Obtaining Informed Consent for Clinical Trials

Policy Details	
Document Type	Standard Operating Procedure
Document name	KHP-CTO/CT/SOP7.0 Obtaining Informed Consent for Clinical Trials
Version	Final v 4.1 28th February 2023
Effective from	28th February 2023
Review date	1st December 2026
Owner	King's Health Partners Clinical Trials Office
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Superseded documents	Final v 4.0 18th December 2019
Relevant regulations/legislation/guidelines	Statutory Instrument 2004 no 1031 Statutory Instrument 2006 no 1928

Change History

Date	Version Number	Change details	Approved by
11 Nov 2013	2.0	Scheduled review and change of branding from JCTO to KHP-CTO	Jackie Powell
28 Nov 2016	3.0	Scheduled review, update of template and glossary to standard format, administrative amendment and update to include changes due to HRA	Jackie Pullen
01 Oct 2018	3.1	Minor amendment to include trials managed by KHP-CTO	Jackie Pullen
18 December 2019	4.0	Scheduled review and replacing subject with participant throughout	Jackie Pullen
28Feb23	4.1	Scheduled review with minor amendments	Jackie Pullen

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1.0 GLOSSARY

Clinical Research Associates (CRAs) – Part of the KHP-CTO Quality Team. Ensure compliance with the Regulations, GCP and SOPs, by monitoring clinical trials.

Clinical Trial - Any investigation in human participants, other than a non-interventional trial, intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal product and/or to identify any adverse reactions to one or more such products and/or to study absorption, distribution, metabolism and excretion of one or more such products with the object of ascertaining the safety and/or efficacy of those products.

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

Health Research Authority (HRA) – An authority in England established in 2011 which exercises functions in connection with the facilitation and promotion of research and the establishment of research ethics committees.

Impartial Witness – A third party who is not connected with the research, such as a non-research team employee, relative of the participant, or person similarly unconnected with the research. The impartial witness must speak both English and the language understood by the participant or representative.

Incapacitated Adult – An adult who is unable to give informed consent, by virtue of physical or mental incapacity.

Informed Consent Form (ICF) – The document which is signed by the participant/legal representative as well as the person who conducted the informed consent discussion confirming the volunteers willingness to participate in the particular trial, having been informed of all aspects of the trial that are relevant to their decision.

International Council for Harmonisation (ICH) – Produced a series of guidelines in 1996, E6 being the guideline on Good Clinical Practice, otherwise known as ICH-GCP. Formerly known as International Conference on Harmonisation.

Investigational Medicinal Products (IMP) - means a pharmaceutical form of an active substance or placebo being tested, or used as a reference in a clinical trial. This includes a medicinal product which has a marketing authorisation but is, for the purposes of the trial -

- **(a)** used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,
- **(b)** used for an indication not included in the summary of product characteristics under the authorisation for that product, or
- **(c)** used to gain further information about the form of that product as authorised under the authorisation

King's Health Partners (KHP) - King's Health Partners Academic Health Science Centre is a pioneering collaboration between one of the King's College London (University) and three of London's most successful NHS Foundation Trusts – Guy's & St Thomas', King's College Hospital and the South London & Maudsley.

King's Health Partners Clinical Trials Office (KHP-CTO) - Established in 2006 by King's College London, Guy's & St Thomas' NHS Foundation Trust, South London and Maudsley NHS Foundation Trust and King's College Hospital NHS Foundation Trust to provide a streamlined approach for all aspects of trial administration.

KHP-CTO Standard Operating Procedures (SOPs) - "Detailed, written instructions to achieve uniformity of the performance of a specific function," SOPs are the base on which Quality Systems and Processes are conducted and monitored against.

Legal Representative – In relation to a minor or an adult unable to give informed consent by virtue of physical or mental incapacity, a person, other than a person involved in the conduct of the trial who;

(a) by virtue of their relationship with that minor or that adult is suitable to act as their legal representative for the purposes of that trial and is available and willing to do so.

(b) If there is no such person, a person, other than a person involved in the conduct of the trial, who is the doctor primarily responsible for the medical treatment provided to that adult, or a person nominated by the relevant health care provider.

Medicines & Healthcare products Regulatory Agency (MHRA) - UK Competent Authority responsible for regulation of clinical trials.

Minor – A person under the age of 16 years.

Participant Information Sheet (PIS) - 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 site.

Research & Development Dept (R&D) – NHS department responsible for confirmation of capacity and capability for all clinical research.

