University of Hertfordshire

INFORMED CONSENT

Clinical Trials Support Network (CTSN)

Standard Operating Procedure for Obtaining and Documenting Informed Consent in Research

SOP Number: gSOP-04-02	**Effective Date:** 28th July 2022
Version Number: v2.0	**Review Date:** 3 years (or as required)

1.0 BACKGROUND

This is a University of Hertfordshire (UH) standard operating procedure (SOP). This document sets out the procedures to be followed by all research staff who consent participants into UH sponsored/co-sponsored or CTSN adopted research studies. Where there are potential conflicts between different collaborating organisations' SOPs, project level working instructions should be developed, to determine precedence.

It aims to provide clear guidance on the legal requirements and the procedures of taking informed consent when recruiting participants to research studies carried out in UH sponsored/co-sponsored studies or CTSN adopted studies.

The Sponsor shall ensure a valid informed consent was obtained prior to participants participating in research to meet ethical and regulatory requirements. Prior to trial initiation, for studies involving Trust participants the Sponsor should ensure that the study has received R&D confirmation from the collaborating hospital trust/s. For those studies conducted outside of NHS Trusts e.g., local authorities, the appropriate approvals/confirmation for trial initiation should have been received.

2.0 PURPOSE

Informed consent is a process by which a trial participant voluntarily confirms his or her willingness to participate in a research study after being duly informed of all aspects of the trial including the risks and benefits to the participant, alternative options, peripheral and altruistic nature of the research. The process should be carried out in stages, allowing sufficient time for the participant to understand oral and written information (e.g., Participant Information Sheet (PIS)) and to clarify any arising queries. The participants must be informed that they are free to withdraw at any point in the trial after consenting if they wish to do so.

Informed consent is at the heart of ethical research. Most studies involving individuals must have appropriate arrangements for obtaining consent, and the ethics review process pays particular attention to those arrangements.

Freely given informed consent should be obtained from every participant prior to clinical trial participation. Consent should be obtained before the first trial-specific activity is undertaken.

The principles of Good Clinical Practice (GCP) state that in obtaining and documenting informed consent, investigators should comply with the applicable regulatory requirement(s) and adhere to GCP. Sponsor/Chef investigator (CI)/Principal Investigator (PI) shall ensure before starting a trial to obtain a written approval/favourable opinion from the ethics committee for the written informed consent form and any other written information to be provided to the participants. For studies involving NHS Trust participants the Sponsor shall also ensure that the research study has R&D confirmation from the collaborating hospital trust/s. For studies involving participants outside of NHS trusts the Sponsor shall also ensure that the research study has confirmation from the appropriate collaborating bodies e.g., local authorities.

Before participants can participate in research a valid informed consent must be obtained by the research team.

For healthy volunteer studies, a separate participant consent form may be required for registration onto The Over-Volunteering Prevention System (TOPS database). A separate PIS with an explanation of the requirement to be registered on to the TOPS system should be provided to participants. Please see gSOP-38 Management of healthy volunteers in research studies.

3.0 APPLICABLE TO

This applies to all staff involved in clinical research that is UH sponsored/co-sponsored or adopted by the CTSN, including: CIs, PIs, Research Fellows, Consultants, Statisticians, Clinical Trial Pharmacists, Research Managers, Research Nurses, Clinical Trial Practitioners, Allied Health Professionals, Trial co-ordinators/Managers, Clinical Studies Officers, Data Managers Research Assistants and Students.

4.0 RESPONSIBILITIES

The Sponsor shall ensure that a valid informed consent was obtained for all participants before recruitment and prior to carrying out any study specific procedures. Consent must be taken by the CI/PI or designated individual (DI).

The CI/PI/DI should fully inform the participant or, if the participant is unable to provide informed consent, the participant's legal representative, of all pertinent aspects of the trial including the written information given approval/favourable opinion by the ethics committee.

The CI/PI shall ensure that participants have fully understood what they are consenting to. Consent is an ongoing process for the duration of the study. The participant should be followed up after being given information as to their decision to take part in the study and this should provide an opportunity for any further questions to be discussed. The Sponsor shall maintain overall responsibility for the consenting process.

The Sponsor/investigator may delegate parts of the informed consent duties to appropriately trained and qualified members of the research teams. Staff delegated to consenting shall have a valid GCP

certificate. Delegation shall be documented on the study delegation log held in the Trial Master File (TMF).

