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Informed Consent for Research

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1.0	14th Jan 2011	Restructure of SOP. 2 yearly review. Training requirements. Cross referencing SOPs	Gemma Earl
2.0	05th Sep 2013	Training section updated and minor typos updated	Gemma Earl
3.0	05th Jan 2017	SOP Training Matrix and removal of appendices 1 & 2	Gemma Earl

1. PURPOSE

This Standard Operating Procedure (SOP) describes the process for obtaining informed consent from a study subject to participate in a Clinical Trial of an Investigational Medicinal Product (CTIMP) or any other research. It outlines the informed consent procedures for adult subjects with capacity who are able to give informed consent, informed consent procedures for more vulnerable subjects (minors and incapacitated adults) and informed consent in the emergency setting.

2. INTRODUCTION

Informed Consent is the process by which a subject voluntarily confirms his/her willingness to participate in a particular study, having been informed of all aspects of the trial that are relevant to their decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.

Informed consent is a three step process which involves:

1. The giving of information
2. The discussion and clarification of the information and finally
3. Receiving the subject's written consent

Informed consent must be given by each participant or from a person with parental responsibility or a legal representative. Informed consent must be in place prior to any enrolment into a clinical trial. This includes any aspect of the trial including screening tests for example. Only in exceptional circumstances can enrolment into a study take place prior to informed consent e.g. if urgent treatment needs to be provided or under the Mental Capacity Act in non-CTIMPs (non-Clinical Trials of Investigational Products).

3.0 Responsibilities

The Principal Investigator (PI) has overall responsibility for ensuring informed consent is obtained from all research participants on the study.

The PI or delegated individual is responsible for ensuring the participant is fully informed and for providing written evidence of this process.

The CI (Chief Investigator) and the sponsor are responsible for determining whether amendments to research studies require participants to be re-consented and, if applicable, the timelines for this to be undertaken.

4.0 Procedure

4.1 The Giving of Information

A Participant Information Sheet (PIS) should be given to the potential participant to read and understand. The PIS should inform the potential participant of the nature, significance, implications and risks of taking part in the trial. This document will be approved by the REC (research ethics committee) as part of the favourable opinion. Templates for PIS's can be found on the Health Research Authority (HRA) website and guidance can be sought from the R&D Department. For all studies where BSUH is the proposed sponsor, the PIS along with the Informed Consent Form (ICF), protocol and all other associated documents will be reviewed by the Sponsor prior to submission of the initial application to the REC (see SOP/RD/008 Sponsorship Approval). The Sponsor will ensure that the information given in the PIS is consistent

with the protocol and for CTIMPs, the Investigator Brochure/Summary of Product Characteristics.
Subjects who potentially fulfil the inclusion/exclusion criteria will be identified and approached according to the procedure given a favourable opinion by the REC. A verbal explanation of the study must be given to the potential participant (and friends and family if appropriate) as well as providing the potential participant with the current PIS.

4.2 The Discussion and Clarification of the Information

The participant giving consent must have had a detailed discussion with the investigator or delegated individual about the trial and the opportunity to ask any questions and have them answered satisfactorily. The participant should not be coerced to participate, and should be reassured that declining to enter the study will not affect their care.
If necessary, diagrams should be used to explain the study. Time for questions throughout the discussion must be given and questions adequately addressed.

When describing the study the person seeking consent should explain:

- That the trial involves research.
- Those aspects of the trial which are experimental.
- What the purpose of the study is and any background information that may be relevant.
- Why the subject has been approached and that confidentiality will be maintained throughout the study, should they decide to participate.
- Details of the study design and details of any drugs used (including any known safety profiles). If there is a placebo arm or randomisation involved then these procedures should be explained.
- 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. It should be explained where the subject will be seen and by whom.
- All trial procedures to be followed, including all invasive procedures.
- The potential benefits and risks of participation in the study, including, when applicable, to an embryo, foetus, or nursing infant. Where there is no intended clinical benefit to the subject, the subject should be aware of this.
- The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.
- The availability of compensation should something go wrong.
- That the subject enters the study voluntarily and can withdraw at any time without any prejudice to them or their future care. Similarly if the Investigator feels that the study medication is not suiting the subject that they have the right to withdraw them from the study in the interests of their safety.
- That a detailed discussion of the subject's medical history (including disclosure of all medication they are taking) will be required should they agree to participate.

