Standard Operating Procedure: The Process of Obtaining Informed Consent for a Research Study

**BACKGROUND**

Informed consent is the foundational principle of the Nuremberg code, the Declaration of Helsinki and Good Clinical Practice (ICH GCP).

A person gives informed consent for a clinical trial only when the decision to participate is:

(a) freely given, after the person has received full information about the nature, significance, implications and risks of the trial

and

(b) evidenced in writing, dated and signed, or otherwise marked by the person so as to indicate consent

or

if the person is unable to sign or to mark a document so as to indicate consent, it is given orally in the presence of at least one witness and recorded in writing.
The same definition applies to the giving of informed consent by a person with parental responsibility, or a legal representative, on behalf of the trial subject (Health Research Authority).

Case law on consent in the UK has established three requirements to be satisfied before a potential research participant can give informed consent:

- the consent should be given by someone with the mental ability to do so
- sufficient information should be given to and understood by the participant
- the consent must be freely given

The UK legal requirements for informed consent of participants in clinical trials of investigational medicinal products (CTIMPs) are set out in Schedule 1 to the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) as amended by SI 2006/1928, SI 2006/2984, SI 2008/941 and SI 2009/1164. The UK Clinical Trial Regulations implement the Clinical Trials Directive (2001/20/EC) and GCP Directive (2005/28/EC), as well as applicable guidelines, such as ICH GCP, into UK law (Health Research Authority).

Performing any research-related procedure on someone without first obtaining their informed consent, is a breach of the UK Clinical Trial Regulations (SI 2004/1031 as amended).

A comprehensive definition of informed consent is to be found in paragraph 24 of the 2008 version of the Declaration of Helsinki:

“In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject’s freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.”

Written documentation consists of three elements:

1. Documentation in the patient’s medical notes describing the process of informed consent
2. The (Patient) Information Sheet (PIS). Describes the trial in layperson’s terms.
3. The Informed Consent Form (ICF). Documents that informed consent has been taken, when and by whom.

Obtaining consent in the study setting is a process involving dialogue between delegated Clinical Research Team members (CRTM) and potential research participants, clarifying objectives and ensuring understanding regarding clinical studies. Effective communication is the key to enabling potential participants to make informed decisions about participation in a clinical trial. When providing information, CRTM will evaluate participants’ individual needs
and priorities including: their understanding of their condition and treatment; beliefs, culture, occupation or other factors that may have a bearing on the information they require.

PURPOSE

This Standard Operating Procedure (SOP) describes the procedure for obtaining written informed consent from a study subject and is complementary to the requirements stipulated by the Study Sponsor in the approved study protocol and/or other relevant documentation and training provided by the sponsor.

This SOP does not outline the procedure for the consent of minors and incapacitated adults.

ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>CRTM</td>
<td>Clinical Research Team members</td>
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<tr>
<td>CV</td>
<td>Curriculum Vitae</td>
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<td>GCP</td>
<td>Good Clinical Practice</td>
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<td>GP</td>
<td>General Practitioner</td>
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<td>ICF</td>
<td>Informed Consent Form</td>
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<td>ICH</td>
<td>The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)</td>
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<td>MREC</td>
<td>Main Research Ethics Committee</td>
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<td>PI</td>
<td>Principal Investigator</td>
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<td>PIS</td>
<td>Patient Information Sheet</td>
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<td>R&amp;D</td>
<td>Research and Development</td>
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<td>SOP</td>
<td>Standard Operating Procedure</td>
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PROCEDURE

1. WHO?

According to section 4.8.5 of ICH GCP, ‘The investigator, or, a person designated by the Investigator should fully inform the subject’ and the written informed consent form should be signed and dated by the ‘person who conducted the informed consent discussion’. The delegation of Informed Consent to an appropriate, suitably qualified member of the research team should be considered on a trial-by-trial basis, taking account of local circumstances and in accordance with the ICH GCP Guidelines.

In addition, section 24 of the 2008 version of the Declaration of Helsinki states that “after ensuring that the subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely given informed consent, preferably in writing”.

If staff other than the Principal Investigator (PI) are to accept responsibility for the informed consent process and/or being the sole signatory on the Informed Consent Form (ICF) then the following criteria must be met:

- i) The designee is prepared to take on this additional responsibility and feels confident to take written informed consent in line with their professional body’s Code of Professional Conduct or other professional organisational guidelines (e.g., the Nursing and Midwifery Council (NMC) Code of Professional Conduct).
ii) The designee has a comprehensive understanding of the study, potential pharmacological interactions/treatment toxicities and the associated disease area. The designee is qualified by experience and/or has received appropriate training for this study. All training must be documented.

iii) The delegation of responsibility is documented on the Study Delegation Log/Site Responsibility Log (refer to SOP 4).

iv) The local Research & Development (R&D) Department have been notified that staff other than the PI will also be responsible for the informed consent process.

v) An effective line of communication is maintained back to the PI who is ultimately responsible for the patient’s care.

vi) All persons who obtain written informed consent have a copy of their signed and dated Curriculum Vitae (CVs) in the study file and have completed the Study Delegation Log, which is also signed and dated by the PI (refer to SOP 4).

It is ultimately the responsibility of the PI to ensure that the correct process is followed and it is usual practice for the PI to sign/counter-sign the consent form.

2. WHEN?

The informed consent process starts when a potential participant is given trial specific information and continues through being offered the opportunity to participate, being given all relevant information and until the written informed consent is signed.

Written informed consent must be obtained from subjects before any study specific procedures are undertaken.

