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This page details the version history and the main changes made for each new version.
The new changes are in red font.

Version Log		
Version number and date	**Author**	**Details of significant changes**
Version 1, 27.10.10	J Pacynko	Original SOP approved by R&D Committee on 27.10.10.
Version 2, 19.01.15	J Pacynko	New wording is in red type and includes • Up-date of references and links • Up-dated consent form – Appendix 1 • Addition of section on consenting minors in emergency situations
Version 3, 27.02.19	J Pacynko	Informed consent template (Appendix 1) removed and is now Working Instruction 18.

Please note for definitions of acronyms refer to Appendix 1 of Management of SOPs. Refer to Appendix 2 of Management of SOPs for the standards to which clinical trials that investigate the safety and/or efficacy of a medicinal product are conducted.

All the R&D GCP SOPs are available at:
https://www.hey.nhs.uk/research/researchers/gcp-sops-for-hey-sponsored-ctimps/

1 Introduction, background and purpose of this SOP

1.1 This SOP describes the procedure for receiving written informed consent from a patient or healthy volunteer participating in a clinical trial involving an investigational medicinal product (CTIMP) sponsored by Hull and East Yorkshire Hospitals NHS Trust.

1.2 This SOP relates to trial subjects who are able to give informed consent themselves and also sets out the consent procedures for more vulnerable subjects (minors and incapacitated adults).

1.3 ICH GCP 1.28 defines informed consent as 'A process by which a study subject **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 subject's decision to participate. Informed consent is **documented** by means of a written, signed and dated informed consent form.'

2 Who should use this SOP

2.1 This SOP should be used by

- All research staff involved with HEY-sponsored CTIMPs – Chief/Principal Investigator, co-investigators, research nurses, clinical trial assistants, project managers, clinical trial co-ordinators, data managers, administrators etc.
- Clinical trials pharmacy staff – technicians and pharmacists.
- All HEY R&D staff who manage the sponsorship of HEY-sponsored CTIMPs.
- Research staff involved with clinical trials sponsored by an external organisation where the sponsor has no SOP for safety reporting. HEY R&D SOPs are defaulted to in this case.

2.2 It is important that this SOP is read and understood before trial staff start taking consent, but it should also be referred to if any doubt arises regarding the process of informed consent during the trial.

3 Procedures

3.1 Who should consent subjects

3.1.1 The Declaration of Helsinki (2013) states that *'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.'*

3.1.2 ICH GCP guidelines state that *'The investigator, or, a person designated by the Investigator should fully inform the subject'* (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'.*

3.1.3 Unless otherwise agreed with the R&D Department, for HEY sponsored CTIMPs, a clinical doctor who has been trained in the informed consent process for the trial and is on the Delegation Log is required to consent subjects and sign the consent form with the subject. The doctor maybe the Chief or Principal Investigator (CI or PI) or a Co-investigator.

3.1.4 The delegation of the informed consent process to a research nurse may be considered for low risk CTIMPs, taking into account the nature of the trial, and must be given a favourable opinion by the Research Ethics Committee (REC) and the Sponsor (HEY R&D).

3.2 How to delegate the informed consent process

3.2.1 If you are the Chief Investigator (CI) or Principal Investigator (PI) for a HEY-sponsored CTIMP you may delegate the informed consent process to a research nurse who is a member of the research team, after prior agreement with HEY R&D, but you remain ultimately responsible for the informed consent of subjects who take part in the trial.

3.2.2 To do this you must ensure the following criteria are met:

- The delegated person is prepared to take on this additional responsibility and feels confident to consent subjects in line with their professional organisation's guidelines.
- The delegated person has a full understanding of the trial, the potential risks/benefits and the associated disease area. They should be qualified by experience and should have received appropriate training for this trial. **All training must be documented on the Study Training Log.**
- The delegation and informed consent process has been given a favourable opinion by the REC reviewing the trial.
- The delegation of responsibility must be documented on the Delegation Log.
- The process has been approved by the Sponsor (HEY R&D).
- An effective line of communication is maintained back to the CI/PI who is ultimately the person responsible for the patient's care and for ensuring that subjects have fully understood what they are consenting to. It is expected that the CI, PI or Co-investigator is on hand during the consent process and countersigns the consent form.