Research Ethics Committee (REC) – The REC that undertakes the review of the research protocol, including the content of the patient information sheet and consent form rather than just site specific approval for each centre.

Participant - An individual who consents to take part in a clinical trial. This individual may also be known as a **Subject**.

Summary of Product Characteristics (SmPC) – This reference document is produced for health professionals and details of how to use a medicinal product safely and effectively.

The Regulations - The Medicines for Human Use (Clinical Trials) Regulations 2004, transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 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. As amended from time to time.

2.0 BACKGROUND AND PURPOSE

Informed consent is defined in ICH 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 informed consent form.

This SOP describes the procedure for obtaining written informed consent from a participant in a Clinical Trial of an Investigational Medicinal Product (CTIMP) study.

The Regulations define informed consent as follows:-
“A person gives informed consent to take part in a clinical trial only if his decision:

a) is given freely after that person is informed of the nature, significance, implications and risks of the trial;

and

b) either:

i) is evidenced in writing, dated and signed, or otherwise marked, by that person so as to indicate his consent, or

ii) if the person is unable to sign or to mark a document so as to indicate his consent, is given orally in the presence of at least one witness and recorded in writing.”

The same definition also applies to the giving of informed consent by a person with parental responsibility, or a legal representative, on behalf of the trial participant.

3.0 SCOPE

This SOP applies to all investigators and research team members involved in the conduct of Clinical Trials (as defined in the Regulations) sponsored by one or more of King’s Health Partner Organisations, or clinical trials where the sponsor responsibilities are managed by the KHP-CTO, and will be followed in accordance with each Partner NHS Organisations’ local policy for consent. The informed consent process will be monitored for compliance with the Regulations and this SOP by the KHP-CTO Quality Team.

4.0 PROCEDURE

4.1 The Informed Consent Process

4.1.1 When?

The Informed Consent process can only commence when the following approvals are in place:

- Clinical Trial Authorisation from the MHRA
- REC favourable opinion
- HRA approval
- Local Site R&D confirmation of capacity and capability

The Investigator Site Initiation and greenlight process must also be complete (as per KHP-CTO SOP 13.0).

4.1.2 Who?

The Declaration of Helsinki clearly states that the person seeking informed consent will be a qualified physician: '*The **physician** should then obtain the participant's freely given informed consent, preferably in writing'* (1996 version).

ICH GCP guidelines are less clear and state that '*The **investigator, or, a person designated by the Investigator** should fully inform the participant*' (ICH GCP 4.8.5) and the written informed consent form should be signed and dated by the '***person who conducted the informed consent discussion***'.

Although ICH GCP has no legal status it is referred to in the UK Clinical Trial Regulations and should be taken into account when conducting clinical trials.

The delegation of Informed Consent to an appropriate and suitably qualified member of the research team is the responsibility of the PI; what is considered appropriate should be considered on a trial-by-trial basis, taking account of circumstances, the NHS Partner Organisation's local general Consent Policy and in accordance with Good Clinical Practice and the Declaration of Helsinki (1996).

The following is to be taken into consideration by the PI when delegating the taking of informed consent from trial participants: -

- The Ethics Committee, HRA, Sponsor and the NHS Organisation hosting the trial have approved the delegation of informed consent for the trial.
- The person taking informed consent is suitably trained and familiar with all aspects of the clinical trial as described in the latest version of the protocol approved by the REC/HRA and the Investigator's Brochure or SmPC for the clinical trial.
- The person taking informed consent have been informed of any amendments to the PIS and ICF and is working to the latest version.
- The General Medical Council (GMC) recommends that when doctors delegate the task of informed consent it is their responsibility to ensure that the person delegated is:
    - suitably trained and qualified,
    - has sufficient knowledge of the proposed investigation or treatment, and understands the risks,
    - acts in accordance with guidance as set out in GMC "Seeking Patients Consent; the ethical considerations"

Although the taking of informed consent may be delegated by the PI, each potential participant must be offered the opportunity of discussing the trial with a delegated trial Physician. In addition, a trial Physician must review the eligibility criteria and ensure that each patient meets the criteria BEFORE they are entered into the trial.

All persons obtaining consent will be clearly identified and recorded on the Authorised Site Signature and Delegation Log' within the Trial Master File or Investigator Site File.

