Header Boxes

The short title of the research

- The program automatically uses this to create a “header” throughout the form. The applicant should include a version number as part of the short title to help the identification of documentation approved and the future monitoring of the application.

- Use this title consistently in all information sheets and consent forms for research participants or others giving consent on their behalf. It must be sufficiently detailed to make clear to participants what the research is about. If acronyms are used the full title should explain them.

Submission date

- Insert the date on which you intend to submit a particular application where requested.

- For the REC application, the submission date should be agreed with the NRES Central Allocation System or the REC office when you book the application.

PART A Core study information

1. ADMINISTRATIVE DETAILS

Question A1 Title of the research

- The full title should be consistent with that on any documents submitted for regulatory purposes, e.g. to the Medicines and Healthcare products Regulatory Agency (MHRA).

Question A2 and A2-1 Student research

- In most cases, it is expected that where projects are undertaken by a student in
fulfilment of educational qualifications below doctoral level, the academic supervisor will take on the role of Chief Investigator. Where acting as the Chief Investigator, the academic supervisor should sign both the Chief Investigator and supervisor declarations.

- It is normally expected that a doctoral student undertaking a project will be named as the Chief Investigator rather than the academic supervisor.

- These guidelines are flexible, depending on the circumstances. For more details see the guidance on student projects on the Help page. [insert link to Help – Other IRAS guidance]

- A copy of a current CV for the student (maximum 2 pages of A4) must be submitted with the application.

Additional guidance for applicants to the Social Care REC

- Student research within the field of social care should ordinarily be reviewed by a University REC, rather than the Social Care REC. If such review is not available to the applicant, they are requested to contact the Social Care REC coordinator at the Social Care Institute of Excellence (SCIE) (0207 089 6840).

Question A3 Chief Investigator (CI)

- This is the person designated as taking overall responsibility within the team of researchers for the design, conduct and reporting of the study.

- For research within the responsibilities of the UK Health Departments, including social care, the responsibilities of Chief Investigators are described in the Research Governance Frameworks for health and social care published in each country (RGF). These are available at:

  - [http://www.sehd.scot.nhs.uk/cso/](http://www.sehd.scot.nhs.uk/cso/)  (Scotland)
  - [http://www.centralservicesagency.n-i.nhs.uk/display/rdo_research_governance](http://www.centralservicesagency.n-i.nhs.uk/display/rdo_research_governance)  (Northern Ireland)
  - [http://www.word.wales.gov.uk/content/governance/governance-e.htm](http://www.word.wales.gov.uk/content/governance/governance-e.htm)  (Wales)

- The named CI must be professionally based in the United Kingdom. For international studies with a chief or “co-ordinating investigator” outside the UK, the form should name as CI the investigator who will take responsibility for the study within the UK.

- For CTIMPs, the CI must be a health professional as defined in the Medicines for Human Use (Clinical Trials) Regulations 2004. This means a person registered in the UK as a doctor, dentist, nurse or pharmacist.

- For multi-site CTIMPs sponsored by a pharmaceutical company, the CI can be an
employee or contractor of the company. However this should be a health professional with current relevant experience. For single-site CTIMPs, the CI must be the Principal Investigator at the site.

- For research funded by a grant the CI should normally be the grant-holder.

- Any subsequent change in the CI should be notified to the main REC as a substantial amendment. A favourable opinion from the REC is required for such a change.

- A CV for the CI should be submitted with all applications to RECs, R&D offices, GTAC and MHRA Devices. The CV should be in summary form, with only information relevant to the current application. For example, it should give evidence of previous research in the same field of study, and other relevant experience and training. The length should be a maximum of 2 pages of A4. It is recommended that applicant use the CV template available on IRAS. This has been endorsed by NRES and the NHS R&D Forum as suitable for all applications to RECs and R&D offices. The CV should be signed and dated prior to submission. (Copies of the signed version can be used for multiple submission.)

- For guidance on who should act as the Chief Investigator in educational projects, please refer to the guidance on student research in Help.

**Question A4 Central study coordinator**

- Please enter details of the central study co-ordinator, if there is one. Not all research will have a central study co-ordinator in addition to the Chief Investigator.

- The central study coordinator is an individual, other than the CI, who assists in the management and administration of the whole study on behalf of the sponsor or CI. The individual may be called a Project Manager, Trial Manager, Clinical Research Scientist or Study Coordinator. Reviewers may contact the central study coordinator to clarify administrative matters relating to the application.

**Question A5-1 Reference numbers**

- This question is largely administrative. It is useful to have all reference numbers recorded in one place.

- If one of the reference numbers listed is not applicable to your study state N/A.

- The International Standard Randomised Controlled Trial Number (ISRCTN) is a simple numeric system for the unique identification of clinical trials worldwide. It will simplify the identification of trials and provide a unique number that can be used to track all publications and reports resulting from each trial. For more details go to: [http://www.controlled-trials.com/isrctn/isrctn_faqs.asp](http://www.controlled-trials.com/isrctn/isrctn_faqs.asp). Alternatively, trials may be registered at [http://clinicaltrials.gov](http://clinicaltrials.gov).

- The EudraCT number is the mandatory reference number allocated by the European Medicines Agency (EMEA) for CTIMPs authorised on or after 1 May 2004. Further details can be found from the EMEA at...

- If the project has a website, give the URL.
- The policy for public registration of the research should be stated in answer to Question A50.

**Question A5-2 Links with previous studies or other applications**

- If this research is a follow-up study to a previous or current application by the Chief Investigator, or if the application is part of a series of closely linked projects in a programme, give details of relevant previous or current applications. This information will allow reviewers to access relevant background information if required. Please do not list all past and current applications unless directly relevant to this application.

**2. OVERVIEW OF THE RESEARCH**

**Introduction**

- This section gives you the opportunity to summarise your project and the ethical and design issues you have addressed. It might help to think of your combined answer to these questions as an introduction you might give to the REC when invited to attend.
- You may find there is some duplication with later questions but the answer here will provide the REC and other reviewers with an easily read description of your study and the main issues. You may “cut and paste” to later questions where appropriate.

**Question A6-1 Summary of the study**

*Writing the research summary*

- Your answer to this question should be a short summary of the proposed research (maximum 300 words) written in plain English. Where technical terms are used they should be explained. All acronyms should be described in full.
- The title should be concise and include the condition under study, the treatment being evaluated and the group to be recruited, framed as a research question.
- The summary should then briefly describe the background to the research, why it is important, the questions it will answer and potential benefits, the study design and what is involved for participants, who is funding the research and where it will be recruiting.
- Questions you may wish to cover in writing the summary:

| Why? | What research question is being addressed? |
How is it of relevance and importance to patients and public?

What?
Broadly what area (disease, therapy or service) is being studied?
For therapeutic studies what is the drug, device or procedure being tested.

Who?
Who would be eligible?

Where?
The type of sites where the study will be conducted.

How?
How long will the study last and what will the participants undergo?

- This summary should be suitable for the public, patients and service users wanting more information about their condition, researchers reviewing current literature and doctors planning treatment. Given its size, we recognise it cannot be comprehensive and will need compromise to meet all audiences. Rather it will be a “signpost” and any reader wishing more information will need to seek further details.

- Applicants are advised to exclude information from the summary where exemptions apply under the Freedom of Information (FOI) Acts (e.g. if disclosure of the information is likely to harm commercial interests, or pose a risk to health and safety of any person, or if the information includes personal data).

- The REC may comment on the summary in the course of the ethical review. For example, it may suggest changes to make the summary more comprehensible or informative for patients, service users and the public. However, any such suggestions will be given separately from the ethical opinion on the research and may be regarded as non-binding advice from the committee. The content of the summary will not determine the committee’s opinion.

Publication of research summaries

- The interests of the public, patients, research participants and researchers are best served by open research and, recognising this, international bodies, medical journal authors and researchers have promoted trial registration. For example, the World Health Organisation states on its website (http://www.who.int/ictrp/en/):

  “The mission of the WHO Registry Platform is to ensure that a complete view of research is accessible to all those involved in health care decision making. This will …..ultimately strengthen the validity and value of the scientific evidence base.”

- The National Research Ethics Service (NRES) shares this view and believes that open research is ethical research. NRES plans to publish summaries of all REC applications, together with a summary of the ethical opinion. In the case of medicinal trials (CTIMPs), an ethics committee is legally required to publish a summary of its opinion by Regulation 15(9) of the Clinical Trials Regulations. This is also required by the Governance Arrangements for Research Ethics
Committees for all types of application reviewed by RECs.

- Publication of research summaries and opinions will also support compliance with requirements under Freedom of Information legislation to publish information held by public bodies.

**Content of the published research summary**

- The published summary will be produced from information provided by applicants in answer to the following questions:

  Summary A6-1
  Study design A7
  Disease/diagnosis A15
  Timescale and duration for participants A21 and A69
  Details of trial registration A5-1 and A50
  Contact point for further details D1

- Publication of a contact point will be subject to agreement by the applicant. For further information, please refer to the guidance in the Declaration section at D1.

**Arrangements for publication**

- Research summaries will be published for all applications submitted from 1 May 2008.

- Publication of research summaries will be on the NRES website at [www.nres.npsa.nhs.uk/researchsummariesregister](http://www.nres.npsa.nhs.uk/researchsummariesregister). Publication will take place no earlier than 3 months following the issue of the committee’s final opinion (or the withdrawal of the application). NRES will write to the Chief Investigator in advance and provide a copy of the intended text for publication. Contact details will only be included in the summary with explicit permission.

- NRES also plans in future to publish summaries of the ethical opinion and is currently exploring the best way of producing the summary. This is likely to be implemented during 2009. The arrangements will not apply retrospectively to applications already concluded at the time of implementation.


**A6-2 Summary of main issues**

- This should be a discussion of the main ethical and design issues arising in the research, how you have addressed them and who you have consulted in developing the proposal.

- You may have made choices when designing your study. Explain the options you considered and the reasons for and against these, summarising why you finally settled on one. The reasons are as important as the final choice itself.
• Indicate any important information not covered elsewhere in the application, and any specific issues on which you would welcome advice from the REC.

• The following paragraphs highlight key areas you may wish to address.

Purpose and design

• RECs pay particular attention to the purpose of a study, asking “What question is the research asking, is it worth asking and can this proposal answer it?” Justify the research, showing how it builds on existing knowledge. Summarise the key choices you have made in formulating the research questions and methodology.

• Indicate who has been involved in developing the research proposal, including scientific critique and input from patient, service user or community groups.

• It is perfectly reasonable for one purpose of the research to be educational.

Recruitment

• Many different methods may be used. RECs will look carefully at the relationship between a potential participant and the “recruiter” to ensure this process is free from undue influence. Recruitment material should make few, if any, therapeutic promises, there should be no coercion or unacceptable inducement.

Inclusion / exclusion

• No one should be unfairly excluded from or included in research. Choices made in both inclusion and exclusion criteria may require justification.