The name and date of the research personnel taking consent should be documented on the consent forms (physically or electronically e.g. via a study database. They must also make a record in the participant's medical notes, of discussions related to the clinical trial with the participant and any further contact. If the participant decides not to consent, a record of this should be recorded in the participant's medical records. If appropriate, the CI/PI may sign/countersign the consent form. All personnel who have completed/signed a consent form must have completed the study delegation log, which shall be countersigned/dated by the CI/PI. The CI/PI or DI should also ensure that PIS contain contact details for nominated personnel within the research team.

All research personnel with consenting responsibility shall ensure that the original copy of the research consent form is held in the Trial Master File (TMF)/Investigator Site File (ISF). Copies of signed consent form may be held in the medical notes and/or TMF and a copy must be provided to the participant. Staff must also ensure appropriate recording of all informed consent discussions in the patient medical records.

5.0 PROCEDURE

5.1 Considerations Before Starting Clinical Trials

5.1.1 Informed consent must be recorded in writing, however electronic methods for documenting consent can be considered to be in writing. A copy of the signed consent form should still be provided to the participants and placed in medical records whether physical or electronic. As part of recording consent electronically, electronic signatures will likely be used. Electronic signatures can take a variety of forms and are classified in different ways (simple, advanced and qualified). The type of electronic signature that is acceptable will depend on the recruitment and consent procedures and will be considered as part of a proportional approach. Refer to the HRA guidance for further information.

5.1.2 All written informed consent forms and any other information e.g., PIS must have approval from ethics. All subsequent versions must also receive ethics approval as substantial amendments (see gSOP-09 Amendments). Blank copies of all versions should be held in the TMF.

5.1.3 None of the information provided relating to the trial shall unduly influence or coerce the trial participant or participant's legal representative.

5.1.4 The written information shall be in a non-technical language, easily understandable to the trial participant or the participant's legal representative or the impartial witness. It is recommended that the templates provided by the Health Research Authority (HRA) be consulted during the preparation stages. Ideally, consent documents should be co-designed or reviewed by a patient and public involvement (PPI) group.

5.1.5 The Sponsor and CI shall ensure that the study teams are adequately trained in obtaining and documenting a valid informed consent. Particular training needs must be met in describing technical languages involved in complex interventions, unlicensed Investigational Medicinal Product (IMP), invasive assessment methods, randomisation and other trial methodologies. In addition, specific training in obtaining informed consent in a paediatric setting or for adults who lack capacity should be given if applicable.

5.1.6 In order to obtain consent, the delegated staff member shall be familiar with the protocol, risks and benefits associated with the study and the peripheral and altruistic nature of the research. The delegated staff member shall be effectively trained in communicating all aspects of the study in a non-technical and understandable language.

5.1.7 The PI must ensure teams are adequately trained in clearly documenting the consenting process in participant records and other trial related documentations.

5.2 Obtaining Informed Consent from Trial Participants

5.2.1 Consenting participants shall be carried out in stages, allowing sufficient time between each stage. Stages shall include preliminary discussion, further discussion and provision of written information (e.g. PIS) and final consent.

5.2.2 The participant must be allowed sufficient time between each stage for understanding the provided oral, written and/or multimedia information. The original research consent forms should be held within the TMF/eTMF/ISF/eISF. A copy should be held within the participant's medical notes and a copy provided to the participant.

5.2.3 Under emergency situations, the consenting methods may vary. If prior consent from the participant was not available, the participant's legal representative must be consulted. If neither the participant nor the legal representative was available, the participant may be enrolled as described in the protocol and/or elsewhere. This must be supported with documented approval from the ethics committee, to protect the rights, well-being, and safety of the trial participants. The investigator shall abide by institutional policies and regulatory compliance.

5.2.4 In order to obtain a valid informed consent, the following best practice guidelines shall be considered:

- Early discussion with participants.
- Answering questions fully by a qualified member of the research team.
- Providing adequate information to make an informed decision.
- Participant must not be under any pressure or duress.
- Participant must be competent to make an informed decision.
- Make sufficient notes of all discussions in participant's notes.
- PIS should be used to enhance the participant's understanding of research however should not be used as a substitute for discussion.

5.2.5 Consent can be configured to be a hybrid combination of paper and electronic consent elements (see Figure 1). When considering remote informed consent, particular attention is required to participant ID verification and data privacy considerations for both paper and eConsent, For further guidance refer to the Electronic Informed Consent Implementation Guide produced by the European CRO Federation (EUCROF) and the eClinical Forum.