3.2.3 All persons who are involved with the informed consent process must have a copy of their signed and dated CVs in the Trial Master File or Investigator Site File and must have completed the Delegation Log, which must also be signed and dated by the CI/PI, prior to consenting subjects.

3.3 Participant information sheet and the informed consent form

3.3.1 Patient information should be provided to potential trial subjects in both an oral and written form.

3.3.2 The Health Research Authority website has excellent guidance, templates and examples on how to prepare participant information sheets and consent forms at the following link: http://www.hra-decisiontools.org.uk/consent/index.html

3.3.3 For HEY sponsored CTIMPs, the R&D department's template for the Informed Consent Form will be used. The template is Working Instruction 18 saved in the ClinicalGov Y drive in Y:\Research\GCP SOPs & forms\Working instructions.

3.3.4 ICH GCP 4.8.10 describes what you should explain to the research subject during the informed consent discussion and also what should be put in the patient information sheet (or any other written information relating to the trial). The following points should be included in the patient information sheet:

- A statement that the trial involves research.
- The purpose of the trial.
- The trial treatment(s) and the possibility of random assignment to each treatment.
- The trial procedures to be followed, including all invasive procedures.
- The subject's responsibilities.
- The experimental aspects of the trial.
- Any foreseeable risks or inconveniences to the trial subject, and when applicable to an embryo, foetus or nursing infant.
- The reasonably expected benefits. If there is no clinical benefit intended, the subject must be made aware of this.
- Alternative treatments and procedure(s) that may be available and the potential benefits and risks.
- The compensation and/or treatment available to the subject in the case of any injury relating to the trial.
- The anticipated pro-rated payment, if any, to the subject for participating in the trial.
- The anticipated out of pocket expenses, if any, to the patient for participating in the trial.
- That the subject's participation in the trial is completely voluntary and that the subject can withdraw or refuse to participate, at any time, without penalty or loss of benefits to which they would otherwise be entitled and without affecting their future care.
- That records identifying the subject will be kept confidential and will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.
- That the subject/legal representative will be informed in a timely manner if any information becomes available that may be relevant to the subject's willingness to continue to participate in the trial.
- The person(s) to contact for further information regarding the trial (if possible record a 24hour phone number where the subject can receive advice out of office if required).
- The foreseeable circumstances under/or reasons under which the subject's participation in the trial may be terminated.
- The expected duration of the subject's participation in the trial.
- The approximate number of patients involved in the trial.
- And in the consent form, that the authorised representatives from the sponsor, regulatory bodies or pharmaceutical company (or other commercial company, if appropriate to the trial) will be given access to the subject's records for the purpose of verification of the trial procedures and

data collected, without violating the confidentiality of the subject. That the subject's General Practitioner will also be informed in writing of their participation in the trial. By signing the informed consent form, the subject is authorising such access.

3.4 Informed consent procedure

3.4.1 The person seeking informed consent must ensure they are completely familiar with all aspects of the clinical trial as described in the current approved version of the protocol.

3.4.2 Informed consent must be received from patients prior to any trial-related procedures being undertaken. This includes screening procedures for the trial.

3.4.3 Respect and dignity of the subject should be taken into consideration and a suitable quiet private area should be used for the consent process.

3.4.4 Subjects who potentially fulfil the eligibility criteria will be identified and approached. A verbal explanation of the trial must be given to the subject (and friends and family if appropriate), and if necessary diagrams may be used to explain the trial. Time for questions throughout the discussion must be given and questions adequately addressed.

3.4.5 The person receiving informed consent should then provide the subject with the current version of the Patient Information Sheet for the trial.