Consent

• Valid consent is underpinned by adequate information and the capacity of participants to decide for themselves. A capable person will:

  - Understand the purpose and nature of the research.
  - Understand what the research involves, its benefits (or lack of benefits), risks and burdens.
  - Understand the alternatives to taking part.
  - Be able to retain the information long enough to make an effective decision.
  - Be able to make a free choice.
  - Be capable of making this particular decision at the time it needs to be made.

• RECs increasingly ask “Can you, or whoever will seek consent, assess capacity and do you understand the ethical principles underpinning informed consent?” If the research involves people who may lack capacity to consent, the provisions of the Mental Capacity Act 2005 will apply. See guidance on Question 7 in the Project Filter.

• If research involves participants who are unable to represent their own interests or are particularly susceptible to coercion (vulnerable individuals), it will be important to explain why this research is needed and how their interests will be protected.
• If research is to be conducted without consent, this needs explanation and justification.

Risks, burdens and benefits

• Summarise and weigh up the risks/burdens and benefits, exploring both likelihoods and the consequences of harm. It helps to “put yourself in the participants’ shoes” and try to imagine how he or she would see the project. If it is possible, discuss it with potential participants. This is an area where consultation with the community, service user or patient groups could provide support.

• It is crucial you have worked to minimise risk and protect your participants and you should demonstrate this to the REC.

• If you are allocating participants to treatments, the committee will expect equipoise, and it will help your application if you summarise the arguments that indicate this.

Confidentiality

• The “Caldicott Principles” set out an ethical framework for use of identifiable data:
  
  Principle 1  Justify the purpose(s) for obtaining the information.
  Principle 2 - Don’t use person-identifiable information unless it is absolutely necessary.
  Principle 3 - Use the minimum necessary person-identifiable information.
  Principle 4 - Access to person-identifiable information should be on a strict need-to-know basis.
  Principle 5 - Everyone with access to person-identifiable information should be aware of their responsibilities.
  Principle 6 - Understand and comply with the law.

• Indicate any problems arising from the processing of identifiable data and/or tissue samples and say how they will be handled.

• Confidentiality is not “secrecy” and there may be (rare) occasions when this has to be broken. RECs expect confidentiality to be broken if participants or others are at serious risk. The possibility needs to be considered and the REC will wish to know how such an occasion will be managed.

Conflict of interest

• You should consider whether your interests as a researcher will conflict with your duties as a health care professional. If there is such a possibility, you will need to explain how it will be handled.

What will happen at the end of your study?

• Consider carefully what will happen after your study has ended, particularly in the case of drug trials, and whether results will be fed back to participants.

Use of tissue samples in future research
• Samples should be used fairly, to the benefit of science and not to the detriment of donors. The idea of sample donations as a “gift” has stood the test of time and has support. Participants should know who will store the samples, for what purpose and who will have access.

For further guidance see:

http://www.nres.npsa.nhs.uk/
http://www.eric-on-line.co.uk/
http://www.dt-toolkit.ac.uk/

3. PURPOSE AND DESIGN OF THE RESEARCH

Question A7 Methodology description

• Please tick all the descriptions that you feel apply to your project. This information is used by organisations to monitor the types of research activity taking place.

Question A8 Type of medicinal trial

• This question applies only to CTIMPs being conducted under the Medicines for Human Use (Clinical Trials) Regulations 2004.

• If the investigational medicinal product in your trial is a gene therapy product or it is a trial of stem cell therapy using cells derived from stem cell lines, you should apply to the Gene Therapy Advisory Committee (GTAC) as the main REC for the trial. In cases of doubt, please contact the GTAC Secretariat for advice. Contact details are at: http://www.advisorybodies.doh.gov.uk/genetics/gtac/contact.htm

• Some products may qualify both as medicinal products under the Medicines Act and medical devices. If so, you should draw this to the attention of review bodies and say which regulatory approvals are being sought. This is a complex area and advice may be sought from the MHRA Clinical Trials Unit by emailing clintrialhelpline@mhra.gsi.gov.uk. The MHRA will indicate whether application for regulatory approval of the trial should be made under the Clinical Trials Regulations or the Medical Devices Regulations. In exceptional cases, both sets of Regulations may apply.

Question A9 Phase of medicinal trial

• Indicate which phase of drug development the trial belongs to. Any trial defined as a Phase 1 trial for the purposes of the Clinical Trials Regulations must be submitted to an ethics committee recognised to review such trials. The Regulations define a Phase 1 trial as:

“A clinical trial to study the pharmacology of an investigational medicinal product when administered to humans, where the sponsor and investigator have no knowledge of any evidence that the product has effects likely to be
beneficial to the subjects of the trial”

- Exceptionally, a trial of a licensed product might be defined as a Phase 1 trial. This would apply where it is being used outside the terms of the authorisation (e.g. with healthy volunteers or patients without the condition the product is intended to treat) to gain additional pharmacological data and no therapeutic benefit to the participants can be expected.

Questions A10-11  Research questions/objectives

- What question(s) are you trying to answer? Reviewers pay particular attention to the purpose of research, asking “What question is the research asking, is it worth asking and can it answer it?”. Your answers should be succinct, excluding methodology, and realistic.

Question A12  Scientific justification for the research

- RECs pay particular attention to purpose, asking “What question is the research asking, is it worth asking and can this proposal answer it?”. RECs balance the potential benefits – whether for science, society or participants themselves - against the potential risks and burdens of the study.

- It therefore helps to place the study in context to demonstrate you are familiar with previous work and show how it will contribute to knowledge. Previous research should not normally be repeated where adequate evidence is already available.

- You should write your answer in a way that will be understood by lay members of the REC and other reviewers without relevant clinical or research expertise. Please avoid technical language. It is not acceptable to cut and paste from the protocol.

- The information provided should clearly and simply answer the following questions:
  - Why is the research considered worth doing and what will be gained by undertaking the project? Does it deepen understanding of disease/illness? Does it answer an important question?
  - What are the main research question(s) designed to answer – i.e. what is the “knowledge gap” the research is designed to fill?
  - What new information will the research provide?
  - Has similar research on this topic been done before?
  - In the case of student research, what training will it provide in research methodology?

- It is the applicant’s responsibility to check the originality of the proposal, using all existing sources of evidence. Where research is to be repeated, this should be
justified. Repeating research that puts participants at more than minimal risk may be considered unethical if the answer to the scientific question is already known from previous studies.

- It is recognised that student research has an educational and training value, and proposals (especially from undergraduates) will not normally be of the same originality or scientific importance as those submitted by professional researchers. However, applications from students should demonstrate knowledge of the relevant scientific background and the methodology to be used, and identify clear and realistic project objectives. Student proposals will be subjected to the same standard of ethical review as all other research proposals.

**Question A13 Design and methodology**

- After reading the answer to this question, a reviewer should have a clear overview of the research protocol or project plan, in particular a complete picture of what will be expected of participants. It helps to put yourself in the participant’s shoes and try to imagine how he or she would see the project. It possible, discuss the design with potential recruits or with community, service user or patient groups.

- Depending on the type of research undertaken, the answer should include the following information:

  - The null and any alternative hypotheses and why such an alternative hypothesis was chosen.
  - Why the study design and methodology has been chosen and what has influenced the choice.
  - The justification for including control arms to a trial, if applicable. Particular justification should be given for use of a placebo arm. In a trial involving allocation to treatments, the REC will expect equipoise - summarise the arguments that indicate this.
  - The broad timetable for the stages of the research e.g. preparation, convening meetings/conducting interviews, interpreting and analysing findings, preparing the final report.
  - Where any interviews will take place.
  - Whether there will be planned interim analyses/reports.
  - What procedures will be in place to detect and compensate for any possible “researcher effects” and “researcher bias”.
  - The details of any observational components of the research methodology and how these will be carried out.

- It is important that the information given in this section clearly reflects the information set out in the protocol and in the Participant Information Sheet.
Additional guidance for research involving prisoners

- The answer to the question should reflect issues specific to prison populations, including in particular literacy levels, mental health needs and prisoner-staff relations.

**Question A14-1 Patient, service user and public involvement**

- Public involvement includes consultation with or working alongside members of the public, patients, service users or carers in the choice of research topic, and the design, planning, conduct and dissemination of research. The UK health departments are committed to active patient and public involvement in all stages of research. For more information see INVOLVE (http://www.invo.org.uk/) or, in Wales, see Involving People (http://www.wales.nhs.uk/sites3/page.cfm?orgid=580&pid=14773)

- This question does not refer to the involvement of patients, members of the public or service users or carers as participants in the research.

**Question A14-2 Acceptability of using identifiable data without consent**

- This question applies only to applications to the National Information Governance Board for Health and Social Care (NIGB).

- As NIGB approval involves the setting aside of the common law duty of confidentiality, it is important that applicants make efforts to test with patients the acceptability of the use of confidential patient information for this particular study, both in terms of the purpose, the degree of identifiability and sensitivity of the data required.

- This does not replace patient consent but if done appropriately can provide useful insights for the research and gives an indication of the general acceptability of the use of the data for this purpose. Please see the NIGB advice on user involvement for further details www.advisorybodies.doh.gov.uk/PIAG/userinvolvementguide.pdf.

**Question A15 Sample group or cohort**

- Please select the main identifying feature(s) of the participants, data or samples being studied. Where research does not involve identification by disease or diagnosis please select the option "Generic Health Relevance".

- Where participants are users of a service, NHS or social care staff, or selected from the general public, please include further details in the inclusion and exclusion criteria at A17.

4. **RISKS AND ETHICAL ISSUES**
Question A16 - 17  Inclusion and exclusion criteria

- No-one should be unfairly excluded from, or included in, research. Inclusion exposes participants to potential risk and burden, while exclusion may deny them benefit from research. Both inclusion and exclusion criteria require justification.

- The policies of the UK Health Departments emphasise equity of access to treatment and service provision in the NHS and social care, and the need to avoid discrimination against individuals, communities or groups.

- You should state clearly any criteria for including and/or excluding potential participants based on the following:
  - Age
  - Disability (including learning disability, physical disability, sensory impairment and mental health problems)
  - Gender (including gender identity)
  - Race, ethnic origin (including Gypsies and Travellers) or nationality
  - Religion or belief
  - Sexual orientation (including lesbian, gay and bi-sexual people).

- Any ethical or design issues that arise from the choice of selection criteria should be discussed in your answer to Question A6-2.

- The guidance on Question A22 includes a table of potential risks and benefits from participation in, or exclusion from, research.

Additional guidance for research involving prisoners

- Applicants should reassure the ethics committee that potential participants who may have the most serious general and mental health difficulties are not excluded from the study, e.g. those with learning difficulties or particularly low literacy levels.

Questions A18–A19  Research procedures to be undertaken

- These questions request detailed information about all the interventions and procedures that will be received by participants, or conducted on samples or data.

- The REC will assess the risk and ethical acceptability of what is involved for potential participants. In particular it will wish to consider the nature and number of procedures compared to what a research participant might receive if undergoing treatment or other service provision alone.