5.2.6 The Sponsor/PI must ensure overall control for the informed consent process. However, the PI may delegate parts of the consenting process to adequately trained and qualified personnel. The investigator shall ensure that the delegated responsibilities are documented, dated and signed by the nominated personnel and a confirmation signature from the Investigator in a 'delegation of responsibilities log'. A copy shall be retained in the TMF/eTMF.

5.2.7 The PI shall ensure that an informed consent form was signed and dated by the participant or participant's legal representative.

5.2.8 An explanation of the standard treatment shall be provided to the participant prior to detailed discussions of experimental research (clinical trials). The participant shall be fully informed that their level of standard care shall not be affected irrespective of whether they decide to participate in research study or not.

5.2.9 Participant information and the informed consent verbal discussion shall contain the key points included in GCP.

5.2.10 The participant or legal representative shall be provided with written information such as the PIS and any other relevant materials to read at their own pace.

5.2.11 Further information sessions should be set up to allow discussion with the participant and to encourage questions. This may be in the form of an appointment or a telephone call. These discussions should also be annotated in the participant's medical record. The investigator should ensure participants fully understand all aspects of the research study including what the participant's responsibilities are.

5.2.12 If the participant's first language is not English, provisions for translational service must be considered.

5.2.13 Obtaining consent is an ongoing process and if the research study protocol or any PIS contain significant amendments (e.g., significant issues with regards to patient's safety), participants may in some cases need to be re-consented. This shall be determined by the Sponsor and ethics committee.

5.3 Trials involving adults not able to consent for themselves

5.3.1 Adults who lack capacity to give consent should receive information at their level of understanding. If participants can form an opinion and assess the information, their explicit wishes should be considered.

5.3.2 The Medicines for Human Use (Clinical Trials) (Amendment No. 2) Regulations 2006 made provisions for trials involving incapacitated adults in emergency settings in which participants can be entered into a trial before informed consent is obtained (see Section 21 of the HRA Guidance).

5.3.3 For research other than CTIMPs, the HRA's online consent guidance provides information about consent in incapacitated adults.

5.4 Trials involving children and young people

5.4.1 The Clinical Trials Regulations define a minor as a person under the age of 16 years.

5.4.2 Where minors can express their own views on a study, they should be involved in a way that is appropriate to their understanding and development and the extent they wish to engage.

5.4.3 Trials involving minors in the emergency setting: The Medicines for Human Use (Clinical Trials) and Blood Safety and Quality Amendment Regulations 2008 have made provisions for trials involving minors in emergency settings in which minors can be entered into a trial without prior consent. The

Regulations require a person with parental responsibility or a legal representative to provide consent as soon as possible after entry into the trial (see Section 16 of the HRA guidance for further information).

5.4.4 For research other than CTIMPs, the HRA's online consent guidance provides information about consent in children and young people.

6.0 RELATED DOCUMENTS

- gSOP-01- SOP on SOPs
- gSOP-06- TMF/Site File
- gSOP-07- Research Training
- gSOP-20- Participant Information
- HRA guidance on information sheets and consent forms
- gSOP-38 Management of healthy Volunteers in Research Studies
- Electronic Informed Consent Implementation Guide – Practical Considerations: https://cdn.ymaws.com/www.tmn.ac.uk/resource/resmgr/electronic_informed_consent_.pdf

7.0 APPENDICES

- Figure 1 – Remote and On-Site Consent Options
- Appendix 1 – Definitions
- Appendix 2 – Key Points of ICH GCP Guidance on Informed Consent

8.0 VERSION HISTORY

Revision Chronology:		
Version Number	**Effective Date**	**Reason for Change**
2.0		Review

9.0 AUTHORSHIP & APPROVAL

Author

Signature  **Date 23 June 2022**
Megan Smith

Pro-Vice Chancellor (Research & Enterprise) Approval

Signature **Date 16 June 2022**
Professor J M Senior

10.0 AGREEMENT

Please detach and retain in your training files

I have read and understood the contents and requirements of this SOP (gSOP-04-02) and accept to follow UH policies in implementing it.

Recipient

Signature: ……..……Date: ……..