3.4.6 Subjects should be given adequate time, usually at least 24 hours, to read the information sheet and to discuss the trial with family and friends (if applicable), prior to agreeing to participate. **The subject must not be coerced to participate in the trial.**

3.4.7 If the patient is willing to take part in the trial after having had time to read the information sheet and having had any questions answered satisfactorily, then the patient should be asked to initial in the box next to each point on the consent form and sign the form. The consent form must be personally signed and dated by the subject and person receiving consent consecutively. Each person should also clearly print their name by their signature.

3.4.8 The subject should be given a copy of the signed and dated consent form. A copy of the consent form must also be filed in the subject's medical notes (casenotes). **The original signed and dated consent form must be filed in the Trial Master File or Investigator Site File.**

3.4.9 All subjects must be provided with contact details where they may obtain further information about the trial. This will either be the CI/PI's number or a contact number of a member of the trial team. If appropriate an out-of-hours contact number should be provided.

3.4.10 It is essential to consent the subject prior to any trial-related procedure and to complete both the consent form and subject's medical notes correctly. The completion of the consent form and the timing of signing of the consent form relative to trial entry and initiation of trial procedures, is subject to inspection by the MHRA.

3.4.11 At all follow-up trial visits, it must be checked at the start of the visit if the subject is willing to continue in the trial and the response must be recorded in the subject's case report form and medical notes.

3.5 Re-consenting subjects

3.5.1 The informed consent process does not end once the consent form has been signed. Should new information become available during the course of the trial which may affect a subjects decision to continue in the trial, then subjects which are ongoing in the trial should be re-consented using the amended approved patient information sheet and consent form.

3.6 Consent of children under the age of 16 Years

3.6.1 The UK Clinical Trial Regulations define a person under the age of 16 years as a 'minor' and require that an appropriate adult gives consent for the child to take part in a CTIMP.

3.6.2 For a paediatric clinical trial a REC with expertise in the consent process for minors will need to review the trial and grant a favourable opinion for the informed consent process for the trial.

3.6.3 There are a number of separate factors listed below that must be considered when taking consent from minors to participate in a CTIMP.

3.6.4 It is essential that the clinical trial relates directly to a clinical condition from which the minor suffers or is of such a nature that the trial can only be carried out on minors.

3.6.5 It is important to show that there will be some benefit for the group of patients involved in the trial and that the clinical trial is necessary to validate data obtained in other clinical trials involving persons able to give informed consent or by other research methods.

3.6.6 The clinical trial needs to be designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the disease and the minor's stage of development. Continuous monitoring throughout the trial of such risks and/or distress must take place. The interests of the minor must always prevail over the interest of science.

3.6.7 A full explanation of the trial (including the objectives, risks, inconveniences) must be given to the person with parental responsibility for the minor in order that they may provide consent for the minor to participate in the trial. If the trial involves **urgent treatment** and the parent/guardian cannot be contacted in time to provide consent, then consent from a **legal representative** can be obtained. The legal representative may be, for example, a doctor primarily responsible for medical treatment of the minor, but must not be connected with the conduct of the trial. The legal representative must receive the same full explanation of the trial so that they can provide consent to the minor taking part. A contact number for the research team must be given in order for them to obtain further information about the trial should they wish to do so.

3.6.8 The minor should be given information regarding the trial according to his/her level of understanding from staff that have experience in dealing with minors and the person receiving consent must respect their wishes.

3.6.9 The minor and parent/legal guardian for the minor (or the legal representative) must be made aware that they can withdraw from the trial at any time without any detriment to future care.

3.6.10 No incentives or financial inducements must be given except for compensation in the event of injury or loss.

3.6.11 If aged 16 or over, it is acceptable for subjects to sign their own consent form.

3.6.12 The Participant Information Sheet should be written in a language that the minor can understand. There should be different versions e.g. for under 5s, 6-12 year olds, 13-15 year olds. There should also be a version produced for the parent/guardian/legal representative.

3.6.13 If the child is deemed competent to understand the research being explained to them, it is best practice to obtain the **assent** of the child in addition to the consent of the parent/guardian. In such circumstances a signature should be obtained from both the minor and the parent/guardian on the consent form.

3.6.14 If able to do so, a minor assents, that is to say, agrees and accepts participation in the research. The parent/guardian/legal representative consents on their behalf.