- NHS reviewers will use the information to:
  - Assess the cost and resource implications
  - Ensure that necessary practical arrangements are made to support research activities
  - Make necessary risk management arrangements
• In Column 1, give the **total** number of interventions or procedures, not the additional number over and above the routine number.

• Where all or some of the interventions or procedures would be regarded generally as routine care, give the number in the second column.

• In column three give the average time taken to conduct each intervention or procedure. Some activities will overlap but the time for each should still be listed separately, e.g. an in-patient hospitalisation of three days and obtaining a blood sample during the stay lasting 10 minutes.

• In column four give either the name and job title of the individual conducting the research intervention or procedure (if it will always be the same person at all research sites), or give a description of the staff group, e.g. research nurse at site. Please also provide a general description of where the intervention/procedure will take place, e.g. out-patient clinic, GP practice or participant’s home.

• Clinical interventions are those that are routinely conducted or requested by a healthcare professional.

• Information given about ionising radiation exposures (e.g. number of diagnostic X-rays, CT scans or courses of radiotherapy) should be consistent with the information provided in Part B Section 3 of IRAS.

**Additional guidance for research involving prisoners**

• It is expected that the applicant will normally only use questionnaires which have been specifically validated for use with the prison population. If the questionnaires have not been so validated the applicant should provide a clear justification for their use.

• It is recognised that literacy levels among the prison population are very low and the researcher is asked to consider this when selecting questionnaires and any related material.

**Question A20 Withdrawal of treatment or other services normally provided.**

• Sometimes a research protocol requires withdrawal of existing treatment or service provision. It may for example be justified to stop current therapy during a “washout period”. Reviewers will be concerned to ensure that treatment is withdrawn only when absolutely necessary. You should explain the possible consequences of withdrawing treatment and how you would minimise the possibility of any harm.

• The participant information sheet should explain where treatment is being withheld, making absolutely clear what is involved, including the likely level of discomfort and risk, procedures to minimise the risks and whether extra assessments will be involved.
Question A21  Duration of study for each participant

- Duration of participation should be calculated from when participants give informed consent until their last contact with the research team.

Question A22  Potential risks and burdens

- Your answer should identify potential risks and burdens (see table below) but it should be more than a comparative list. You should weigh up the risks in relation to the benefits, exploring the likelihood of both and the consequences of potential harm. It helps to put yourself in the participants’ shoes and try to imagine how he or she would see the project. If it is possible, discuss with potential recruits. This is another area where consultation with community, service user or patient groups may provide support.

- Include any potential for distress, discomfort and/or inconvenience which might be experienced by a research participant, with an explanation of why it is necessary and what has been done to minimise the effects. Most research has potential to cause some distress even if this is felt to be minimal, e.g. breach of confidentiality, upsetting participants in interviews.

- Where the research only involves the use of data, consideration should still be given to the risks for patients associated with any breach of confidence or failure to maintain data security.

- Potential risks and burdens should be described in the participant information sheet in such a way that potential participants can clearly understand what is involved if they consent to take part.

- Research sponsors should have in place systems to monitor and respond to developments as the research proceeds, particularly those which put the safety of individuals at risk, and to ensure the design and conduct of the research is modified accordingly.

- It is not acceptable to state “not applicable” in answer to this question.

Balance of risks and benefits of participation in, or exclusion, from research

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<td>Risk of research procedures or withholding standard procedure</td>
<td>Better supervision</td>
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<td>Risk of new therapy</td>
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<td>Intrusion</td>
<td>Evidence that results of treatment/care may be better within a trial</td>
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<td>Risk of breach of confidentiality</td>
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<td>Change of relationship with care professional</td>
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<td>Exclusion</td>
<td>Possible misunderstanding (especially for those who have difficulty with English)</td>
<td>Belonging to an under-researched group (e.g. children or women)</td>
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<td>Stagnant or inappropriate care</td>
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**Question A23  Disclosure of information from interview/questionnaire**

- If interviews touch on sensitive areas, reviewers will consider the experience of researchers and how they will handle these aspects.

- Where the research might lead to unexpected disclosure of information by participants that could require notification or other follow-up action by the researcher, please describe how this would be handled.

- Reviewers will wish to be assured that appropriate arrangements are in place including support for the researcher.

- The participant information sheet should make it clear under what circumstances action may be taken by the researcher.

**Additional guidance for research involving prisoners**

- Applicants should consider how they will deal with potential disclosure of information required by Prison Rules, i.e. any intention on the part of the participant or another prisoner to self-harm, harm another named person or pose a threat to security. Careful consideration should also be given to the policy for disclosure of any other sensitive information which might come to light during the research, e.g. misuse of drugs or other breaches of Prison Rules. The information sheet should state clearly what information would be disclosed by the researcher.

- The REC would expect the applicant to provide participants with access to an appropriately trained person should they become upset, agitated, angry, etc during any interviews/group discussions/completion of questionnaires. The applicant should be aware in this context of the general levels of mental health of the prison population.

**Question A24  Benefits to the research participant**
• You should state here any potential benefits to be gained by the research participant through taking part in the research either now or in future. However, don’t over-emphasise the benefits. In some cases there may be no apparent benefit.

• Some studies purport to show a benefit to taking part in any therapeutic trial but a recent meta-analysis could not support this and demonstrated significant methodological problems in previous work. It seems that the majority of those who participate find it a positive experience, but it is probably best to refrain from claiming any therapeutic benefit simply from being in the trial.

• There is clearer evidence that patients and service users experience benefit from taking part in observational research.

Additional guidance for research involving prisoners

• The applicant must ensure that the participants clearly understand that by participating in the study their care, life in prison or parole will not be affected in any way.

Question A25 Arrangements at the end of the trial

• Describe the arrangements the sponsor is making, if any, for continued access by the participant to any benefits or intervention, which he or she may have obtained during the research.

• There is no legal or policy requirement to provide continued treatment to participants once they have completed the trial. It is an issue to be considered on a trial by trial basis. However, the sponsor’s plans must be made clear to potential participants before consent is sought. Where a commitment is made to provide continued treatment, review bodies will seek assurance that agreement has been reached on funding responsibilities.

• Researchers should consider the following options:
  
  (i) No treatment available after the trial.
  
  (ii) Treatment available to all those in the trial already taking it.
  
  (iii) Treatment available to all participants.
  
  (iv) Treatment available to patients on a named patient basis.
  
  (v) Drug available on an open label basis for a cohort observational study.

• Reviewers will wish to consider the following issues:
  
  □ Will the subjects understand the arrangements at the end of the trial prior to agreeing to participate?
  
  □ Who, if anyone, is in a position to provide treatment after the trial?
What are the resource and financial implications of providing continued treatment? Would these jeopardise the trial?

Who would carry the liability for provision of treatment outside the trial?

How soon will the results be available for use after the conclusion of the trial?

Will the results of the trial provide unequivocal evidence of efficacy?

**Question A26  Potential risks to the researchers**

- The research sponsor should consider the safety and well-being of researchers. For example, there may be risks for lone researchers visiting participants at home. Describe the measures proposed to address such issues.

**Additional guidance for research involving prisoners**

- You should ensure that the safety of the researcher has been considered and that the researchers have the relevant experience to be able to assess and to deal with possible risks.

**Question A27-1  Identifying potential participants**

- Where potential participants will be referred to a separate research team, the arrangements for identification and referral must be clearly described here. Details of the centres undertaking such referral of NHS patients must be given in Part C of IRAS. Where potential participants are referred as NHS patients to a separate research team outside the NHS, any publicity, letter of invitation and/or written information for participants must explain this arrangement clearly.

**Additional guidance for research involving prisoners**

- Justification is required if prison staff are being used to select or approach suitable participants as this could well bias the results of the study. It is generally unacceptable for prison staff to be used as gatekeepers.

**Questions A27-2 and A27-3  Screening of identifiable personal information**

- Please give details of the sources of identifiable personal information that will be used to identify potential participants.

- Normally only a member of the patient’s or service user’s existing care team should have access to their records without explicit consent in order to identify potential participants, check whether they meet the inclusion criteria or make the initial approach to the patient or service user. If the research proposes to use someone outside the clinical team to identify suitable participants, or as first contact with the participant, the reason for this should be explained.

- Where patient, client or disease registers are used to identify potential participants give brief details of the consent and confidentiality arrangements of the register.
**Question A27-4  Access to personal data outside the care team**

- Normally only a member of the patient’s direct healthcare team should have access to patient records without explicit consent in order to identify potential participants, check whether they meet the inclusion criteria or make the initial approach to patients. If the research proposes to use someone outside the clinical team to identify suitable participants, or as first contact with the participant, the reason for this should be explained.

- The “direct healthcare team” are clinicians directly responsible for providing routine care and treatment to individual patients together with their administrative support staff. Normally such clinical staff will have direct contact with the patients. However, as pathology staff also directly support the care provided to patients they would also be included within the boundaries of the healthcare care team. Social Workers are not usually part of the healthcare team and disclosures of confidential information to social services staff should be undertaken with explicit patient consent, at least initially, in order to provide a basis for further disclosures based on implied consent.

**Question A27-5  Consent to access identifiable data**

- Consent for secondary uses of identifiable data such as health research must be explicit. Implied consent is only acceptable where there is a basis for implying consent such as where the patient agrees to be referred to another service. Although custom and practice has been that researchers have often been given access to records in order to identify relevant patients in order either to extract relevant data or to invite those patients to seek consent, this involves a breach of confidentiality. Consent should be sought by the clinical care team therefore to allow researchers access to the records in order to extract information or to identify patients with a view to informing them about a research study, where clinicians or their staff are unable to do this themselves. (See guidance at [http://www.nigb.nhs.uk/](http://www.nigb.nhs.uk/).)

- If you plan to access identifiable data without prior consent you should ensure that you have selected the option to apply to the National Information Governance Board (see question 4 of the Project Filter).

**Question A28  Advertisements**

- All advertising material designed to recruit participants must be reviewed by the REC. This includes posters, television and radio broadcasts, videos, CDs and web pages. Copies of these (printed material, audio or video tapes, transcripts etc) should be included with your application and give a version number and date.

- Recruitment material should be restrained in tone. Care should be taken not to over-emphasise potential benefits or make other inducements.
• You should state who would be the first contact point for anyone answering an advertisement, and give brief details of their professional background and training for this task.

Additional guidance for research involving prisoners

• Recruitment material needs to take into account the general literacy levels of the prison population, and applicants should consider how they will recruit non-literate participants. Participants should clearly understand from any advertising material that their participation is entirely voluntary and that they can decide not to participate or withdraw from the study at any time without their parole, care or life in prison being affected in any way.

Question A29 Approaching participants

• Please explain how participants will be approached and who will be involved.

• Participation in a research project must be entirely voluntary, and no one must be coerced to participate in a research project against his/her will. Researchers should avoid exerting undue influence when approaching potential participants. No sanctions should follow if the participant decides to leave the research at any time.

