signing and thus provides greater assurance.

Things to think about when using electronic methods to seek and document informed consent

All research studies

- Can the signature be dated either manually by the participant or automatically by the eConsent system?
- Is it possible to verify which version of the information sheet and consent form the electronic signature applies to?
- For interventional studies, are there methods in place to ensure that the person signing the electronic consent form is the person who will be participating in the research study?

CTIMPs

- How will you ensure that the source consent documentation is available for inspection during and after the end of the trial according to the legally required retention period for CTIMPs?
- Can the site retain control of the informed consent process and documentation so that personal identifiable data are not inappropriately disclosed beyond the site to either sponsors or third party vendors?
- Where a sponsor has commissioned a third party to provide an eConsent system, are the necessary information governance arrangements in place to ensure that participant confidentiality is protected with appropriate access and retention controls to the system? Where the sponsor is responsible for auditing, ensuring compliance, and maintaining access controls to the eConsent system they may provide the appropriate certifications to the site as needed.
- How will a copy of the informed consent documentation (information sheet and signed consent form) be provided to the participant and retained in the investigator site file?

- How will you enable MHRA Inspectors to access the eConsent system in a readily available way during triggered, short notice or unannounced inspections?
- Where advanced or qualified electronic signatures have been used, can an inextricable link be maintained between the metadata (the information in the electronic record that gives context, meaning, and security attributes to the data) and the document, thus demonstrating the electronic signature's authenticity for as long as applicable legislation requires, dependent on the type of trial?

Further Information

Guidance

HRA Consent and Participant Information Sheet Preparation Guidance
http://www.hra-decisiontools.org.uk/consent/

HRA Guidance: Applying a proportionate approach to the process of seeking consent (2017)
https://www.hra.nhs.uk/planning-and-improving-research/best-practice/informing-participants-and-seeking-consent/

TransCelerate Biopharma eConsent Implementation Guidance
http://www.transceleratebiopharmainc.com/initiatives/econsent/

Electronic Signatures and Trust Services Guide. Department for Business, Energy & Industrial Strategy (August 2016) https://www.gov.uk/government/publications/electronic-signatures

U.S. Food and Drug Administration. Use of Electronic Informed Consent in Clinical Investigations, Questions and Answers. Guidance for Institutional Review Boards, Investigators, and Sponsors (December 2016)
https://www.fda.gov/downloads/drugs/guidances/ucm436811.pdf

Legislation

EU Regulation on electronic identification and trust services for electronic transactions in the internal market and repealing Directive 1999/93/EC (No 910/2014)
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv%3AOJ.L_.2014.257.01.0073.01.ENG

EU regulation No 910/2014 is supplemented by the Electronic Identification and Trust Services for Electronic Transactions Regulations 2016 (SI 2016/696) (the UK eIDAS Regulations) http://www.legislation.gov.uk/uksi/2016/696/pdfs/uksi_20160696_en.pdf

The Medicines for Human Use (Clinical Trials) Regulations (2004)
http://www.legislation.gov.uk/uksi/2004/1031/contents/made

Electronic Communications Directive 2002/58/EC
http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32002L0058

Electronic commerce: Formal Requirements in Commercial Transactions. Advice from The Law Commission (December 2001)
http://www.lawcom.gov.uk/wp-content/uploads/2015/09/electronic_commerce_advice.pdf

Electronic Communications Act 2000
http://www.legislation.gov.uk/ukpga/2000/7/contents