- If there are any payments made for participation in the study or for out of pocket expenses.
- The responsibilities of the subject if they choose to take part, particularly if the study duration is lengthy.
- That giving informed consent does not necessarily mean the subject will be enrolled into the study if it is discovered they do not meet the inclusion/exclusion criteria e.g. a study specific diagnostic test.
- That the monitor(s), auditor(s), REC and regulatory authorities 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.
- That if the results of the trial are published, the subject's identity will remain confidential.
- That the subject 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.
- 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.

Once the above information has been verbally discussed with the subject, the subject has read and understood the current PIS and the participant is willing to take part, informed consent must be evidenced in writing.

4.3 Receiving the subject's written consent

The application form submitted to REC must set out a general policy for the trial in terms of what types of personnel will be consenting participants.
The delegation of Informed Consent to an appropriate, suitably qualified member of the research team should be considered on a study-by-study basis. If staff other than the Principal Investigator (PI) are to accept responsibility for the informed consent process, it is important the following criteria are met:

- S/He is prepared to take on this additional responsibility AND feels confident to seek informed consent in line with their professional organisational guidelines.
- S/He has a full understanding of the study, potential risks/benefits and the associated disease area. They should have undertaken appropriate training in the specific clinical trial as well as in obtaining informed consent. All training must be documented.
- This delegation of the task should be documented on the Delegation Log and signed and dated by the PI prior to these tasks being undertaken.
- The process has been approved by the relevant Research Ethics Committee (REC).
- An effective line of communication is maintained back to the PI who is the person ultimately responsible for the subject's care with the Trust.

It is ultimately the responsibility of the PI to ensure that subjects have fully understood what they are consenting to. Where taking consent is a delegated task of someone who is not a medically qualified doctor, it is expected that a medically

qualified doctor who is part of the trial team will be readily available during or following the consent process if required.

The time given for the participant to consider whether they would like to take part in the trial will be specified in the approved REC application. This should include time to consult with family and friends if applicable.
Informed consent must be evidence in writing on an informed consent form (ICF). There are templates on the HRA website and advice can be sought from the R&D department.

The Informed Consent Form must include the following:

- It should be on departmental headed paper
- The correct title and version number for the study should be clearly visible and relate to the written information sheet given to the participant.
- A statement to say the participant has had the study explained to them. The risks, benefits and alternative treatments have been discussed and all the subject's questions have been satisfactorily answered.
- A statement that their participation is voluntary and they are free to withdraw at any time, without the loss of any treatment to which they would otherwise have been entitled.
- A statement that their medical records may be reviewed by authorised personnel and that confidentiality will be maintained at all times.

Depending on the study it may be necessary to include statements regarding additional invasive tests or samples required for study purposes only, consent to use of audio/video-taping or for example transfer of data or samples to countries with less data protection.

The participant should initial the box next to each statement on the ICF. There should be a process to ensure the appropriate management of any statements that are not consented to. The participant must also sign, print their name and date the ICF themselves. Where the person giving consent is unable to sign or mark a document to indicate consent, they may give consent orally in the presence of at least one independent witness, who must then sign the consent form as evidence that the information was accurately explained to and understood by the participant and that the participant had verbally confirmed willingness to take part in the research study. Details of the witness should also be documented.

In addition to the participant, the informed consent form must be personally signed, dated and name printed in indelible pen by the PI or delegated member of the research team seeking consent.