• The initial approach to potential participants should normally be made by a member of the health or social care team. If researchers other than members of the health or social care team propose to approach potential participants directly, the reason for this approach should be explained.

• Copies of documentation used to approach potential participants should be enclosed with all applications (e.g. letters to clinicians or other health professionals, letters from clinician to patient).

Question A30-1 Informed consent

Legal and ethical requirement for informed consent

• For most types of research, it is both a legal and ethical requirement to obtain informed consent from participants able to consent for themselves.

• There are exceptions in which it is not a legal requirement to obtain informed consent, for example where the research is limited to use of the following:

  - Data that has been completely and irrevocably anonymised and is no longer personal data within the meaning of the Data Protection Act.

  - Personal data where approval has been given by the National Information Governance Board for Health and Social Care (NIGB) (formerly PIAG) for processing of the data without consent under Section 251 of the NHS Act 2006 (or formerly by the Patient Information Advisory Group under Section 60 of the Health and Social Care Act 2001) - see http://www.nigb.nhs.uk for further guidance.
“Existing holdings” of tissue under the Human Tissue Act 2004, i.e. “relevant material” which was already held prior to 1 September 2006.

Tissue from the living, which is not identifiable by the researcher and where the research is ethically approved by a NHS REC under section 1(9) of the Human Tissue Act.

Studies which only use postal survey approaches may not require additional consent, since completion and return of the survey implies consent. However, adequate participant information of the purpose of the study is required. Any intention or mechanism to issue reminders, and the recipients rights to ignore them, should be fully explained in this information. It would be expected that postal surveys would be disseminated by bodies who are entitled to hold contact details, probably at the request of the research team.

If you propose not to seek consent, please explain why in your answer to this question. Where consent is not a legal requirement, you should still consider whether it would be feasible and ethically justified to seek consent. Research evidence indicates that the public value their right to choose whether or not to participate in research, even where a study has been approved by a REC.

Arrangements for seeking consent

For consent to be ethical and valid in law, participants must be capable of giving consent for themselves. A capable person will:

- Understand the purpose and nature of the research.
- Understand what the research involves, its benefits (or lack of benefits), risks and burdens.
- Understand the alternatives to taking part.
- Be able to retain the information long enough to make an effective decision.
- Be able to make a free choice.
- Be capable of making this particular decision at the time it needs to be made (though their capacity may fluctuate, and they may be capable of making some decisions but not others depending on their complexity).

In general, exclusive reliance on distributing the participant information sheet as a way of informing and recruiting participants should be avoided. Researchers should be able to explain the study clearly to potential participants. Reviewers will consider what training and experience the researchers have had in seeking consent. RECs will seek reassurance that researchers understand the ethical principles underpinning informed consent and are able to assess capacity.

Where the research team will be recruiting participants whose capacity is likely to be borderline or to fluctuate, please say how capacity will be assessed and by whom, and what relevant knowledge and/or expertise this person will have. Where adults unable to consent for themselves are to be included, separate information about recruitment should be provided in Part B Section 6.

Participant information sheets

Advice on writing the participant information sheet and a pro-forma can be found on the NRES web site at [http://www.nres.npsa.nhs.uk/applicants/guidance/](http://www.nres.npsa.nhs.uk/applicants/guidance/). Reviewers will generally expect applicants to follow the NRES guidelines. They
should be regarded as setting out the basic minimum information, which can be supplemented if required.

- Information should explain the study clearly, and the language used should be suitable for a lay person. All technical words must be explained. The tone of the information sheet should be invitational and not coercive.

- The REC expects a copy of the participant information sheet to be given to the research participant to be kept for reference.

- Where the schedule of study procedures is complex, it is recommended that a flow chart or table should be prepared for participants and included with the application.

Vulnerable participants

- Consent must always be voluntary. Where participants are capable of consenting for themselves but are particularly susceptible to coercion, it is important to explain how their interests will be protected.

- Particular consideration should be given to informed consent arrangements where participants are in a dependent relationship with the research team. Examples include:
  - Students participating in research by their tutors.
  - Members of staff participating in research carried out, or formally supported by, the management of their organisation.
  - Residents of care homes.

- In such cases, participants may feel under an onus to participate. It is important that every effort is made to avoid coercion and ensure consent is voluntary. Your answer to this question should say what steps will be taken.

Additional guidance for research involving prisoners

- The participant information sheet should include specific guidance for prisoners on the following:
  - the obligation on the researcher to disclose any intention on the part of the participant or another prisoner to commit self-harm, harm a named person or pose a threat to security, if this comes to light during the research
  - any other information the researcher plans to disclose if it comes to light during the research
  - that participation will not affect their parole, care or life in prison in any way.

- When drafting the information sheet the researcher should bear in mind that the average reading age of prisoners is lower than that in the general population.

Question A30-2  Recording consent in writing
• The consent to take part in a study should be recorded in a patient’s notes and in the study records.

• Please enclose a copy of the proposed consent form when submitting your application. Advice on the consent form and a pro-forma can be found on the NRES web site at http://www.nres.npsa.nhs.uk.

• If you do propose not to obtain consent in writing, you should justify this. The REC usually requires that written consent be obtained for all but the most minor procedures. In studies involving postal questionnaires where the burdens are insignificant and sensitive topics are not involved, the REC will normal regard the return of the questionnaire as adequate evidence of consent. This is sometimes called “implicit consent”.

• Where a participant is unable to sign or mark a document to indicate their consent, arrangements should be made for their consent to be witnessed and this should be documented.

Question A30-3 Justification for not seeking consent to process identifiable data

• This question applies only to applications to the National Information Governance Board for Health and Social Care (NIGB) to process identifiable patient data without consent.

• Explain why it is not practicable for either your organisation or the current holder(s) of the information you require to obtain consent from patients to use their information. Robust arguments are sought here. For example, the data may be very historical and people would be difficult to trace and/or deceased.

• Often it is argued that 100% coverage of patients is needed and therefore that consent is inappropriate. While NIGB understands that this is desirable, it is often neither possible nor necessary to have 100% coverage to produce valid results. If it is required, you should provide a detailed explanation of why and what the consequences of lesser coverage might be, giving evidence to support any assertions.

• As a general principle, the process of seeking consent should be undertaken by the original holder of the data. NIGB occasionally gives approval for a research body to act as data processor for the Trust(s) responsible for the data and to write to patients direct in order to seek consent but the letter should appear to come from the relevant Trust / GP practice.

Question A31 Time allowed to decide to take part

• Potential participants need time to consider fully the implications of taking part in research. They should be able to ask questions and reflect. Participants should not be rushed into decisions.

• There are no fixed guidelines for the time to be allowed to participants. It has been common practice to suggest a minimum of 24 hours, but this is not an absolute rule. Each study should be considered on its own merits. If you feel
that a shorter period is reasonable in the circumstances and taking into account
the nature of the study, please justify this in your answer.

**Question A32  Multiple participation**

- Particular care must be taken to ensure that participation in multiple studies will
  not compromise patient safety or undermine the scientific basis of the study. The
  REC may also wish to consider the overall burden on participants.

**Medicinal trials**

- It is important to distinguish medicinal trials (CTIMPs) from other studies. For
  CTIMPs, the guidance from the Association of the British Pharmaceutical Industry
  (ABPI) is that there should be a gap of 4 months between trials. The US Food
  and Drug Administration (FDA) stipulate 28 days. The investigator should also
  consider whether there are reasons for extending this period.

- For Phase 1 CTIMPs, investigators should use a process such as The Over-
  Volunteering Prevention System (TOPS) to identify any volunteers who are
  putting themselves at risk by participating on more than one trial. Further
  information about TOPS is available at [www.tops.org.uk](http://www.tops.org.uk).

**Other research**

- For studies other than CTIMPs, there are no established guidelines. Multiple
  participation is an ethical issue for the REC to consider as part of its review.
  There is little published literature on this issue, but what there is suggests that
  the public are willing to take part in more than one study. However, you should think
  about the following:

  - The burden of participation in more than one study and the psychological
    impact.
  - Any possible impact on the results of each study.
  - The consequences for the design and scientific validity of your study.
  - Recovery periods.

- The decision should be the patient’s provided that there are no overriding safety
  or design considerations.

**Question A33-1  Research participants who may have difficulties in
adequate understanding of English**

- The inclusion or exclusion of potential participants who may have difficulties in
  adequately understanding written or verbal information in English raises ethical
  issues.

- If they are to be included, you should explain what measures will be taken to
  provide necessary translation of written information and interpretation. In a multi-
  site study, the CI is responsible for ensuring that Principal Investigators and
  collaborators will make the necessary arrangements at each research site. There
  are strong arguments in terms of cost and consistency for translation of the
documents to be commissioned centrally and then made available to each site as necessary.

- Any proposal to exclude such participants should be clearly justified in the application.

- The acceptability of the plan to implement these arrangements in a particular locality falls within the scope of site-specific assessment by the NHS R&D office or the local REC for the site, or should be raised in negotiations to access local authority sites.

- If you have concerns about how these issues relate to your research you should seek specific guidance from the REC in your application.

**Question A33-2 Information for participants in Wales**

*Recruitment of participants in Wales*

- If you are recruiting patients for a trial in Welsh centres you should note that provision of information for patients and service users is governed by the Welsh Language Act (1993). The Act established the principle that in the conduct of public business and administration of justice in Wales, the English and Welsh languages should be treated on the basis of equality. This principle of equality offers the public the right to choose which language to use in their dealings with public organisations (including the National Health Service) and recognises that members of the public can express their views and needs better in their preferred language. In research, this presents particular ethical issues relating to informed consent.

- There is considerable geographical variation in the use of the Welsh language within Wales. Before submitting your application it is recommended that you seek advice from local NHS R&D office(s) or local authorities about the language requirements of the local population and the Welsh language policies in place at the site.

- Please indicate in your answer to this question whose advice you have sought on this issue, as this will provide assurance to the main REC that the local issues have been appropriately addressed. This will be especially helpful where the main REC is in another UK country. The main REC may seek its own advice from local RECs for the research sites if necessary.

- If Welsh translations of patient information and consent forms are required, a list of translators can be obtained from the Welsh Language Board (0129 20 224744).

**Additional guidance for research involving prisoners**

- Certain prisons have a large population of non-English speaking prisoners and the applicant is asked to ensure that the information sheets are translated into the relevant languages or to provide interpreters. Excluding those prisoners who have the most problems with understanding English might well exclude those with the most significant physical and mental health needs and thus bias the results of the study.
Question A34 Providing information during the study

- Participants should be aware of any new information that emerges during the research, which might affect their participation. You should describe your strategy for looking for, and disseminating, such information.

Question A35 Loss of capacity to consent

- The following guidance applies to all research except for clinical trials of investigational medicinal products (CTIMPs). (Issues relating to consent in CTIMPs are governed by Schedule 1 to the Medicines for Human Use (Clinical Trials) Regulations 2004.)

For other research:

- Consent under common law cannot generally be said to endure the loss of capacity to consent by a participant.

