Informed Consent for Research

NJRO-GEN-SOP-011

Contents

1. Background/Introduction

Informed consent is defined in ICH GCP as:

"A process by which a participant 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 participant's decision to participate. Informed consent is documented by means of a written signed and dated consent form."

Informed consent is a three step process which involves:

- The giving of study related information
- The discussion and clarification of this information and
- The receipt of the participant's written consent

When carrying out research involving patients or volunteers, it is particularly important to ensure that the research is not contrary to the individual's interests; that participants understand that it is research and that it may not be possible to predict with complete confidence the effect of, or reactions to, the interventions used in the study.

2. Purpose

This SOP describes the procedure for providing information to potential study participants, participating co-workers and obtaining informed consent from these parties. This document also outlines the procedure for obtaining consent from vulnerable participants (minors and incapacitated adults).

This SOP includes the use of e-Consent and its application in CTIMP and non-CTIMP studies.

There is a separate SOP which describes the use of virtual and e-consent; NJRO-GEN-SOP-028 Virtual and eConsent in Research at NuTH

3. Scope of Document

The SOP is applicable to all personnel and those delegated to take informed consent for participation in a research study. It does not cover those projects that purely involve the obtaining of tissue samples for the purpose of Biobanking. This process is covered in Informed Consent for Biobanking SOP NJRO-TISS-SOP-011.

If additional/spare tissue from research is to be placed into a biobank, consent must be obtained at the same time as consent to participate. This process must meet the criteria

specified in NJRO-TISS-SOP-011 "Informed Consent for Biobanking" as well as GCP requirements.

4. Definitions

Assent
Agreement from a child to take part in a research study/trial, prior to the age of legal consent (16 years). Advice is available at http://www.hra-decisiontools.org.uk/consent/principles-children-EngWalesNI.html

ICH GCP
International Council for Harmonisation Good Clinical Practice

Electronic signatures
The following information is extracted from the MHRA/HRA Joint Statement on seeking consent by electronic methods (Reference Number 7.5)

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

CTIMP
Clinical Trial Investigational Medicinal Product

Non-CTIMP
None Clinical Trial Investigational Medicinal Product

ATIMP
Advanced Therapy Investigational Medicinal Products

Capacity

The person must be capable of giving consent, which means they understand the information given to them and can use it to make an informed decision

CI
Chief Investigator

GCP
Good Clinical Practice

HRA
Health Research Authority

ICF
Informed Consent Form

Informed Consent
The person must be given all of the information about what the treatment involves, including the benefits and risks, whether there are reasonable alternative treatments, and what will happen if treatment does not go ahead

MHRA
Medicines and Healthcare products Regulatory Agency

PI
Principle Investigator

PIS
Participant Information Sheet

5. Roles & Responsibilities

It is the responsibility of the individuals delegated to obtain consent to ensure that they are suitably qualified, appropriately trained and the procedure is followed.

6. Procedures

6.1. Providing Information to Potential Participants

6.1.1. Staff Obtaining Consent

The delegation of obtaining informed consent to an appropriate, suitably qualified member of the research team will be considered on a study-by-study basis. If staff other than the Chief Investigator (CI) or local Principal Investigator (PI) are to accept responsibility for the informed consent process, then that individual must:

- Feel confident to seek informed consent in line with the organisation's guidelines.
- Have a full understanding of the study, associated disease area and knowledge of the potential risks/benefits of the research.
- Be qualified by experience and have received appropriate training for this study. For medically qualified personnel this is afforded by their training in consent for medical procedures supplemented by attendance at GCP training. All other nursing and Allied Health Professionals intending to obtain Informed Consent must attend a specific obtaining informed consent training event. All training must be documented and refreshed every three years.
- Delegation of responsibility must be approved by the relevant Research Ethics Committee (REC) and documented on the delegation log

It is ultimately the responsibility of the CI/PI to ensure that participants have fully understood what they are consenting to.