4.2 Adults with Capacity

Consent from the participant may only be taken when all the following have occurred: -

- Copies of the PIS and Consent Form have been approved by the REC and have been printed on local hospital/departmental headed paper and the correct title and version number for the trial is clearly visible.
- Information about the trial has been provided to the participant in both an oral and written form.
- The participant has had an interview with the investigator, or another member of the investigating team, in which he/she was given the opportunity to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted.
- The participant has been informed of his/her right to withdraw from the trial at any time without being subject to any resulting detriment, by revoking his informed consent.
- The participant has been provided with a contact point where he/she may obtain further information about the trial.
- The participant has been given sufficient time to make a decision with regard to trial entry. The definition of 'sufficient time' may vary according to the nature of the trial and will be defined in the application form to the REC and approved by the REC.

A signed ***and personally dated*** (by the participant) informed consent form will be obtained from each potential participant prior to his or her involvement in the trial. Where boxes need to be initialled, the participant must complete each box.

Once all parties have signed and dated the consent form, a copy of the information sheet and consent form will be given to the participant. The original signed copy will be filed in the Investigator Site File. A further copy will be stored with the participant's health record.

The informed consent process will be appropriately documented in the participants health record.

The informed consent process does ***not*** cease once the informed consent form has been signed; the practice of giving information about the trial to participants will be an ongoing process performed by all members of the research and/or multidisciplinary team. If the protocol is amended or information becomes available that may affect the participant's willingness to continue in the trial, it may be necessary to re-consent the participant on an updated consent form. The updated PIS/Consent forms must receive approval from the REC, HRA and, if applicable, each local site R&D prior to its use. If any revision is made to the written information sheet/consent form, the entire document will be assigned a new version number/date.

If a participant is unable to read (e.g. blind, illiterate etc.), an impartial witness is required. The impartial witness must ensure that the verbal information given correlates to that written on the information sheet and must sign the consent form as witness to the process. The process for identifying a suitable witness should be as per HRA & REC guidelines. The participant is required to mark the consent form, if able.

4.3 Mentally or Physically Incapacitated Adults

Provision has been made within the Regulations for obtaining consent for participation in clinical trials for incapacitated adults. Consent can only take place when the following have occurred: -

- The participant's legal representative has had an interview with the investigator, or another member of the investigating team, in which he/she has been given the opportunity to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted.
- The legal representative has been provided with a contact point where he/she may obtain further information about the trial.
- The legal representative has been informed of the right to withdraw the participant from the trial at any time.
- The legal representative has given his/her informed consent to the participant taking part in the trial.
- The legal representative may, without the participant being subject to any resulting detriment, withdraw the participant from the trial at any time by revoking his/her informed consent.
- The participant has received information according to his/her capacity of understanding regarding the trial, its risks and its benefits.
- The explicit wish of a participant who is capable of forming an opinion and assessing the information referred to in the previous paragraph to refuse participation in, or to be withdrawn from, the clinical trial at any time is considered by the investigator.

4.4 Minors

There are a number of factors that must also be considered when seeking consent from minors:-

- The minor has received information according to his/her capacity of understanding, from staff with experience with minors, regarding the trial, its risks and its benefits.
- The explicit wish of a minor who is capable of forming an opinion and assessing the information referred to in the previous paragraph to refuse participation in, or to be withdrawn from, the clinical trial at any time is considered by the investigator.
- A person with parental responsibility for the minor or, if by reason of the emergency nature of the treatment provided as part of the trial no such person can be contacted prior to the proposed inclusion of the participant in the trial, a legal representative for the minor has had an interview with the investigator, or another member of the investigating team, in which he/she has been given the opportunity to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted.

- That person or legal representative has been provided with a contact point where he/she may obtain further information about the trial.
- That person or legal representative has been informed of the right to withdraw the minor from the trial at any time.
- That person or legal representative has given his/her informed consent to the minor taking part in the trial.
- That person with parental responsibility or the legal representative may, without the minor being subject to any resulting detriment, withdraw the minor from the trial at any time by revoking his/her informed consent.

The **HRA** online guidance on consent and participant information should be used when drafting a **PIS** and consent form within the UK. Local advice should be sought for trials being conducted outside the UK.

5.0 RELATED TEMPLATES

Not applicable

6.0 RELATED DOCUMENTS

6.1 Weblink to HRA guidance on consent and participant information including NRES Guidance paper on Informed Consent in CTIMPs: https://www.hra-decisiontools.org.uk/consent/index.html

7.0 APPROVAL and SIGNATURE

28 February 2023

Jackie Pullen
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King's Health Partners Clinical Trials Office

Date