Once all parties have signed the written informed consent form, the participant should receive a copy, together with a participant information sheet and any other written information provided to the participants. A copy of the above must be placed in the participant's medical notes and the original kept by the study team in the investigator site file.

A record of the informed consent process must be recorded in the medical notes by the person receiving consent. The entry in the medical notes must include as a minimum the following:

- Details of the study name and a unique identifying reference for the study that the participant has consented to e.g. IRAS number.
- Confirmation that the patient is eligible for study participation
- The version number and date of the Participant Information Sheet and Consent Form that the participant was given.
- The time the patient was given the PIS and the time that elapsed before consent was obtained.
- The date consent received.
- Name, date and signature of person receiving consent.
- Details of anyone else present during the consent process; e.g. research nurse or family members.
- Confirmation that the participant was provided with all information as described in the section above in order to make an informed choice to participate in the trial with adequate time to make this decision.

Emergency out of hours contact details should be given to the participant at the time of consent if deemed appropriate for the study by the Sponsor. The giving of this information should be documented. The out of hours contact should be tested where appropriate before the study commences and periodically to ensure the details are correct and the contact is adequate.

A research sticker should be attached to the inside cover of the patient notes to ensure the patient's notes are not destroyed prematurely (see SOPRD004 Archiving).

4.4 Ongoing Procedure throughout the study

Informed consent is an ongoing process and does not end once the informed consent form has been signed. At each contact with the participant, the research team should be re-confirming that the participant is happy to continue in the study. This discussion should be documented in the hospital notes as evidence. The practice of giving information about the study to participants should be an ongoing process performed by all members of the research team and any associated healthcare professionals. This is particularly important if protocol amendments are introduced, or if important new information that may be relevant to the participant's willingness to continue taking part in the study is discovered.

4.5 Amendments

If there are changes to the trial design, the medication used or risks associated with trial participation, then the participants may be required to re-consent to the trial. Re-consenting of participants should be considered by both the Investigator and the sponsor and a measured approach to determine which participants should be re-consented should be applied. Participants should be re-consented in a timely manner. It is generally accepted that participants are re-consented at the next visit

but investigators and the sponsor should also consider contacting subjects to arrange an unscheduled visit depending on the new information that has become available. For urgent safety measures, please refer to SOP/RD/016 Amendments, Urgent Safety Measures and Temporary Halt of Trial.

4.6 INFORMED CONSENT OF MINORS

4.6.1 CTIMPs

A minor is defined as a person under the age of 16 years. The inclusion of minors in CTIMPs is governed by the Medicines for Human Use (Clinical Trials) Regulations 2004. Special protection should be given to minors with regard to inclusion into clinical trials. Minors should not be included in clinical trials if the same results can be obtained using persons capable of giving consent. The minor's parent or person with parental responsibility should always be approached if available. If a parent or person with parental responsibility cannot be contacted before the proposed trial inclusion of the minor by reason of the emergency nature of the treatment provided, a personal legal representative can be approached. The personal legal representative must not be connected to the conduct of the trial and must be suitable to act as a legal representative by virtue of their relationship with the minor. A professional legal representative may be approached if there is no suitable person to act as personal legal representative for the minor. The professional legal representative should not be connected to the conduct of the trial and should either be the doctor responsible for the medical treatment of the minor or a doctor nominated by the Trust.

When seeking consent from the parent/person with parental responsibility or legal representative the process should include the procedure outlined in section 4.1-4.4 in this SOP. It addition to that:

- The minor should receive information, according to his/her capacity of understanding about the trial and its risks and benefits.
- This information must be given by members of the research team with experience of communicating with minors.
- The investigator must consider the explicit wish of a minor capable of forming an opinion and assessing the information provided. This applies both to the wish of a minor to refuse to take part, or to withdraw from the trial at any time.
- No incentives or financial inducements should be given either to the minor or to the parent or legal representative.
- The clinical trial must relate directly to a condition from which the minor suffers or is a trial that can only be carried out on minors.
- It should be shown that there is some direct benefit for the group of patients involved in the trial. The 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 study of such risks and/or distress must take place
- The trial should be necessary to validate data obtained (a) in other clinical trials involving persons able to give informed consent, or (b) by other research methods.