3.6.15 It is important to note that, a mother automatically has parental responsibility for her child from birth. Fathers do not always have parental responsibility for their children if they are not married to the mother at the time of the birth.

3.6.16 Detailed information is available from Gov.uk – Parental rights and responsibilities.

3.7 Consent of minors in emergency situations

3.7.1 The Medicines for Human Use (Clinical Trials) Amendment Regulations 2008 made additional provision relating to trials involving minors in emergency situations.

3.7.2 Where the treatment to be given to a minor as part of the trial needs to be administered urgently, time may not allow for the written consent of a person with parental responsibility or a legal representative to be obtained first.

3.7.3 The amended Regulations allow minors to be entered into a trial prior to informed consent being obtained provided that, having regard to the nature of the trial and the particular circumstances of the case, it is necessary to take action for the purpose of the trial as a matter of urgency but it is not reasonably practicable to obtain informed consent prior to entering the subject, and the action to be taken is carried out in accordance with a procedure approved by the REC.

3.7.4 Where a minor is recruited in an emergency situation without prior informed consent, steps must be taken to seek informed consent from a person with parental responsibility or a legal representative as soon as practicable after the initial emergency has passed.

3.7.5 Where consent is withheld, the subject must be withdrawn from the trial.

3.8 Consent of subjects with communication problems or comprehension difficulties

3.8.1 The legal position is that adults must be presumed capable of taking decisions unless the opposite has been demonstrated. This applies just as much to people with learning disabilities as to any other adult. Where there are comprehension or communication difficulties then subjects must be given all appropriate help to enable them to make their own decisions e.g. using visual aids, sign language etc.

3.8.2 If a decision is taken to enrol subjects with communication problems or comprehension difficulties then investigators must have a clear plan about how these matters will be managed and documented in the consent process. For example, if the difficulties are due to visual impairment then the information sheet can be read to the potential participants and audio recorded at the same time to provide a copy for the participant to keep.

3.8.3 Where there are communication difficulties, a relative or an independent patient's advocate should be involved in the consent process. Their role is to help the prospective subject express their views. Therefore two types of information sheet may be required: one for the relative/advocate and one for the patient. The patient's information sheet should be designed to overcome or minimize some of the communication problems, for example, a pictorial information sheet. Sufficient time must be allowed for the person receiving consent to explain and discuss the trial with the subject and the relative or advocate, and for the relative or advocate to discuss with the prospective subject.

3.8.4 For the consent to be valid the research subject must always be able to communicate their decision. If the person is unable to sign or to mark the consent form so as to indicate his/her consent, then consent may be given orally in the presence of at least one witness, usually a relative or patient advocate. The role of the relative or advocate in the consent process, for example, acting as a witness or explaining the trial to the subject, must be documented in the medical records. Consent could also be video recorded to provide a complete record with a copy of the video for the participant.

3.8.5 All hospital staff that provide information and request consent from patients with communication problems or comprehension difficulties must be appropriately trained and experienced with such patients.

3.8.6 The REC and the Sponsor must agree the plan, including the delegation of responsibilities.

3.9 Consent of incapacitated adults

3.9.1 There are a number of separate factors listed below that must be considered when receiving consent from adults that lack the ability to give consent to participate in a clinical trial. More information is provided on the HRA website at the following link: http://www.hra-decisiontools.org.uk/consent/principles-ALC-EnglandandWales.html

3.9.2 For clinical trials that involve incapacitated adults, a REC with expertise in the consent process for adults lacking capacity will need to review the trial and grant a favourable opinion for the informed consent process for the trial.

3.9.3 Legally, adults must be assumed to be capable of taking decisions unless the opposite has been demonstrated for a particular decision. Where doubt exists, the CI/PI or another experienced and independent clinician should formally assess the capacity of the individual to make an informed decision about participation in a research project. You must take account of the advice on assessing capacity in the Codes of Practice that accompany the *Mental Capacity Act 2005*. This assessment and the conclusions should be recorded in the patient's medical records. A patient is deemed to lack capacity to consent or refuse only when they cannot be helped to reach their own decision with memory aids or sign language for example.