For Trust sponsored CTIMPs informed consent may be obtained by other clinically qualified/professionally registered personnel, e.g. Research Nurse or Genetic Councillor. However, each study will be assessed on a case by case basis by representatives of the Trust, informed by the outcome of the risk assessment, and this arrangement must comply with the conditions in the favourable opinion of the NHS Research Ethics Committee (REC) and the approval of the Medicines and Healthcare products Regulatory Agency (MHRA).

It is best practice for any other research personnel involved in giving information during the informed consent procedure to sign and date the Informed Consent Form (ICF).

All those responsible for obtaining written informed consent must:

- Have a signed and dated CV stored in the Trial Master File or Investigator Site File.
- Have completed the delegation log, which also must have been counter-signed and dated by the CI/PI.

6.1.2. Informed Consent

Informed consent **must** be obtained **prior** to the participant undergoing any trial-related procedures.

If the intervention involves a surgical procedure e.g. biopsy, consent must be obtained for this separately following Trust Policy “Consent to Examination or Treatment (with reference to the Mental Capacity Act 2005)"

All individuals asked to consider taking part in research will be given the fullest possible information, presented in a form that is understandable. This must include, but is not limited to, the Participant Information Sheet (PIS) approved by a REC. Provision of information should be fully documented in the clinical records including the type of document i.e. when there are different version for different age groups, version number and version date. Guidance on the content of the PIS is provided by the Health Research Authority (HRA).

Participants must be given enough time to read the information about the research. This is usually at least 24 hours except where research is conducted in an acute or emergency setting or the study is a non-interventional study. However, in all cases if less than 24 hours is to be given then the timeframe must have received a favourable ethical opinion from a REC.

If a potential participant is unsure about participation, extra time must be given for their consideration and they will also be offered the option of speaking to another member of the research team, or someone independent of the research such as a colleague or their GP. This person will also be provided with information about the research.

6.2. The Informed Consent Form

The PIS and ICF must be approved by a REC and will be used together with any documents the participant may need to use, for example study diary or questionnaires.

Only the currently approved, most recent version of the PIS and ICF must be used for obtaining consent.

The following information is extracted from the MHRA/HRA Joint Statement on seeking consent by electronic methods (Reference No. 7.5)

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

For CTIMPs

Informed consent must be recorded 'in writing'. Electronic methods for documenting consent can be considered to be in writing

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.

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).

6.3. Obtaining Consent

Potential participants must be fully aware of the research project and not pressured into taking part, the dignity of the potential participant must be taken into consideration, and a private area used for the consent process if required.

If there is doubt as to the potential participant's understanding, the individual will not be recruited.

When describing the study, the person seeking consent will explain the following in conjunction with providing the written PIS:

- The purpose of the study and any background information that may be relevant.
- Why the potential participant has been approached and that confidentiality will be maintained throughout the study.
- Details of the study design and details of any drugs used (including any known safety profiles).
- The number of people taking part in the study and how many have been recruited to date.
- The duration of the study and the number of study visits involved.
- All procedures, such as blood tests, x-rays etc that are required as part of the study.
- The potential benefits and risks of participation in the study, and any alternative treatments available to the participant will be discussed. A clear description of the exit strategy for CTIMPs will be given.
- That the participant enters the study voluntarily and can withdraw at any time without any prejudice to them or their future care.
- That the clinician may withdraw the participant upon any concerns that may arise from the treatment.
- A detailed discussion of the potential participant's medical history (including disclosure of all medication they are currently prescribed) will be required if they agree to participate.
- If there are any payments made for participation in the study for expenses.
- The responsibilities of the potential participant if they chose to participate.
- That giving informed consent does not necessarily mean the participant will be enrolled into the study if it is discovered they do not meet the inclusion/exclusion criteria.

NB: This is standard practice but there may be exceptions prescribed and approved by the REC.

Once the above information has been verbally discussed, the written PIS will be provided and the participant consented after having fully considered the implications of participation.

The ICF must be fully completed including the participant's initials next to each consent statement. The ICF should then be signed and dated so that it is easily visible on photocopies/printouts by the participant and by the person seeking consent, both of which must be present for this.