The informed consent process does not cease once ICF has been signed. The practice of giving information to subjects about the study is an ongoing process performed by CRTM. This is particularly significant when protocol amendments occur and new information becomes available that may be relevant to the subject’s willingness to continue participation in the study. In these circumstances the study subject may be required to re-consent on an amended consent form in order to continue involvement in the study.

3. HOW?

Prior to the start of any trial, a favourable ethical opinion from the Main Research Ethics Committee (MREC), is obtained for the use of the Patient Information Sheet (PIS), ICF and any other trial specific patient information.

Informed consent is a two-step process: (1) informing the subject and, (2) obtaining written consent.

Potential study subjects, i.e. those thought to fulfil the Inclusion/Exclusion Criteria of the study are identified and approached by either the PI or designee as defined in ‘Section 2, Who?’

Informing the subject
Patient information is provided to potential study subjects in both an oral and written form or other appropriate format (information may be presented to potential subjects using many formats and different media, including video, posters, recordings, CD ROM, Braille, deaf interpreter).

In obtaining and documenting informed consent, the PI or designee complies with the applicable regulatory requirement(s) and adheres to ICH GCP and to the ethical principles that have their origin in the Declaration of Helsinki.

Neither the PI nor any CRTM will coerce or unduly influence a subject to participate or continue in a trial.

Any information imparted to the subjects (written, verbal or other formats), will not contain any language that causes the subjects to waive (or appear to waive) any legal rights, or that releases (or appears to release) the PI, institution or sponsor from liability for negligence.

The language used in the written, verbal (or other format) information about the study including the written consent form, is as clear and non technical as practicable. A comprehensive list of information that is included in any explanation to a potential subject is found in Appendix A.

The Patient Information Sheet (PIS) and Informed Consent Form (ICF) are identifiable by date and version number and are printed on headed paper associated with the particular hospital or site where the study is being conducted.

The PIS includes the name and telephone numbers of the local PI and/or research nurse who can be contacted if the potential subject has any questions or requires further information.

Potential participants are provided with ample time and opportunity to read the PIS, review the study information, and discuss the study with family friends or others. Prior to subjects signing the consent form all questions are answered by the delegated member(s) of the CRTM.

Obtaining Informed Consent

When the person obtaining written informed consent is satisfied that the potential subject has had ample time and opportunity to ask questions, been fully informed and understands what study participation entails, the ICF is signed and personally dated by both the subject and by the designee who conducted the informed consent discussion. The PI retains overall responsibility for gaining subjects' informed consent and it is good practice for the PI or designee to counter-sign the consent form when consent is taken by another team member.

Two copies of the original signed and dated consent form are made. The original is filed in the Trial Site File (refer to SOP 2 and SOP 3). One copy is filed in the subject's medical notes. One copy is given to the subject.

The process of obtaining informed consent should be documented in the subject's medical records, detailing the study title and/or acronym, the date the study was offered to the subject and the date the ICF was signed. The entry should be dated and signed by a delegated CRTM.
When new information requires revision of the PIS, subjects may be required to repeat the consent procedure to document their continued willingness to participate in the study.

With the subject’s consent, their General Practitioner (GP) will be informed in writing about their study participation and will receive appropriate information regarding the study.

Every effort will be made to include patients for whom English is not their first language. These patients will only be included if there is access to an interpreter who can adequately explain the concept and requirements of the trial and the PI is satisfied that the subject has a full understanding of what is involved. If this cannot be achieved then such patients will not be recruited.

Every effort will be made to include patients who are visually or hearing impaired. These patients will only be included if there is access to communication aids to enable the PI to ensure the subject has a full understanding of what is involved. If this cannot be achieved then such patients will not be recruited.

4. OTHER RELATED PROCEDURES/DOCUMENTS/SOURCES

SOP 2 - Study Files and Filing
SOP 3 - Archiving
SOP 4 - Definition of Responsibilities

5. APPENDICES

Appendix A - Information to be Provided to Potential Trial Subjects.

6. REFERENCES


ICH GCP – ICH Harmonised Tripartite Guideline for Good Clinical Practice E6(R1) (CPMP/ICH/135/95), May 1996.

Nursing and Midwifery Council (NMC) Code of Professional Conduct


THIS IS A CONTROLLED DOCUMENT, ANY PRINTED VERSIONS OF THIS DOCUMENT WILL BE CLASSED AS UNCONTROLLED.
As amended:


- **SI 2006/2984** – The Medicines for Human Use (Clinical Trials) Amendment (No.2) Regulations 2006.


APPENDIX A: Information to be provided to Potential Trial Subjects

According to section 4.8.10 of the ICH GCP guidelines, both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:

a) That the trial involves research.
b) The purpose of the trial.
c) The trial treatment(s) and the probability of random assignment to each treatment.
d) The trial procedures to be followed, including all invasive procedures.
e) The subject’s responsibilities.
f) Those aspects of the trial that are experimental.
g) The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, foetus, or nursing infant.
h) The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
i) The alternative procedure(s) or treatment(s) that may be available to the subject, and their important potential benefits and risks.
j) The compensation and/or treatment available to the subject in the event of trial-related injury.
k) The anticipated prorated payment, if any, to the subject for participating in the trial.
l) The anticipated expenses, if any, to the subject for participating in the trial.
m) That the subject’s participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.

n) That the monitor(s), the auditor(s), and the regulatory authority(ies) will be granted direct access to the subject’s original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject’s legally acceptable representative is authorising such access.
o) That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the study are published, the subject’s identity will remain confidential.
p) That the subject or the subject’s legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject’s willingness to continue participation in the trial.
q) The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
r) The foreseeable circumstances and/or reasons under which the subject’s participation in the trial may be terminated.
s) The expected duration of the subject’s participation in the trial.
t) The approximate number of subjects involved in the trial.