3.9.4 When making the decision about the enrolment of an adult who is unable to provide informed consent for his/herself for participation in a clinical trial it is important that the CI/PI ensures that:

3.9.5 The trial relates directly to a life-threatening or debilitating clinical condition from which the subject suffers and that there are grounds for expecting that the trial procedure/intervention to be tested will produce a benefit to the subject, outweighing the risks or producing no risks at all.

3.9.6 The clinical trial must be essential to validate data obtained in other clinical trials involving persons able to give informed consent or by other research methods.

3.9.7 The clinical trial needs to be designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the disease and the cognitive abilities of the subject and continuous monitoring throughout the trial of such risks and/or distress must take place. The interests of the subject must always prevail over the interest of science.

3.9.8 The research investigator must identify a **legal representative** who can be consulted about the involvement of the subject in the trial. If no suitable personal legal representative (e.g. relative) is available then a professional legal representative may be approached (e.g. doctor primarily responsible for medical treatment or a person nominated by the trust). However, this professional legal representative must not be connected with the conduct of the trial in any way.

3.9.9 Where a legal representative has been appointed, they must have an interview with a member of the trial team to understand the objectives, risks, inconveniences/discomforts and associated conditions for the trial and be provided with a contact number for the trial team should they wish to ask further questions about the trial. The legal representative must be informed of their right to withdraw the subject at any time resulting in no detriment to care or treatment for the subject.

3.9.10 Subjects should not be enrolled into the trial if it is contrary to a formal advance decision or any other form of statement made in advance by the subject whilst competent. This does not have to be in writing and an investigator should take reasonable steps to find out if there are any advance wishes by consulting relatives. Any patient's 'dissent' must always be respected.

3.9.11 The subject must also be given information regarding the trial according to their level of understanding. For those subjects able to form an opinion based on the information provided, their wish to participate must be respected by the person receiving consent.

3.9.12 The role of the patient's representative, their relationship to the patient and the response of the subject should be documented in the patient's medical records.

The opinion of the patient's representative about enrolment should be formally documented and a written and signed statement obtained.

3.9.13 No incentives or financial rewards must be used to influence a subject to participate (or the subject's legal representative to agree to participation on their behalf) in a trial other than provision for compensation in the event of loss or injury.

3.10 Incapacitated adults in emergency situations

3.10.1 The Medicines for Human Use (Clinical Trials) (Amendment No.2) Regulations 2006 made additional provision relating to trials involving incapacitated adults in emergency situations.

3.10.2 Where the treatment to be given to an incapacitated adult as part of the trial needs to be given urgently, time may not allow for the written consent of a legal representative to be obtained first.

3.10.3 The amendment allows incapacitated adults to be entered into a trial prior to consent being obtained from a legal representative provided that, having regard to the nature of the trial and the particular circumstances of the case, it is necessary to take action for the purpose of the trial as a matter of urgency, but it is not reasonably practicable to obtain informed consent prior to entering the subject, and the action to be taken is carried out in accordance with a procedure approved by the REC.

3.10.4 Where an incapacitated adult is recruited in an emergency situation without prior informed consent, steps must be taken to seek informed consent either from the subject (if capacity has been recovered) or from a legal representative as soon as practicable after the initial emergency has passed. See above for the process of finding an appropriate legal representative.

3.10.5 Where consent is withheld, the subject must be withdrawn from the trial.

4 Related Documents

The Medicines for Human Use (Clinical Trials) Regulations 2004 Statutory Instrument 2006/1031, implemented on the 1st May 2004 as amended

ICH Harmonised Tripartite Guideline for Good Clinical Practice (1996) and E6 (R2) (2017)

The Mental Capacity Act 2005

Code of Practice for Mental Capacity Act 2005

Declaration of Helsinki (2013 Version)

UK Policy Framework for Health and Social Care Research (2017)

5 Implementation

- Implementation of this SOP will conform to the process outlined in R&D SOP 01 Management of SOPs.