ICFs held in the ISF/TMF should not be annotated to include personal/ identifying details such as full DOB, address, telephone number or email details

There are circumstances whereby consent may be obtained remotely e.g. by post or by telephone in which case the participant and person obtaining consent will not

be able to sign and date the ICF concurrently. The obtaining of consent by this method must be justified and approved by REC before implementation.

The person obtaining consent will annotate in the clinical records;

- Date
- Time
- Name of person obtaining consent
- Document type i.e. when there are different versions for different age groups
- Version number and version date of the ICF used and PIS provided
- Confirmation that ICF/PIS copies have been given to the patient

The person obtaining consent will not complete any of the participant's details on their behalf, however if the participant is unable to sign/mark the document to indicate consent, it will be given orally in the presence of at least one witness and recorded in writing. The witness will also sign and date the ICF. The need for a witness for the process should be risk assessed and the outcome documented as it may not be required for some low risk studies. The person obtaining consent will not direct participants to complete details through use of annotation or highlighting next to required fields.

The study Sponsor may revise the informed consent form when new information becomes available which may be relevant to the participant's consent. Any revisions must be approved by the relevant REC before use (unless incorporated as part of an urgent safety measure) and the participant will be informed of new information in a timely manner. The communication of this information must be documented in the participant's medical notes.

6.4. After Consent Has Been Obtained

Once all of the parties have signed the ICF, two copies will be taken. One copy is returned to the participant, one copy is stored within the participant's medical notes (along with the PIS) and the original is stored within the Investigator Site File or Trial Master File. The signed ICF must be retained regardless of how long the participant is active in the trial, including if the participant withdraws from the study.

A copy of the ICF **must not** be stored together with data from the Case Report Forms.

The practice of giving information regarding the trial to participants will be ongoing throughout and performed by all members of the research team. It is good practice

to confirm with the participant at each interaction that they are willing to continue in the study. This should be documented in the medical notes.

If protocol amendments are introduced, or if new safety information released, the participant will be approached for their continued willingness to be involved in the study. This must be documented in the source data or medical notes. In these circumstances it may be necessary to re-consent using an amended consent form.

HRA/MHRA Joint statement observes “a copy (physical or electronic) of the signed consent form should be provided to the participant” (Reference Number. 7.5)

6.4.1 Eligibility

For Clinical Trials of Investigational Medicinal Products (CTIMPs) and Advanced Therapy Investigational Medicinal Products (ATIMPs) the eligibility of potential participants **must** be determined by medically qualified personnel (i.e. doctor or dentist). This responsibility cannot be delegated to non-medically qualified individuals within the study team.

For non-CTIMP studies eligibility assessment by non-medically qualified personnel must be approved by REC.

The outcome of the eligibility assessment must be documented in the participant’s medical notes. This must state clearly that the patient is eligible to participate.

The entry in the notes must be clearly signed and dated by the individual undertaking the eligibility assessment.

6.4.2 Withdrawal of Consent

If a participant wishes to withdraw their consent to participate in research activity this must be accepted and the decision documented in the participants notes. The record must define the level of withdrawal as described in the Protocol so that it is clear if some data collected can still be utilised or if the participant has withdrawn completely.

6.5. Informed Consent of Minors

Under the Medicines for Human Use (Clinical Trial) Regulations, a participant is classified as a minor if they are under the age of 16. In addition to the above, there are a number of factors that must also be considered when seeking consent from minors:

- It is essential that the study either relates directly to a clinical condition from which the minor suffers, or that the study can *only* be performed in minors.
- It will be demonstrated that there will be some direct benefit for the research participants and that the clinical study is necessary to validate data obtained in other clinical studies.

The clinical study needs to be designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the investigated disease and the minor's stage of development. Risk and distress must be monitored continually for the duration of the study.

Consent will ensure that:

- The minor has received information according to their capacity and understanding from experienced staff.
- The wish of a capable minor to refuse consent or withdraw from the study at any time is considered by the investigator.
- A parent/guardian or legal representative has been consulted and agrees participation if the study takes place in an emergency setting or the minor has lack of capacity.
- The PIS is written in language the minor can understand and this will reflect the potential participant's age.
- Assent should be obtained from the Minor where possible. Justification for not obtaining their consent should be documented in the medical notes

Consent can be provided for the minor by:

- A parent or person with parental responsibility.
- Personal legal representative – a person not connected with the conduct of the trial who is suitable to act as a legal representative by virtue of their relationship with the minor.
- Professional legal representative – a person nominated by the relevant healthcare provider who is not connected with the trial.
- The minor assessed as competent in law (Reference 7.4).