Name & Position: ……

Figure 1: Remote and On-Site Consent Options

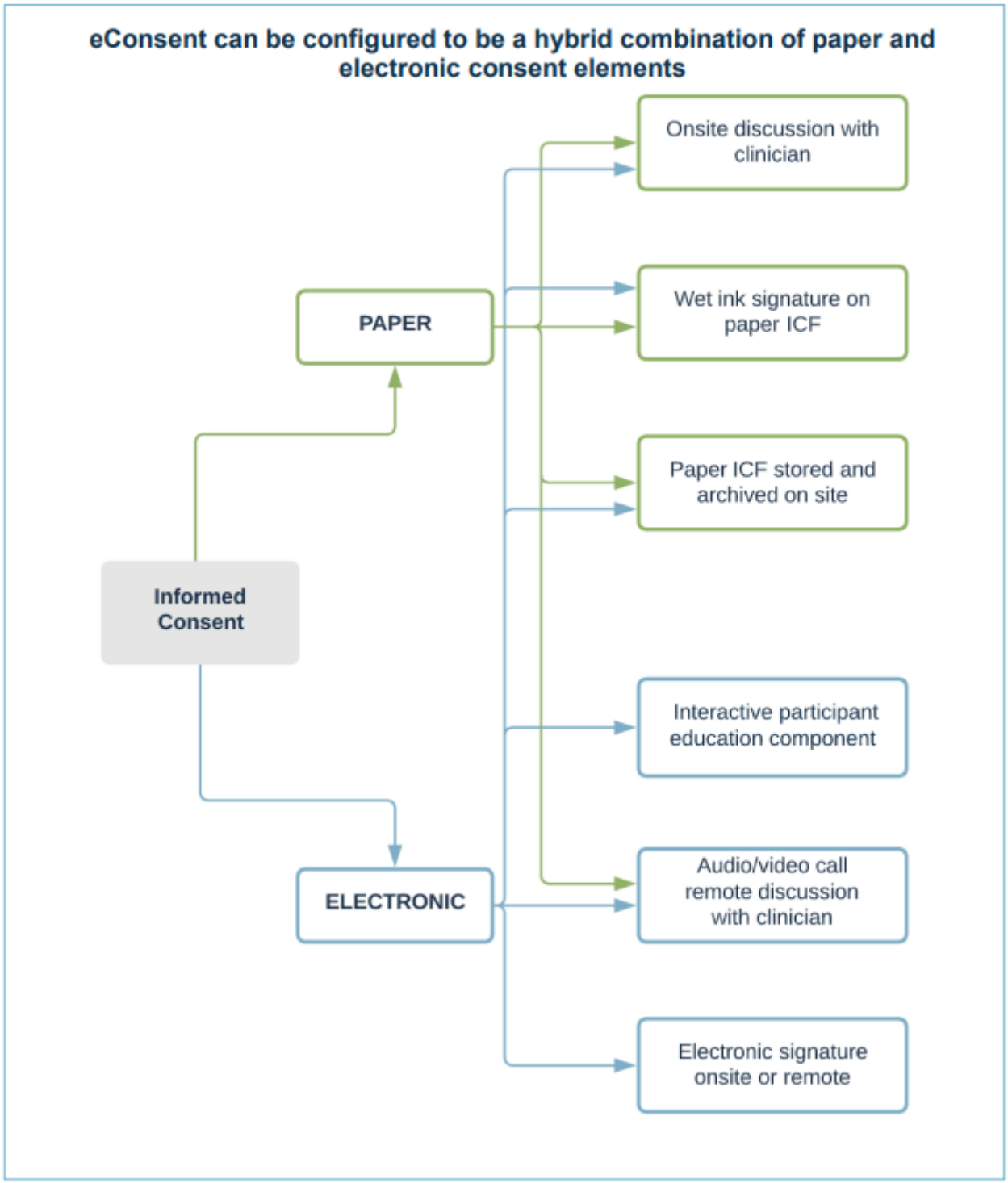

Figure 1: The arrows demonstrate how paper consent is enhance by adding electronic consent elements. This is non-exhaustive view of the possible combinations of paper consent and eConsent aspects of informed consent. Retrieved from https://cdn.ymaws.com/www.tmn.ac.uk/resource/resmgr/electronic_informed_consent_.pdf

Appendix 1: Definitions

Adverse Event (AE)
Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product

Chief Investigator (CI)
A Registered Physician, Dentist, Pharmacist or Registered Nurse who has overall responsibility for the conduct of the trial.

Clinical Trial
A research study in which one or more human participants are prospectively assigned to one or more interventions (which may include placebo or control) to evaluate the effects of those interventions on health outcomes.