If the child turns 16 years of age during the course of the trial, then they should be re-consented to the study as an adult.

4.6.1.1 Emergency Situations

The Medicines for Human Use (Clinical Trials) and Blood Safety and Quality Amendment Regulations 2008 made additional provision relating to involvement of minors in clinical trials in an emergency setting.

Where trial treatment needs to be given to minor immediately, there may not be time to obtain consent from the parent or legal representative. The amendment allows for minors to be entered into a trial before written informed consent is obtained provided that it is not reasonably practicable to obtain informed consent prior to trial treatment and that the action taken is in line with procedure given a favourable opinion by the ethics committee. Steps must be taken as soon as is practicable to obtain consent from the parent/person with parental responsibility or legal representative once the immediate emergency has passed. If consent is withdrawn, the minor must be withdrawn from the trial.

4.6.2 Non CTIMPs

Consent to participate in a non-CTIMP study can be given by a *Gillick* competent child, or if the child is not competent, by a person with parental responsibility for the child.

If the child has the maturity, understanding and is capable of making reasonable assessment of the risks and benefits of the study participation, then consent can be given by the minor. If a competent child consents to taking part in research, a parent cannot override that consent.

Further guidance is available on the National Research Ethics Committee's website (www.nres.nhs.uk). The NRES guideline makes specific recommendations on the type of information which may be provided for different age groups and different levels of understanding. The PIS should be written in a language that the minor can understand e.g. under 5's, 6-10 year olds, 11-15 years olds and over 16, if applicable.

4.7 INCAPACITATED ADULTS

The inclusion of incapacitated adults into research studies is given special protection. CTIMPs are governed by the Medicine for Human Use (Clinical Trials) Regulations 2004. Non-CTIMPs are governed by the Mental Capacity Act 2005.

The investigator and other research team members involved are responsible for assessing decision-making capacity of potential participants over 16 years of age. The assessment of capacity must be documented in the hospital notes.

4.7.1 CTIMPs

The inclusion of incapacitated adults in CTIMPs is governed by the Medicines for Human Use (Clinical Trials) Regulations 2004. Those who are incapable of providing legal consent for inclusion in clinical trials should be given special protection. Such persons should not be included in clinical trials if the same results can be obtained using persons capable of giving consent. Legal representatives must be approached to obtained consent on behalf of the patient. Legal representatives must not be involved in the conduct of the trial. A personal legal representative should be suitable to act as legal representative by virtue of their relationship with the adult and should be approached first if willing and available.

In the absence of a personal legal representative, a professional legal representative may be approached. The professional legal representative should be either the doctor responsible for the medical treatment of the potential participant who is not involved in the clinical trial or another nominated independent member of staff..

Medicinal products for a trial may be administered to all such individuals only where there are grounds for assuming that the direct benefit to the patient outweighs the risks.

If a capable adult gives informed consent and then subsequently loses capacity with regard to decision making, then the consent previously remains valid.

If a capable adult refuses informed consent and then subsequently loses capacity with regard to decision making, then the refusal to consent previously remains valid and consent cannot be sought from a legal representative.

When seeking consent from the legal representative the process should include the procedure outlined in section 4.1-4.4 in this SOP. It addition to that:

- The subject has received information, according to his or her capacity of understanding, about the trial and its risks and benefits.
- The investigator must consider the explicit wish of a subject capable of forming an opinion and assessing the information provided. This applies both to the wish of a subject to refuse to take part, or to withdraw from the trial at any time.
- There are grounds for expecting that administering the medicinal product to be tested in the trial will produce a benefit.
- The trial is essential to validate data obtained (a) in other clinical trials involving persons able to give informed consent, or (b) by other research methods.
- The clinical trial relates directly to a life-threatening or debilitating clinical condition from which the subject suffers.