6.6. Informed Consent of Incapacitated Adults

When seeking consent from an adult unable by virtue of physical/mental incapacity to give informed consent the Investigator must ensure that:

- The study relates directly to a life threatening or debilitating clinical condition from which the participant suffers, and it is expected that the study will produce a benefit which will outweigh the risks/produce no risk at all.

- The clinical study must be essential to validate data obtained in other clinical studies involving persons able to give informed consent.
- The clinical study needs to be designed to minimise pain, discomfort, fear and any other foreseeable risks to the participant. Continuous monitoring throughout the study of risks and/or distress must take place and the interests of the participant must prevail over the interest of the science.

- The participant's legal representative must have the objectives, risks, inconveniences and associated conditions for the study explained to them. They must be informed of their right to withdraw the participant at any time resulting in no detriment to care. They must then give informed consent on behalf of the participant.
- The potential participant must also be given information about the study according to their level of understanding.
- No incentives or financial gains will be used to influence a potential participant to participate (or the participant's legal representative to consent on their behalf), other than provision for compensation in the event of loss or injury.

6.7. Informed Consent in Emergency Research

Where research involves adults or minors in emergency situations there are several requirements that need to be met before the individual can receive a trial intervention.

6.7.1. Emergency Research Involving Minors

The Medicines for Human Use (Clinical Trials) and Blood Safety and Quality (Amendment) Regulations 2008 gives provision for CTIMPs involving minors in emergency situations. The obtaining of consent for a minor to participate in such a trial may be deferred whilst:

- the minor requires urgent treatment.
- urgent action is required for the purposes of the trial.
- meeting the requirements of the legislation is not reasonably practical, providing that a REC has approved.

Where a minor is recruited in an emergency situation without prior informed consent, steps must be taken to seek consent from an individual with parental responsibility or a legal representative as soon as possible after the initial emergency has passed. If consent is withheld then the minor must be withdrawn from the trial.

6.7.2. Emergency Research Involving Incapacitated Adults

Where research involves adults that temporarily or permanently lack capacity to consent, due to the nature of the study and initiation is required swiftly two approaches are required depending on the classification of the trial.

For a CTIMP, The Medicines for Human Use (Clinical Trials) (Amendment No.2) 2006 gives provision for trials involving incapacitated adults in emergency situations. The obtaining of consent may be deferred whilst:

- it is necessary to take action for the clinical trial as a matter of urgency;
- meeting the requirements of the legislation is not reasonably practical, provided that a REC has approved.

For non-CTIMP research the Mental Capacity Act (2005) will be followed. Researchers are required to consult a carer, someone interested in the adult's welfare, or an independent nominee for their advice and opinion on whether the patient will be recruited. However, the Act also allows an adult to be enrolled in a research study in an urgent situation without such consultation, providing there is an agreement from an independent clinician. If this is not practical, then the protocol must be approved by the appropriate research ethics committee.

7. References

7.1 Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments
7.2 UK Policy Framework for Health and Social Care Research: Version 3.3
7.3 The Mental Capacity Act 2005
7.4 British and Irish Legal Information Institute. Gillick v West Norfolk & Wisbech Area Health Authority, UKHL 7 (17 October 1985)
7.5 HRA/MHRA Joint Statement on seeking consent by electronic methods (September 2018)
7.6 eIDAS Regulation (EU) No 910/2014
7.7 eIDAS Regulations (UK) SI 2016/696
7.8 Trust Policy "Consent to Examination or Treatment (with reference to the Mental Capacity Act 2005)
7.9 Informed Consent for Biobanking SOP NJRO-TISS-SOP-011
7.10 Virtual and eConsent in Research at NuTH SOP NJRO-GEN-SOP-028