- It is therefore necessary for researchers to consider what steps they would take in the event of a participant losing capacity to consent during the project.

- You should tick the most appropriate option in A35 and give brief details of the action that would be taken, particularly in relation to tissue samples or data already collected.

- Researchers are not obliged to monitor the capacity of participants proactively during the study. However, they should be ready to address the consequences of a loss of capacity should this come to their attention at any point.

Option 1 – Withdrawal of participant and anonymisation of tissue/data

- The participant would be withdrawn from the study. No further clinical or non-clinical interventions or procedures would be carried out on the participant under the study protocol. No new samples or personal data would be collected.

- Subject to ethical approval, tissue samples or data already collected in relation to the participant may be retained and used for the purposes for which consent has already been given, provided they are effectively anonymised and no longer identifiable to the research team or any other persons to whom access will be given. Further data may be collected provided that it is received in anonymised form and is not identifiable; consent for this is not a legal requirement.

- Alternatively, samples and data may be disposed of.

Option 2 – Withdrawal of participant, retention of identifiable tissue/data

- The participant would be withdrawn from the study. No further clinical or non-clinical interventions or procedures would be carried out on the participant
under the study protocol. No new samples or personal data would be collected.

- Subject to ethical approval, tissue samples and data already collected may be retained in identifiable form and used in the research provided that properly informed and expressed consent for this was given prior to the onset of incapacity.

- If you select this option, you should cover the issue explicitly in the participant information sheet. Participants should be aware that in the (perhaps unlikely) event of a loss of capacity, the research team would retain tissue and personal data collected and continue to use it confidentially in connection with the purposes for which consent is being sought. This could include further research after the current project has ended provided that this is made clear in the information for participants.

- The researcher may then continue to rely on such consent following loss of capacity.

- Approval will not be required under either the Mental Capacity Act 2005 (in England and Wales) or the Adults with Incapacity (Scotland) Act 2000.

**Option 3 – Participant remains in the research study**

- Under this option, the participant would remain in the research study and may undergo further interventions and procedures, including collection of new samples and personal data, as required by the protocol.

- This would constitute “intrusive research” for the purposes of the Mental Capacity Act 2005 in England and Wales and would require approval under section 30 of the Act. In Scotland, approval would be required under section 51 of the Adults with Incapacity (Scotland) Act 2000. In Northern Ireland, the common law requirements would apply.

- If you select this option, you should complete the detailed questions in Part B Section 6 of the application form. Note that these questions would apply only to the situation following loss of capacity, not to the initial inclusion of participants with consent. Your answers in Part B Section 6 should justify the proposal to undertake further research following loss of capacity and give information about the procedures you would follow if this occurred.

- This option may apply where research participants are suffering from an impairing condition and their capacity to consent is borderline or fluctuating. Participants could be initially recruited with consent but lose capacity during the research. It may be reasonable to continue to include them in the research, subject to appropriate safeguards, to achieve the research objectives and realise the benefits either to participants themselves and/or to science and society.

- Continued research on participants following loss of capacity would only be approved by the REC if the research met in full the criteria for including such participants in research, i.e. the nature of the research is such that it would have been justified to include participants lacking capacity from the outset.
Option 4 – Not applicable as informed consent will not be sought from any participants

- In some cases, the issues around loss of capacity will not arise at all because it is not proposed to seek informed consent from any participants in the study.

- This could apply in the following cases:
  - Research using tissue samples where consent is not a legal requirement under the Human Tissue Act or the Human Tissue (Scotland) Act.
  - Research using data where no identifiable data will be processed by researchers outside the clinical team.
  - Research involving the processing of identifiable patient data without consent with the approval of the National Information Governance Board for Health and Social Care (NIGB) (formerly PIAG).

- You may also select “not applicable” where the research only involves children without capacity and will rely in all cases on informed consent from a person with parental responsibility. However, if informed consent is to be obtained from children considered capable of giving consent for themselves under the Gillick principles, consideration should be given to the implications of loss of capacity during the study and one of the other options should be selected.

Further guidance

- The Department of Health is preparing further guidance on loss of capacity in an information note on “The Mental Capacity Act and consent for research”. The guidance will be made available on the NRES website at http://www.nres.npsa.nhs.uk/applicants/help/guidance.htm as soon as it is published.

Questions A36-A45 Confidentiality - general guidance

- The safe acquisition, storage and transmission of personal data are major ethical considerations, and there are also legal requirements in the Data Protection Act.

- It is the researcher’s responsibility to ensure compliance with the legal requirements of the DPA.

- The REC cannot give a legal opinion, but its advice, based on its experience, may help you decide when further legal advice might be necessary.

- For research conducted with patients, tissue or data identified through the NHS, the NHS organisation will review the compliance of the arrangements described with the Data Protection Act and NHS codes of practice. Similar responsibilities in relation to Data Protection Act and codes of practice fall to local authorities and other care providers hosting research involving access to service user data.

- The researcher should give full details of any plans to share data with others
(particularly if it is identifiable), and especially if it is to be exported outside the UK.

- For general guidance on use of personal information in research, see the MRC guidelines available at: http://www.mrc.ac.uk/PolicyGuidance/EthicsAndGovernance/PublicationsinEthicsGovernance/index.htm

The Caldicott Principles

**Principle 1 Justify the purpose**

Every proposed use or transfer of person-identifiable information within or from an organisation should be clearly defined and scrutinised by an appropriate guardian, with continuing uses regularly reviewed.

**Principle 2 Do not use person-identifiable information unless it is absolutely necessary**

Person-identifiable information items should not be included unless it is essential for the specified purpose(s) of that data flow. The need for patients to be identified should be considered at each stage of satisfying the purpose(s).

**Principle 3 Use the minimum necessary person-identifiable information**

Where use of person-identifiable information is considered to be essential, the inclusion of each individual item of information should be considered and justified so that the minimum amount of identifiable information is transferred or accessible as is necessary for a given function to be carried out.

**Principle 4 Access to person-identifiable information should be given on a strict need-to-know basis**

Only those individuals who need access to person-identifiable information should have access to it, and they should only have access to the information items that they need to see. This may mean introducing access controls or splitting information flows where one information flow is used for several purposes.

**Principle 5 Everyone with access to person-identifiable information should be aware of their responsibilities.**

Action should be taken to ensure that those handling person-identifiable information – both clinical and non-clinical staff – are made fully aware of their responsibilities and obligations to respect confidentiality.

**Principle 6 Understand and comply with the law**

Every use of person-identifiable information must be lawful. Someone in each organisation handling confidential information should be responsible for ensuring that the organisation complies with legal requirements.
<table>
<thead>
<tr>
<th>Activity</th>
<th>Guidance</th>
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<tbody>
<tr>
<td>Access to medical or social care records by those outside the direct</td>
<td>This should only be undertaken with consent or S60 approval.</td>
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<tr>
<td>healthcare or care team</td>
<td></td>
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<tr>
<td>Electronic transfer of data by magnetic or optical media, email or</td>
<td>Where personal data is transferred electronically, data should be encrypted during transfer.</td>
</tr>
<tr>
<td>computer networks</td>
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<tr>
<td>Sharing of data with other organisations</td>
<td>Except where such disclosure has consent or approval under S60, only anonymised data should be shared. Where data has been effectively</td>
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<td>pseudonymised it should only be shared on the basis that the recipient cannot disclose pseudonymised data to third parties and is not</td>
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<td></td>
<td>permitted to link the data with other data which might render the information more identifiable.</td>
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<tr>
<td>Export of data outside the EEA</td>
<td>In general, patient level data should not be transferred outside of the European Economic Area (EEA). This is because other countries do not</td>
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<td>have the same legal framework or protections for patient data. Even where this is the case, it is difficult to manage and monitor the use of</td>
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<td>data to ensure it is safeguarded appropriately and is not misused.</td>
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<td>Use of personal addresses, postcodes, faxes, emails or telephone</td>
<td>It should be remembered that such personal contact details can be sensitive information, either because individuals are concerned about</td>
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<td>numbers</td>
<td>identity theft or because of domestic violence etc.</td>
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<tr>
<td>Publication of direct quotations from respondents</td>
<td>Should be anonymised (but linked to identifiable securely-held transcripts).</td>
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<tr>
<td>Publication of data that might allow identification of individuals</td>
<td>In general, publication of case histories should be effectively anonymised. Where identification is possible it is essential that this is</td>
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<td>only undertaken with consent.</td>
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<tr>
<td>Storage of personal data on manual files (including X-rays)</td>
<td>Paper and other manual files should be appropriately filed and stored securely.</td>
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<tr>
<td>Storage on NHS computers</td>
<td>Appropriate access controls need to be in place to ensure that access to confidential research information is restricted to those who need</td>
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<td>access.</td>
</tr>
<tr>
<td>Storage on home or other personal computers</td>
<td>Under no circumstances should patients’ or research participants’ personal data be stored on a home or other personal computer.</td>
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<tr>
<td>Storage on university computers</td>
<td>Appropriate access controls need to be in place to ensure that access to confidential research information is restricted to those who need</td>
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<td>access.</td>
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</table>
**Storage on private company computers**

Appropriate access controls need to be in place to ensure that access to confidential research information is restricted to those who need access.

**Storage on laptop computers**

Use of laptops and other portable devices is to be avoided. Where it is necessary for them to be used, data must be encrypted and the data uploaded onto a secure server or desktop as soon as possible and the data removed from the portable device as soon as possible and using appropriate data destruction software.

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**Question A37  Physical security of data storage**

- Please describe where all personal data of participants will be stored. Explain if filing cabinets, cupboards and/or rooms will be locked and who has access. Give details of security arrangements for personal data held on computer, especially where laptop computers are used.

- Information about security arrangements should *not* be detailed enough to enable access by anyone viewing this application.

- Signed consent forms should not be stored with participant data, including interview notes and transcripts.

**Question A38  Confidentiality of data**

- Please give details of the overall arrangements to respect confidentiality of personal data and meet the requirements of the Data Protection Act. Give details of policies or guidance that will be followed, e.g. NHS Code of Confidentiality.

- For NIGB applications, please provide details of confidentiality policies, confidentiality clauses in staff contracts and measures to ensure that all staff are aware of and work to appropriate confidentiality standards.

**Question A39  Separation of identifiers from clinical data**

- This question applies only to applications to the National Information Governance Board (NIGB) to process identifiable patient data without consent.

**Question A40  Access to personal data during the study**

*Access to data for monitoring and audit*

- Monitors and auditors from pharmaceutical companies, trial centres and NHS R&D offices, and regulatory inspectors may require access to patients’ clinical notes to verify or cross check data. Review bodies are likely to accept protocols that incorporate such arrangements provided that the following guidelines are
observed:

- Participants are told in the information sheet who may have access to their medical records and trial data, and why.
- Such individuals must have an appropriate professional background. If there is concern regarding the appropriateness of a person this should be checked with the REC.
- Participants have signed a consent form to state they have read the participant information sheet and understood the information it contains.
- In some circumstances it may be appropriate to add that the data in an anonymous form may be used for preparation of the trial report, and for submission to Government agencies as part of the procedures for marketing any new medicine.