4.7.1.1 Emergency Situations

The Medicines for Human Use (Clinical Trials) Regulations 2006 Amendment 2 made additional provision relating to trials involved incapacitated adults in emergency situations.

Where trial treatment needs to be given to an incapacitated adult immediately, there may not be time to obtain consent from a legal representative. The amendment allows for adults lacking capacity to be entered into a trial before written informed consent is obtained provided that it is not reasonably practicable to obtain informed consent prior to trial treatment and that the action taken is in line with procedure given a favourable opinion by the ethics committee. Steps must be taken as soon as is practicable to obtain consent from the subject (if capacity is regained) or the legal representative once the immediate emergency has passed. If consent is withdrawn, the subject must be withdrawn from the trial.

4.7.2 Non-CTIMPs

Non-CTIMPs are governed by the Mental Capacity Act 2005. Those who lack capacity can be invited to participate in clinical trials if the research has been approved by a research ethics committee, the researcher considers the views of carers and other relevant people, the research treats the person's interests as more important than those of science and society and the researcher respects any advance decisions or expressed preferences of a person who lacks capacity. The opinion of a consultee, who is involved in the patients care or has an interest in the patient's welfare should be sought for inclusion in the study. A personal consultee may be a family member or attorney acting under the Legal Power of Attorney. If a personal consultee cannot be consulted, the researcher must find someone not connected to the research who can fulfil the role of a nominated consultee. This could be an independent mental capacity advocate. The patient's wishes and feelings should be considered by the consultee and the patient should be helped as far as possible to be involved in the decision to participate in a research study. If the consultee says that the person who lacks capacity would not have wanted to take part or continue to take part in the research study, then the subject must not be involved in the research.

If the adult lacking capacity shows any sign of resistance or indicates in any way that they do not want to participate in the research then they must be withdrawn immediately, unless withdrawal of any treatment as part of the research would impose a significant risk to the subjects health. It is important to note that consent cannot be obtained from a consultee rather that , advice is sought from them.

In an emergency, if it is not possible to consult with a consultee in sufficient time, then the researcher must obtain agreement from an independent registered medical practitioner or comply with any other requirement of the REC.

If an adult loses capacity after consenting to a study then the subject should be withdrawn unless ethical favourable opinion has been given for the adult to remain on the study.

5.0 Training

For nurses, allied healthcare professionals and any other non-medics consenting patients to research studies, who are not experienced in receiving consent, will undertake the BSUH Informed Consent Competency Training. This will be completed and signed off prior to the role being undertaken.

For medics, this is a 'read and understand' SOP. To evidence that you have read and understood this SOP, please complete the SOP Training Matrix.

Please note that the R&D department discourages the retention of hard copies of SOPs and can only guarantee that the most up-to-date version is on the Trust website.

6.0 Cross Referenced SOPs

SOP/RD/016 Amendments, Urgent Safety Measures and Temporary Halt of Trial
SOP/RD/008 Sponsorship Approval

7.0 References

The Medicines for Human Use (Clinical Trials) Regulations 2004 as amended 2006 (amendment no 2), 2008 (Blood Safety and Quality Amendment)
Mental Capacity Act 2005
ICH GCP section 4.8 Informed Consent of Trial Subjects
National Patient Safety Agency: National Research Ethics Service 'Information Sheets and Consent Forms: Guidance for Researchers and Reviewers', March 2011
NHS R&D Forum 'A Simple Guide to the Mental Capacity Act 2005 in Relation to Research', version 2, 26/02/2008
NSPCC Fact Sheet 'Gillick Competency and Fraser Guidelines' July 2012
'Informed Consent in Clinical Trials' CT Regulations, version 3 01-May-2008