

## The Leeds Teaching Hospitals NHS Trust

### Department of Research & Development

#### Obtaining Written Consent from Subjects Taking Part in Research

##### 1. Introduction

This information summarises the requirements for informed consent of participants in all research studies, with emphasis in clinical trials of investigational medicinal products (CTIMPs).

Please note the provisions relating to giving informed consent on behalf of **minors and adults who are unable to consent for themselves** (referred to in this note as “incapable adults”), including the role and responsibilities of **legal representatives**.

In obtaining and documenting informed consent, the Principal Investigator is responsible for ensuring that they and members of their research team comply with the applicable UK Regulatory requirements and should adhere to GCP and to the ethical principles that have their origins in the Declaration of Helsinki.

Any written information and consent form provided to subjects must have ethical approval / favourable opinion. The information / consent document should be revised when new important information becomes available that may be relevant to the subject's consent. Any revised information / consent document, should receive ethical approval / favourable opinion in advance of its use.

The language used in the information / consent documents should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and where applicable, an impartial witness.

***Prior to commencement of any study related procedures / investigations, the subject (or their legally acceptable representative) must personally sign and date the consent form as must the person who conducted the informed consent discussion.***

##### 2. Informed Consent

Can be defined as:

*A person gives informed consent to take part in a research study only if their decision:*

- (a) is given freely after that person is informed of the nature, significance, implications and risks of the trial; and either:*
  - (i) is evidenced in writing, dated and signed, or otherwise marked, by that person so as to indicate their consent, or*
  - (ii) if the person is unable to sign or to mark a document so as to indicate their consent, is given orally in the presence of at least one witness and recorded in writing.*

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

##### 3. Contents of the patient information sheet and consent form

The following should be included in all patient information sheets

- i. That the study involves research
- ii. The purpose of the study.
- iii. The approximate number of subjects involved in the study.

- iv. The study treatments and probability of random assignment to each treatment.
- v. Study procedures to be followed.
- vi. The subject's responsibilities and expected duration in the study.
- vii. Aspects of the study that are experimental.
- viii. Reasonable foreseeable risks, inconvenience to the subject and when applicable, to the embryo, fetus or nursing infant.
- ix. Reasonable expected benefits. If there is no intended benefit to the subject, the subject should be made aware of this.
- x. Any alternative procedure / treatment that may be available and their risks / benefits.
- xi. Compensation or treatment available in the event of study related injury.
- xii. Prorated payment the subject may receive, if any.
- xiii. Anticipated expenses that may be paid to the subject, if any.
- xiv. The subject's participation is voluntary and that they may refuse to take part or withdraw at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
- xv. That monitors, the ethics committee, sponsor and regulatory agencies will be granted direct access to the subjects medical notes for verification of study procedures / date, without violating the confidentiality of the subject and that by signing the consent form, the subject or the subject's legally acceptable representative is authorising such access.
- xvi. That records identifying the subject will be kept confidential, according to local applicable laws / regulations and will not be made publicly available. If the results of the study are published, the subject's identity will remain confidential.
- xvii. Foreseeable circumstances under which the subject's participation in the study may be terminated
- xviii. Any new information that becomes available during the course of the study that may be relevant to the subject's willingness to continue in the study, will be made available in a timely manner.
- xix. Contact details for further information regarding the study.

The patient information sheet should be printed out on letter headed paper of the participating site.

A version number and date should be used to ensure a clear audit trail of all approved documents

The following should be included on the consent form:

1. The study title
2. Space for the patient's name and date of birth or study number and a centre number (if multi-centre study).
3. Space for the subject or their legally acceptable representative, the person providing the consent and any impartial witness (if applicable) to write their full name, signature and date.
4. Additional comments, to which the subject adds their initials to:
  - I understand that I have read and understood the information sheet, version date & number for the above study and have had the opportunity to ask questions.
  - I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason, without my medical care being affected.
  - I understand that: (1) study monitors (2) the independent ethics committee reviewing this study (3) the sponsor (4) the regulatory authority will need permission to look at my health records, in respect to this study, even if I withdraw. I agree to this access.
  - If applicable where study data may be sent out of the UK - I consent to the collection, processing, reporting and transfer within and outside Europe of my personal and sensitive data for healthcare and/or medical research purposes
  - I agree to take part in the study
5. Version number and date of the consent form.

#### 4. Capable Adults

The following conditions apply to the giving of informed consent by a capable adult:

1. *The subject has had an interview with the investigator, or another member of the investigating team, in which they have been given the opportunity to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted.*
2. *The subject has been informed of their right to withdraw from the trial at any time.*
3. *The subject has given their informed consent to taking part in the trial.*
4. *The subject may, without being subject to any resulting detriment, withdraw from the clinical trial at any time by revoking their informed consent.*
5. *The subject has been provided with a contact point where they may obtain further information about the trial.*

If a capable adult gives informed consent to take part in a CTIMP in accordance with these conditions, and subsequently becomes unable to give informed consent by virtue of physical or mental incapacity, the consent previously given when capable remains legally valid.