**Question A41  Analysis of data and location**

- Explain where the data will be analysed and the arrangements for ensuring confidentiality of personal data during transfer of data. Give details of any plans to export data outside the UK.

**Question A42  Data custodian**

- Give details of who will be responsible for the use, security and management of all data generated by the study.

**Question A43  Retention of identifiable data**

- Please note this question only relates to retention of personal data.
- Where valid consent is in place, identifiable data may be retained, but consideration should be given at the end of the study to whether it is possible to reduce the identifiability of data retained following record linkage and validation.
- For general guidance on use of personal information in research, see the MRC guidelines available at: [http://www.mrc.ac.uk/PolicyGuidance/EthicsAndGovernance/PublicationsinEthicsGovernance/index.htm](http://www.mrc.ac.uk/PolicyGuidance/EthicsAndGovernance/PublicationsinEthicsGovernance/index.htm)
- Where data is to be processed without consent using Section 251 support (i.e. with approval from the National Information Governance Board), there is a requirement to reduce the identifiability of the data at the earliest reasonable point and to anonymise/pseudonymise the data effectively at the end of the study. Describe how patient identifiable information will be destroyed once work is complete. You should not include details of any data destruction software to be employed here but include it instead in Part B Section 9 of IRAS.

**Question A44 and A45  Data storage**
• Please indicate in your answer to A45 whether the proposed retention period and storage arrangements are subject to any policy or guidance from the research host or your employer. Explain how and when data will be destroyed.

Audio/video recording and the observation of patients

• Informed consent should be obtained from the research participant(s) involved. The participant information sheet should specify the uses to which the material might be put, how the material will be stored and how and when it will be destroyed. It should be noted that videos should not be used for commercial purposes.

Question A46  Payment to research participants

Payments and benefits

• Payment of participants should be ethically justified. The REC will wish to be reassured that research participants are not being paid for taking risks or that payments are set at a level which would unduly influence participants.

• Information on any payments or benefits must be included in the participant information sheet.

• If proposing payments, you should consider the possibility of non-cash payments, particularly for children (e.g. book tokens).

• If you decide to introduce payments after receiving a favourable opinion from the main REC, these must be notified to the REC as a substantial amendment and ethically reviewed before being implemented.

Reimbursement of expenses

• Research participants should not be substantially out of pocket as a result of taking part in a research study.

• Payment in cash or kind to participants must only be for costs such as travel expenses, child-care expenses, meals and demonstrable loss of earnings etc.

• Consideration should be given to any expense involved in returning postal questionnaires.

• If it is not possible to reimburse such expenses this should be explained before the research participant is recruited. A clear statement should be included in the participant information sheet setting out the position on reimbursement.

Payment models

<table>
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<tr>
<th>Justification</th>
<th>Market Model</th>
<th>Wage Payment Model</th>
<th>Reimbursement Model</th>
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<tr>
<td>Recruitment of participants is vital to research and the</td>
<td>Participation in research takes time and effort and</td>
<td>There should not be any financial sacrifice by the research</td>
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monetary incentive will facilitate this. may include uncomfortable procedures. participant.

Function Incentive Compensation for time and effort Reimbursement of expenses

Requirements of ICH GCP (applies to medicinal trials)

3.1.2 The IRB/IEC should obtain information about payments and compensation available to subjects.

3.1.8 The IRB/IEC should review both the amount and method of payment to subjects to assure that neither presents problems of coercion or undue influence to trial subjects. Payments to a subject should be prorated and not wholly contingent on completion of the trial by the subject.

3.1.9 The IRB/IEC should ensure that information regarding payment to subjects, including the methods, amounts and schedule of payment to trial subjects, is set forth in the written informed consent form and any other written information to be provided to subjects. The way payment will be prorated should be specified.

4.8.10 Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following: the anticipated, prorated payment, if any, to the subject for participating in the trial.

Additional guidance for research involving prisoners

- Applicants who are considering offering a payment to participants should seek the advice of the prison governor on its suitability. Payment includes vouchers or gifts as well as actual cash.

Questions A47 Payment to researchers

- This question is concerned with “in pocket” financial payments or additional benefits to be provided direct to researchers personally, over and above the costs of conducting the research. Such payments could include, for example, contributions to a library, additional equipment not actually required for the research, social events etc. The question is not concerned with payments agreed between the sponsor and NHS care organisations or other sites to reimburse the costs of hosting the research.

- Personal payments or benefits to researchers should not be set at a level to cause undue influence.

- You should record the fact that researchers are receiving personal payments or benefits in the participant information sheet. See the guidance on informed
Question A48  Conflicts of interest

- Information should be given about any potential conflict of interest for the Chief Investigator or any other investigator or key collaborator in undertaking the proposed research.

Question A49-1  General Practitioner

- In the case of any clinical research, the participant’s GP (or other health care professional responsible for the care of the participant) should be informed that his/her patient has agreed to take part. It is the Chief Investigator’s responsibility to ensure that the necessary arrangements are made.

- A copy of the proposed information sheet or letter to the GP/health professional must be submitted with all applications.

- It is important to ensure that the health of the research participants at the time of recruitment and during the study is appropriate to the demands made by the research. Special care must be taken to advise the GP/health professional of any aspects of the project that will affect day-to-day treatment given by them. In particular they should be informed about any trial medication, making clear any side effects and potential interactions with other drugs.

- In the case of non-clinical research, it is a matter of judgement whether GPs or other health professionals should be informed. Applicants should consider whether study participation could have implications for care by other professionals or it is possible that participants could approach them for advice about any aspect of the study. If so, it may be helpful for the GP/health professional to be aware of their patient’s involvement. Advice on this may be sought from the REC.

Question A49-2  Permission to notify the GP

- The research participant should be advised in the participant information sheet that his/her GP/health professional will be approached.

- Normally the REC would expect that any clinical research participant who refused permission to approach their GP should be excluded from the project. If you propose an exception to this requirement (e.g. in a GUM clinic) you must fully justify this to the REC making clear any special arrangements.

Question A50  Study registration

Policy and guidance

- The Declaration of Helsinki of the World Medical Association (revised 18 October 2008 at Seoul) states:
“19. Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.”


- It is government policy in the UK to promote registration of clinical studies and public access to research findings affecting health and social care. For more information see [http://www.dh.gov.uk/en/Researchanddevelopment/A-Z/Researchgovernance/index.htm](http://www.dh.gov.uk/en/Researchanddevelopment/A-Z/Researchgovernance/index.htm)

**Options for registration**

- The International Standard Randomised Controlled Trial Number (ISRCTN) is a simple numeric system for the identification of clinical trials worldwide. The ISRCTN Register accepts the registration of randomised controlled trials and any other research study designed to assess the efficacy of health interventions in a human population. This includes both observational and interventional studies. The Register provides a unique number that can be used to track each trial throughout its lifecycle from initial protocol to publication of results. For more details go to: [http://www.controlled-trials.com/isrctn/isrctn_faqs.asp](http://www.controlled-trials.com/isrctn/isrctn_faqs.asp).

- Alternatively, clinical research may be registered at [http://clinicaltrials.gov](http://clinicaltrials.gov) (a register of studies in the United States and around the world) or through the metaRegister of controlled trials at [http://www.controlled-trials.com/mrct/mrct_about](http://www.controlled-trials.com/mrct/mrct_about).

- For other types of research, registration is also encouraged wherever possible. You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists.

- The Department of Health wishes to encourage the registration of social care research with the National Research Register for Social Care. This is hosted by the Social Care Institute of Excellence (SCIE): visit [www.scie.org.uk](http://www.scie.org.uk) or call 0207 089 6840 and ask for the Register.

- Further guidance will be added on options for registering non-clinical studies in due course.

- In general, registration is not expected for projects undertaken entirely for educational purposes below doctoral level.

**Question A51 Dissemination of results and publication**

- The results of research should be reported, whether through publication in peer reviewed journals or other means of dissemination. Negative as well as positive
results should be published, or at least made publicly available.

- Consideration should be given to providing feedback on the results to research participants, interested groups and communities (see Question A53).

**Question A52  Ensuring anonymity of identifiable data in publications**

- Care should be taken when considering publishing data or case histories to ensure the anonymity of the relevant patients, service users, staff and other participants. For example, where tables of data are to be published, care should be taken where the values of cells are small numbers as, in combination with other information, this could render information potentially identifiable. Particular care needs to be taken in relation to 0 as this can create an inference in relation to other cells. For further information on this, please see the ONS guidance on the publication of statistics in relation to small numbers, [www.statistics.gov.uk/about/consultations/disclosure.asp](http://www.statistics.gov.uk/about/consultations/disclosure.asp).

- In relation to case histories care should be taken that the combination of incidental details e.g. details about occupation, location, age and ethnicity, do not lead to individuals being identifiable.

**Question A53  Informing participants of the results**

- It is good practice to disseminate the results of research to research participants and other interested groups or communities. This provides feedback to participants on the outcome of research towards which they have contributed. Consideration should be given to providing a summary sheet of the findings or letting participants know where they can access the results.

- In addition, it may be important to inform patient groups, service user groups or communities of any findings that are relevant to future care.

- Information about publication arrangements should be included in the participant information sheet.

5. **SCIENTIFIC CRITIQUE, STATISTICS AND ANALYSIS METHODS**

**Question A54  Scientific critique**

- The sponsor of the research is responsible for the assessment of the scientific quality of the proposed research. The research proposal must be subjected to review by experts in the relevant fields able to offer independent advice on its quality. Arrangements for review should be commensurate with the scale of the research and the potential risks or burdens involved for participants.

- Protocols should already have been subjected to scientific critique before formal applications to conduct research are submitted. Exceptions may be permitted if there is a satisfactory explanation.

- Please support your answer by explaining the nature of the review process. A
copy of any available comments or scientific critique reports from referees or review committees should be enclosed with the application, together with any correspondence which explains how issues raised by scientific critique have been resolved.

- In the absence of any evidence of scientific critique, the REC may require such an assessment to be arranged by the applicant or sponsor before confirming its final opinion on the application. The 60 day clock for the ethical review will stop during this process. Alternatively the REC may issue an unfavourable opinion and advise that scientific critique should be obtained before a fresh application is submitted.

- It is recognised that student research has an educational and training value, and proposals (especially from undergraduates) will not necessarily be of the same importance or scientific quality as those submitted by professional researchers. However, research proposals from students should be reviewed at least by the academic supervisor. Review bodies will expect the academic supervisor to sign the declaration in Part D of IRAS. This provides assurance that the proposal has identified a valid research question and is suitably designed taking into account the limitations of time and resources.

Additional guidance for applications to the Social Care REC

- Please select the multi-centre research group option for review by the Association of Directors of Adult Social Services.