Clinical Trial of Investigational Medicinal Product (CTIMP)
A study that looks at the safety or efficacy of a medicine/food stuff/placebo in humans as defined by the Medicines for Human Use Regulations (2004).

Delegated Individual (DI)
An individual delegated by the PI to carry out their task(s).

Good Clinical Practice (GCP)
As defined in the Regulations.

International Conference on Harmonisation (ICH)
The ICH produced a series of guidelines in 1996, E6 being the guideline on Good Clinical Practice, otherwise known as (ICH-GCP).

Investigator Site File (ISF)
The file(s) held at each site taking part in the trial which hold the essential trial document set necessary for local approval and trial conduct at site**.**

Public and Patient Involvement (PPI)

Patient Information Sheet (PIS)
A document that explains all relevant study information to assist the trial participant in understanding the expectations and requirements of participation in a clinical trial.

Principal Investigator (PI)
A Registered Physician, Dentist, Pharmacist or Registered Nurse who has responsibility for the conduct of the trial at a host site.

Site File
Site Files are held by the Principal Investigator at sites and contain copies of the essential documents, local approvals, signed consent forms and completed data forms.

The Regulations

Medicines for Human Use (Clinical Trial) Regulations 2004 transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031. This became effective on the 1st May 2004. An amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928.

Trial Master File

The Trial Master File (TMF) will be held at the principal site by the sponsor, Chief Investigator or at the co-ordinating Centre. The TMF should contain all essential documents defined as documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. A Trial Master File should be set up at the beginning of a trial and maintained up-to-date throughout the trial until trial conclusion.

For trials currently running, it is recommended that Section 8 of the ICH-GCP Guideline is followed as guidance in order to meet statutory requirements. However, some of the documents listed may not be available or applicable in many non-commercial trials. The appropriate documentation will vary according to the trial and sponsor requirements.

Appendix 2: Key points of ICH GCP Guidance on Informed Consent

This document refers to the ICH GCP Guidance on informed consent of trial participants. Key points are listed below:

- Participants shall be provided with what the trial involved, explanation of the parts that are experimental and other relevant background information.
- Why the participant/legal representative was approached and the purpose of the trial and eligibility criteria.
- Participant/legal representative must be ensured that the trial participation and related activities will be confidential. However, participants should be informed that their medical records and other trial related documents will be accessed by research staff and other related personnel such as regulatory authorities, monitors, auditors and ethics committee for verification of trial data. The participant must authorise such access in the form of written consent (physical or electronic), personally signed and dated.
- An explanation of the trial treatment(s), details of any medications, details of any invasive procedures, and the probability of random assignment to each treatment. If a placebo or use of medication outside licensed indication was involved, the participant should be provided with clear explanation of what that entails.
- An explanation of foreseeable risks or inconveniences to the participant and, where applicable, to any embryo, foetus, or nursing infant.
- An explanation of the expected benefits and altruistic nature of research must be provided. If the participant was not to gain any clinical benefit from the study, this should be explained.
- The participant/legal representative should be made aware of any available alternatives and the risks/benefits related to these.
- An explanation of compensation and/or care and supporting treatment available to the participant in the event of trial related injury must be explained.
- The anticipated prorated payment or travel expenses, if any, to the participant for participating in the trial.
- An explanation for use and storage of the collected biological samples (e.g., blood, tissue) must be provided. Appropriate use of these and supporting written consent must be obtained in compliance with the Human Tissue Act.
- Participant/legal representative must be advised that the trial participation is voluntary and that the participant may refuse to take part or to stop participation in the trial at any time.
- Participants must be informed of their responsibilities of participation in a trial, the duration of the trial, the likely number of trial participants, and the responsibilities for reporting any adverse

events to the study team immediately to ensure their safety and that of other participants. If applicable, the participants must be advised to provide the emergency card during every hospital admission to alert the study team.

- Participants must be provided with details of the study team and an emergency contact number.

- Participants must be informed that they will be provided with up-to-date information of all trial related issues and if necessary, the protocol and/or patient information sheets may be amended. In some cases, the participant may need to be re-consented. The participant should be provided with copies of all up-dated consent forms and PIS.

- Participants must be informed that following consent, under certain cases, they might not be able to continue with the trial. If they failed to meet eligibility criteria at a later stage following diagnostic tests or other foreseeable circumstance and/or reasons under which the participant's participation in the trial may be terminated.