If a capable adult refuses informed consent, and subsequently becomes unable to give informed consent, the refusal is legally binding. He or she cannot be entered into the trial by seeking consent from a legal representative.

#### 5. Minors

The following guidance applies to England, Wales, Scotland and Northern Ireland without distinction.

A minor is a person under the age of 16 years.

Table 1 prescribes a hierarchy for determining who should be approached to give informed consent on behalf of a minor prior to their inclusion in the trial. The provisions for informed consent by a legal representative only apply in the case of **emergency treatment** where no person with parental responsibility can be contacted prior to the proposed inclusion of the minor.

	<i>Person who may give consent</i>	<i>Definition</i>	<i>Commentary</i>
1.	Parent	A parent or person with parental responsibility.	Should always be approached if available.
2.	Personal legal representative	A person not connected with the conduct of the trial who is:	May be approached if no person with parental responsibility can be contacted prior to the proposed

		(a) suitable to act as the legal representative by virtue of their relationship with the minor, <u>and</u>  (b) available and willing to do so.	inclusion of the minor, by reason of the emergency nature of the treatment provided as part of the trial.
3.	Professional legal representative	A person nominated by the relevant health care provider (e.g. an acute NHS Trust or Health Board) who is not connected with the conduct of the trial.	May be approached if no person suitable to act as a personal legal representative is available. Informed consent must be given before the minor is entered into the trial.

All the conditions and principles listed in Annex A must be satisfied if a minor is to be included in a clinical trial. They relate mainly to the informed consent procedure.

## 6. Incapable Adults

Is defined as: “an adult unable by virtue of physical or mental incapacity to give informed consent”.

Table 2 sets out the hierarchy prescribed for determining what type of legal representative should be approached to give informed consent on behalf of an incapable adult prior to inclusion of the subject in the trial. The provisions in England, Wales and Northern Ireland differ from those in Scotland.

<b>Table 2: Hierarchy of informed consent for an incapable adult</b>	
<b><i>England, Wales and Northern Ireland</i></b>	<b><i>Scotland</i></b>
<p><i>1. Personal legal representative</i></p> <p>A person not connected with the conduct of the trial who is:</p> <p>(a) suitable to act as the legal representative by virtue of their relationship with the adult, <u>and</u></p> <p>(b) available and willing to do so.</p>	<p><i>1. Personal legal representative</i></p> <p>1A. Any guardian or welfare attorney who has power to consent to the adult’s participation in research.</p> <p>1B. If there is no such person, the adult’s nearest relative as defined in section 87(1) of the Adults with Incapacity (Scotland) Act 2000.</p>
<p><i>2. Professional legal representative</i></p> <p>A person not connected with the conduct of the trial</p>	<p><i>2. Professional legal representative</i></p> <p>A person not connected with the conduct of the</p>

<p>who is:</p> <p>(a) the doctor primarily responsible for the adult's medical treatment, or</p> <p>(b) a person nominated by the relevant health care provider (e.g. an acute NHS Trust or Health Board).</p> <p>A professional legal representative may be approached if no suitable personal legal representative is available.</p>	<p>trial who is:</p> <p>(a) the doctor primarily responsible for the adult's medical treatment, or</p> <p>(b) a person nominated by the relevant health care provider.</p> <p>A professional legal representative may be approached if it is not reasonably practicable to contact either 1A or 1B before the decision to enter the adult into the trial is made. Informed consent must be given before the subject is entered into the trial.</p>
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All the conditions and principles listed in Annex B must be satisfied if an incapable adult is to be included in a clinical trial. They relate mainly to the justification for inclusion of incapable adults in the trial and to the informed consent procedure.

## 7. Legal Representatives

Under the UK Regulations, the definition depends on whether the subject is a minor or an adult with incapacity. The definition also varies where the subject is an adult with incapacity in Scotland.

Common to the definition of the legal representative in any scenario is that the individual concerned must not be "a person connected with the conduct of the trial". This is defined in the UK Regulations as:

- (a) the sponsor of the trial,
- (b) a person employed or engaged by, or acting under arrangements with, the sponsor and who undertakes activities connected with the management of the trial,
- (c) an investigator for the trial,
- (d) a health care professional who is a member of an investigator's team for the purposes of the trial, or
- (e) a person who provides health care under the direction or control of a person referred to in paragraphs (c) and (d) above, whether in the course of the trial or otherwise.

## 8. Responsibilities of the ethics committee in studies involving all subject, especially minors or incapable adults

An application to an ethics committee must include:

- (a) The procedures for obtaining informed consent
- (b) A copy of all written information to be given to a potential subject or their legal representative prior to seeking informed consent, and
- (c) A copy of the form to be used to record consent.