Question A55    Assessment by Expert Advisory Group and CHM

- If your clinical trial falls into the category of trials that require advice from EAG/CHM (see also Question 16), please give details of the status of the application to MHRA for Clinical Trial Authorisation and, where applicable, any changes made to the proposed trial in the light of the expert advice. Any relevant correspondence with the MHRA should be enclosed with the REC application.

- Consider carefully when to make a submission for ethical review. You may opt to apply either sequentially or in parallel. The following points should be considered:
  - It is possible that for trials involving higher risk compounds, advice from EAG/CHM will lead to changes in your protocol, with potential implications for ethical review. If you apply to the REC prior to having received EAG/CHM advice, you must notify the REC promptly of any changes made that may be relevant to the ethics application.
  - In general, a sequential process may be preferable; consider whether factors such as the novelty of the compound including its mode of action and target, the relevance of animal models and the completeness of the data package available may result in protocol changes following EAG/CHM review.
  - Making sequential applications to EAG/CHM first, followed by ethics, allows the REC to receive the final version of the protocol and be fully informed about the outcome of the CTA application when undertaking its review.
• The Commission on Human Medicines (CHM) will require certain information when you make an application for First-in-Human trials with novel compounds, and applications for trials with integrin antagonists. The details are published on the MHRA’s website: http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=986

Question A56  Statistical review

• Assurance should be provided that the statistical aspects of the protocol have been reviewed by an individual or a department with relevant expertise.

• Any person involved in providing expert statistical advice should be satisfied that they have the necessary expertise, taking into account the nature of the research and the methodology involved. Statistical advice may be provided by one of the investigators or key collaborators named on the application form, provided that they have relevant expertise.

• The individual providing statistical advice should normally be named. If he/she has provided advice in confidence, the name of the department and institution should be given.

• If it is not clear to a review body that the individual statistician or department concerned has relevant expertise, it may request sight of a CV or contact the statistician or department directly to seek clarification of their qualifications and experience.

• If the statistical aspects of the protocol are based on expert advice and appear sound, RECs will usually accept this without requirement for further review. If expert advice has not been sought and/or the REC has doubts about the statistical soundness of the protocol, it may request that the Chief Investigator obtains independent statistical review as part of the request for further information after the REC meeting. Alternatively the REC may commission its own review.

• In the case of undergraduate research using simple designs, it will normally be acceptable for statistical advice to be provided by the academic supervisor or another person with expertise in research methodology.

Question A57  Primary outcome measure

• In quantitative research, the primary outcome measure takes the form of a statement expressing how, in numerical terms, the primary objective of the study will be met from the data collected. For example, in a study of hypertension, the primary outcome measure might be the systolic blood pressure at the final visit.

• There should normally be only one primary outcome measure, though exceptionally there may be more.

Question A58  Secondary outcome measures
• Statements expressing how, in numerical terms, other results of the study will be determined from the data collected. There may be no secondary outcome measures, or one, or more than one.

**Question A59 Sample size**

• The sample for the research may include “participants” who are not approached but whose records or samples are to be studied.

• The number of participants is an ethical and methodological issue in any study. The number should be sufficient to achieve worthwhile results but should not be so high as to involve unnecessary recruitment and burdens for participants.

• In the case of research involving qualitative methods only, it is recognised that the number of participants may be small and will not be determined using a statistical power calculation. However, reviewers will find it helpful to know who you are targeting and why you are targeting them. Describe the sampling approach that will be used (theoretical, purposive, snowball, convenience sampling, etc) and give a rationale. Indicate the basis for deciding on the required number of participants and why this number will result in data saturation.

• If a formal sample size calculation is used, this should refer to the primary objective, or in the case of more than one primary objective, the one giving rise to the largest sample size. Sufficient information should be given to allow review bodies to reproduce and check the calculation.

• Sample size calculations will typically involve the following steps:

  - In the case of a **comparison between two or more groups**, the calculation should include the significance level and power of the test to be carried out, as well as stating and justifying the difference in the primary outcome to be detected between the groups. It is important that the difference is not unrealistically high as this could lead to an underestimate of the required sample size.

  - For a **single-group study**, the sample size should be justified by reference to a confidence interval (normally 95%), e.g. around the mean of the primary outcome measure.

• If a more complex study design is chosen, for example seeking to show that two groups’ responses are equivalent, specialist advice will be needed.

• The number of participants may have been decided pragmatically rather than by a formal calculation, for example where a rare disease is being studied, or where study resources are limited. If this is the case, any limitations that have restricted the sample size should be stated, e.g. what size of effect can be detected for the given power and significance.

**Question A61 Randomisation**

• It is helpful to give the intended mechanism of randomisation, for example a sequence of opaque envelopes, or telephone or internet randomisation. It should
be evident to reviewers that the concept of random allocation has been correctly understood, and will be seen to be free from bias.

**Question A62  Methods of analysis**

- For studies with a quantitative (numerical) outcome, give details of the methods that will be used to obtain the results for the primary and secondary outcomes, including methods of summarising the data with numbers and graphs, and the main statistical tests to be used where comparisons are to be made. It is not necessary to give every detail in advance.

- Describe how you will handle missing data, for example due to withdrawal or non-compliance.

- For studies using qualitative methods, researchers should:

  - Outline in simple terms exactly how the data from the study will be managed and analysed. For example, will it be arranged into themes? If so, will this be done by use of a qualitative data analysis tool, by manual analysis and coding of the data, or by some other means? You should state why this is your chosen method of analysis. Give a brief description of any techniques to be used (e.g. framework, content or thematic analysis) for the benefit of lay members. Refer to any qualitative data software to be used.

  - Indicate whether or not member checking will be used (with a brief explanation of what this means for the benefit of lay members). Member checking is not essential but is good practice. Alternatively, you can ask others who are part of the study or independent researchers to check your themes and categories to make sure you have not over-represented some aspect of your data.

6. **MANAGEMENT OF THE RESEARCH**

**Question A63  Other key collaborators**

- Give names of any other key collaborators of the Chief Investigator or key members of the CI’s research team. All co-holders of grants or protocol co-authors should be named. (N.B. Do not include researchers at all the local sites in a multi-centre project – these are to be entered in the Site-Specific Information Form for each site by the Principal Investigator – unless any of them are also a key collaborator at “national” level.) The sponsor of the research is responsible for ensuring key researchers involved in the research have the relevant experience and expertise.

- Where the CI or any of the key collaborators named at A63 are members or deputy members of an ethics committee, the committee is not permitted to review the application. Advice should be sought from the REC concerned or from NRES operational management about arrangements to allocate the application to another REC.
Question A64 Sponsorship

- Any research requiring the collaboration of the NHS must have an individual or organisation willing and able to take on the responsibilities of the research sponsor.

- The prospective sponsor must be named in this section. You should contact your R&D office for advice about sponsorship issues before submitting the application.

- It is possible that the duties of the sponsor could be shared between more than one party. If this applies, enter as the "lead sponsor" the one nominated to receive copies of correspondence from review bodies relating to the application. Enter further details of the co-sponsors and explain how the responsibilities of sponsorship will be assigned, in particular those relating to monitoring of the research and provision of insurance or indemnity.

- The sponsor is the individual, company, institution or organisation, which takes on ultimate responsibility for the initiation, management (or arranging the initiation and management) of and/or financing (or arranging the financing) for that research. The sponsor takes primary responsibility for ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting.

- The sponsor is usually, but does not have to be, the main funder of the research. It can also, for example, be the employer of the Chief Investigator, the educational institution (e.g. for student research), or the care organisation where the research is to take place.

- It is your responsibility to ensure that the sponsor(s) are aware of your proposal and accepts these responsibilities. A representative of the lead sponsor should complete the sponsor declaration in Part D of IRAS.

Sponsorship of CTIMPs

- For any clinical trial of an investigational medicinal product (CTIMP) it is a legal requirement for the trial to be sponsored.

- If a sponsor of a CTIMP is a commercial or other non-NHS body, a copy of the insurance or indemnity policy for the trial should be included with the application. The insurance should be sufficient to cover any potential liability of the sponsor arising from the management of the research.

Requirement to appoint a legal representative in a CTIMP

- If the main sponsor of a CTIMP is not based in the European Economic Area (EEA), e.g. an American or Japanese company, it is a statutory requirement to appoint a legal representative based in the EEA for the purposes of the trial.

- The EEA comprises the countries in the European Union together with Iceland, Liechtenstein and Norway.

- The legal representative:
  - May be an individual person or a representative of a corporate entity
- Does not have to be a legally qualified person
- Should be willing to act as the agent of the sponsor in the event of any legal proceedings instituted in the EEA (e.g. for service of legal documents)
- Should be established and contactable at an address in the EEA
- Does not assume any of the legal liabilities of the sponsor(s) for the trial by virtue of the role of legal representative and does not therefore require insurance or indemnity to meet such liabilities, but
- May in some cases enter into specific contractual arrangements to undertake some or all of the statutory duties of the sponsor in relation to the trial, in which case the legal representative would also be regarded as a co-sponsor and would then require insurance or indemnity cover.

In all cases, evidence should be provided with the application that the legal representative is willing to take on the role of legal representative and is established at an address in the EEA. For example, a copy of correspondence between the sponsor and legal representative on appropriate headed paper could be enclosed, or a copy of a contract.

Where the legal representative is also a co-sponsor, this should be separately recorded on the application form and details given of the allocation of sponsorship responsibilities. Evidence of insurance or indemnity cover should be provided.

**Clinical investigations of medical devices sponsored by the manufacturer**

- The Medical Devices Directive 93/42/EEC requires that a manufacturer who places devices on the market under his own name and does not have a registered place of business in a Member State must designate an Authorised Representative, who does have a registered place of business in the Community, to act on their behalf.

- In the case of clinical investigations of non-CE marked medical devices, the Medical Devices Directive does not require a manufacturer to appoint an Authorised Representative until the point that the device is placed on the market in Europe. In this circumstance, details of the Authorised Representative are only required if the Authorised Representative has been appointed at the time of application. Please enter the details in the Legal Representative section.

**Legal representatives – studies other than CTIMPs and devices investigations**

- For studies other than clinical trials of investigational medicinal products or clinical investigations of medical devices sponsored by the manufacturer, a legal representative in the UK must be nominated if the sponsor is established outside the UK. This is a requirement of the Research Governance Framework for Health and Social Care.

- If a legal representative is required, please enter the details in the Legal Representative section.

- The legal representative:
  - May be an individual person or a representative of a corporate entity
  - Does not have to be a legally qualified person
  - Should be willing to act as the agent of the sponsor in the event of any legal proceedings instituted in the UK (e.g. for service of legal documents)
  - Should be established and contactable at an address in the UK
Does not assume any of the legal liabilities of the sponsor(s) for the study by virtue of the role of legal representative and does not therefore require insurance or indemnity to meet such liabilities, but may in some cases enter into specific contractual arrangements to undertake some or all of the statutory duties of the sponsor in relation to the study, in which case the legal representative would also be regarded as a co-sponsor and would then require insurance or indemnity cover.