The ethics committee that reviews a clinical trial (referred to in this note as "the main REC") must consider various matters before giving its opinion. These include:

- (a) The adequacy and completeness of the written information to be given, the procedures to be followed, for the purpose of obtaining informed consent to the subjects' participation in the trial.
- (b) If the subjects are to include incapable adults, whether the research is justified having regard to the conditions and principles specified in Annex B.

If the main REC does not have a member with suitable expertise, it must obtain expert advice before giving its opinion on a clinical trial involving minors or incapable adults.

In the case of a minor, where the REC does not have a member with professional expertise in paediatric care, it must obtain advice on the clinical, ethical and psychosocial problems that may arise in relation to the trial.

In the case of an incapable adult, where the REC does not have a member with professional expertise in:

- (a) the treatment of the disease to which the trial relates *and*
- (b) the treatment of the patient population suffering that disease

It must obtain advice on the clinical, ethical and psychosocial problems in the field of that disease and patient population that may arise in relation to the trial.

Procedures for consulting expert referees are set out in section 2 of the COREC Standard Operating Procedures for Research Ethics Committees.

## **9. Annex A - Conditions and principles which apply to the inclusion of a minor in a clinical trial**

### **Conditions**

1. The parent or legal representative has had an interview with the investigator, or another member of the investigating team, in which opportunity has been given to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted.
2. The parent or legal representative has been provided with a contact point where further information about the trial may be obtained.
3. The parent or legal representative has been informed of the right to withdraw the minor from the trial at any time.
4. The parent or legal representative has given informed consent to the minor taking part in the trial.
5. The parent or legal representative may, without the minor being subject to any resulting detriment, withdraw the minor from the trial at any time by revoking the informed consent.
6. The minor has received information, according to his or her capacity of understanding, about the trial and its risks and benefits. The information must be given by staff with experience with minors.
7. 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.
8. No incentives or financial inducements are given either to the minor or to the parent or legal representative, except the provision of compensation for injury or loss.
9. The clinical trial relates directly to a condition from which the minor suffers or is of such a nature that it can only be carried out on minors.
10. Some direct benefit for the group of patients involved in the trial is to be obtained from the trial.
11. The trial is necessary to validate data obtained (a) in other clinical trials involving persons able to give informed consent, or (b) by other research methods.
12. The corresponding scientific guidelines of the European Medicines Agency (EMA) are followed.

## Principles

13. Informed consent by a parent or legal representative shall represent the minor's presumed will.
14. The trial has been designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the disease and the minor's stage of development.
15. The risk threshold and the degree of distress have to be specially defined and constantly monitored.
16. The interests of the patient always prevail over those of science and society.

## 10. Annex B - Conditions and principles which apply to the inclusion of an incapable adult in a clinical trial

1. The legal representative has had an interview with the investigator, or another member of the investigating team, in which opportunity has been given to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted.
2. The legal representative has been provided with a contact point where further information about the trial may be obtained.
3. The legal representative has been informed of the right to withdraw the subject from the trial at any time.
4. The legal representative has given informed consent to the subject taking part in the trial.
5. The legal representative may, without the subject being subject to any resulting detriment, withdraw the subject from the trial at any time by revoking the informed consent.
6. The subject has received information, according to his or her capacity of understanding, about the trial and its risks and benefits.
7. 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.
8. No incentives or financial inducements are given either to the subject or to the legal representative, except the provision of compensation for injury or loss.
9. There are grounds for expecting that administering the medicinal product to be tested in the trial will produce a benefit to the subject outweighing the risks or produce no risk at all.
10. 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.
11. The clinical trial relates directly to a life-threatening or debilitating clinical condition from which the subject suffers.

## Principles

12. Informed consent given by a legal representative shall represent the presumed will of an incapacitated adult.
13. The trial has been designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the disease and the cognitive abilities of the patient.
14. The risk threshold and the degree of distress have to be specially defined and constantly monitored.
15. The interests of the patient always prevail over those of science and society.

## 11. Special Notes

Subjects / patients who are incapable of giving legal consent to clinical trials should be given special protection. Such persons may not be included in clinical trials if the same results can be obtained using persons capable of giving consent. Normally these persons should be included in clinical trials only when there are grounds for expecting that the administering of the medicinal product would be of direct benefit to the patient, thereby outweighing the risks. However, there is a need for clinical trials involving children to improve the treatment available to them. Children represent a vulnerable population with developmental, physiological and psychological differences from adults, which make age- and development-related research important for their benefit. Medicinal products, including vaccines, for children need to be tested scientifically before widespread use. This can only be achieved by ensuring

that medicinal products which are likely to be of significant value for children are fully studied. The clinical trials for this purpose should be carried out under conditions affording the best possible protection for the subjects. Criteria for the protection of children in clinical trials therefore need to be laid down.

In the case of other persons incapable of giving their consent, such as persons with dementia, psychiatric patients, etc, inclusion in clinical trials in such cases should be on an even more restrictive basis. Medicinal products for 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. Moreover, in such cases the written consent of the patient's legal representative, given in co-operation with the treating doctor, is necessary before participation in any such clinical trial.