In all cases, evidence should be provided with the application that the legal representative is willing to take on the role of legal representative and is established at an address in the UK. For example, a copy of correspondence between the sponsor and legal representative on appropriate headed paper could be enclosed, or a copy of a contract.

**Question A65  Funding**

- The information required here is the funding of the project costs of the researcher (which might include a contribution to salaries, other costs of research staff time, additional equipment and reagents, IT costs, administrative expenses etc). It does not include any funding agreed with the host institution through a research contract to pay for the costs of hosting the research.

- Applicants are strongly advised to secure any project funding required from bodies outside the NHS before submitting the application for ethical review. If funding has not been secured, and the funding body later requires changes to be made to the proposal, these would require further review by the REC. If the change were major, the REC would require submission of a new application.

**Question A66  Subcontractors**

- The sponsor retains the ultimate accountability for the research. However, if responsibility for any aspects of the research have been delegated to a subcontractor such as a Contract Research Organisation or Site Management Organisation, reviewers will wish to know this and you should make clear the remit of the delegated responsibility.

- Give the name of the organisation, including the name of a contact person within it. This should be the person reviewers can contact in case of queries.

**Question A67  Previous rejection of the research by an ethics committee**

- If the research has been rejected previously, the REC will wish to see a copy of the unfavourable opinion letter. You should also provide a covering letter explaining how the issues of concern have been addressed in this application.

- It does not necessarily follow that rejection in another country will result in rejection in the UK.

**Question A68  Lead R&D contact**

- The lead NHS R&D contact may be the R&D contact for:
- The Chief Investigator’s employing NHS organisation
- A partner NHS organisation of the university employing the Chief Investigator
- A main NHS collaborator

- The lead R&D office should be contacted at the earliest possible stage to advise and support the research through the review process.

**Question A69 Proposed study dates and duration**

- Give the proposed start date and the proposed end date of the research. You may not know these dates exactly, but a rough estimate should be supplied.

- Allow sufficient time in the start date for your applications to all bodies who need to approve the research.

- For CTIMPs, please give planned end dates both for the final clinical intervention (e.g. last administration of IMP) and the conclusion of all trial procedures (i.e. last data capture). The protocol should include a definition of the end of the study, and any change to this definition would need to be notified to the main REC as a substantial amendment.

- For all other studies, the end date is the date on which all procedures specified in the protocol are concluded.

**Question A70 Definition of the end of the trial**

- This question applies only to CTIMPs being conducted under the Medicines for Human Use (Clinical Trials) Regulations 2004.

- Please indicate how the end of the trial is defined in the protocol. The guidance from the European Commission states that the protocol should include a definition of the end of the study. Any change to this definition would need to be notified to the main REC and the MHRA as a substantial amendment.

- Further guidance is available in paragraph 4.3 of the *Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial* (ENTR/CT1, Revision 2, October 2005), available at:


**Question A72 Host organisations**

- Please give the approximate number of each type of research site you plan to involve in the study, even if you have not yet approached the host organisations concerned.

- A research site is defined as the single organisation responsible for conducting the research at a particular locality. Where the research will be conducted at more than one location within the same organisation (for example, where the departments or clinics involved are dispersed at different hospitals within an
• Research sites are organisations responsible for participant-related research procedures specified in the protocol - including recruitment and informed consent. Referral of a patient or service user for assessment and possible recruitment is not part of the conduct of the study. The following are not considered to be research sites:

  - Clinicians or clinical units making referrals to the research team.
  - Clinicians, clinical units or organisations involved only in the identification of potential participants and/or facilitating recruitment by the research team, not responsible for informed consent or any other protocol procedures ("participant identification centres")
  - Research units undertaking support functions, e.g. project management, site monitoring, data analysis or report writing.

• For further guidance on research sites, see Section 4 of the NRES Standard Operating Procedures [http://www.nres.npsa.nhs.uk/news-and-publications/publications/standard-operating-procedures].

**Question A73  Identification of participants**

• Any organisations involved only in identification of potential participants are described as “participant identification centres”. If any of these centres are NHS organisations, details should be entered in Part C of IRAS.

• For NHS participant identification centres, describe the use of staff, time and resources at each participant identification centre and the arrangements for covering these costs. Please estimate the time that will be taken to identify potential participants for the study at each centre. Include the time taken to send letters of invitation or provide information to potential participants.

**Question A74  Monitoring and auditing research**

• It is the responsibility of the research sponsor(s) to ensure arrangements and systems are in place for the management and monitoring of research. Particular tasks within this responsibility may be delegated to particular individuals or organisations.

• The arrangements for monitoring and auditing the conduct of the study should reflect the allocation of responsibilities set out in the Research Governance Framework.

• In the case of CTIMPs, sponsors and investigators have statutory obligations relating to pharmacovigilance under Part 5 of the Medicines for Human Use (Clinical Trials) Regulations 2004.

**Question A75  Data Monitoring Committee**

• For certain kinds of clinical trial, for example those with predicted high morbidity or mortality, or double-blind trials with unknown or uncertain risks, sponsors are
strongly recommended to establish an independent Data Monitoring Committee (sometimes called a Data Safety and Monitoring Committee) to advise on safety issues. A DMC is usually composed of statisticians and clinical investigators not directly involved with the trial. The DMC is responsible for reviewing the data and performing interim analyses.

- For such trials, stopping rules relating to toxicity or outcome should also be considered and agreed with the DMC.

- A detailed Guideline on Data Monitoring Committees was issued in July 2005 by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMEA) and is available at:
  

**A76 Indemnity, insurance and compensation – general guidance**

(Further guidance on each question in A76 and A77 is available by clicking on the links next to the questions.)

- **Indemnity** is an assurance that payment will be made to cover the legal liability of another person in the event of a claim. **Insurance** is a contractual arrangement to pay a sum of money to another person in the event of verified loss or damage. **No fault compensation** is an arrangement to pay compensation for harm where no legal liability arises or is admitted.

- Legal liability may arise from fault in the management, design or conduct of the research. The liabilities may fall on different parties in each case.

- It is the sponsor’s responsibility to ensure that arrangements are in place before the study starts to cover the potential legal liabilities of the various parties arising from the research.

- The main REC must be assured that there are appropriate arrangements to compensate participants in the event of harm due to fault in the management, design or conduct of the research. The REC will not expect to see full details and proof of all arrangements. However, applicants must be clear about all the arrangements for compensation before making an application to the REC.

- In general, such arrangements will normally be in place through NHS indemnity, and/or employer’s liability insurance, and/or professional indemnity and/or clinical trials insurance, as appropriate. In certain circumstances, e.g. high-risk research activities or vulnerable participants, additional arrangements may need to be made. Employers and sponsors must be made aware of such situations in sufficient time to make necessary arrangements.
Question A76-1  Liability arising from the management of the research

- The liabilities of the sponsor relate to the overall management of the study, i.e. the systems and processes through which the sponsor meets its responsibilities. (See guidance on sponsorship at A64-1.) This could include responsibilities for monitoring and training, for example.

- Normally the sponsor(s) will hold insurance or provide indemnity to cover their liabilities as sponsors. Where the sponsor is the employer of the Chief Investigator this is likely to be covered through insurance or indemnity for employer’s liability. Where there is more than one sponsor, details for all sponsors should be provided. You should make sure that you have discussed the study with the sponsor and that they have agreed, in principle, to act as sponsor.

- If an NHS organisation is a sponsor, then indemnity is provided through NHS schemes. Tick the response to indicate that NHS indemnity will apply - no proof of indemnity needs to be provided.

- If a university or higher education institution is a sponsor, tick the response to indicate that other insurance or indemnity arrangements will apply and give details. A copy of the relevant policy must be provided.

- If a company is a sponsor, tick the response to indicate that other insurance or indemnity arrangements will apply and give details. A copy of the relevant policy must be provided.

- Where sponsor activities are delegated to sites or sub-contracted to another party, the contract or agreement between the organisations should set out the responsibilities of the parties and the arrangements for covering any liabilities. The sponsor is responsible for ensuring that these arrangements are in place.

Question A76-2  Liability arising from the design of the research

- The design of the research is the responsibility of the author and any co-authors of the protocol. Employers are responsible for the actions of their staff who design research studies as part of their employment.

- Normally the employer(s) of the author(s) will hold insurance or provide indemnity to cover their liabilities for the design of the research.

- The main author will usually be the Chief Investigator in the UK. For some international studies it may be the co-ordinating investigator for the study as a whole.

- Where the employees of an NHS organisation are responsible for designing the study, indemnity is provided for harm arising from the design of the study through NHS schemes. Tick the response to indicate that NHS indemnity will apply - no proof of indemnity needs to be provided.

- If the author is employed by a university, or the design of the research has been undertaken in the course of an honorary arrangement with a university, tick the response to indicate that other insurance or indemnity arrangements will apply.
and give details. This situation applies to researchers employed by a university, regardless of whether or not they hold any honorary contract with an NHS organisation. The university is likely to hold insurance that is additional to normal employer’s liability insurance, to cover CTIMPs or other interventional trials. For other non-interventional clinical research, employer’s liability insurance is likely to be sufficient. A copy of the relevant policy must be provided.

- If the author is employed by a company, is self-employed or is an independent contractor, tick the response to indicate that other insurance or indemnity arrangements will apply and give details. A copy of the relevant policy must be provided.

Question A76-3 Liability arising from the conduct of the research

- The conduct of the research refers to the study procedures, as described in the protocol or proposal, which are conducted by the research team with participants, data or tissues.

- Employers are normally responsible for the actions of their staff who conduct research procedures as part of their employment.

- However, where the research involves NHS patients under the care of NHS organisations (including independent contractors), indemnity for harm to participants resulting from clinical negligence is provided either through NHS schemes or through professional indemnity. Formal permission from the NHS organisation (R&D approval) must be obtained in writing before the start of the research. Tick the response to indicate that NHS or professional indemnity will apply - no proof of indemnity needs to be provided.

- Independent contractors, e.g. GPs, should ensure that their professional indemnity provides cover for the activities they will be undertaking.

- Where the research involves private patients under the care of an independent contractor, the main REC requires assurance that appropriate indemnity arrangements will be in place before the study starts. Tick the response to indicate that non-NHS sites are involved and give details of the insurance or indemnity arrangements that will apply. A copy of the relevant policy must be provided.

- Where the investigator is an employee or contractor of a university or Higher Education Institution (HEI) and the research involves members of the public taking part in research outside the care of the NHS, the HEI should have insurance or indemnity to meet the investigator’s liabilities. Such research may take place in the HEI, in the community or in other private or state institutions. Tick the response to indicate that non-NHS sites are involved and give details of the insurance or indemnity arrangements that will apply. In some cases, the HEI may need to arrange additional insurance. A copy of the relevant policy must be provided.

- Where the investigator is an employee or contractor of a Contract Research Organisation or Site Management Organisation and the research is taking place through a commercial organisation, the company should have insurance or indemnity to meet the investigator’s liabilities. Tick the response to indicate that
non-NHS sites are involved and give details of the insurance or indemnity arrangements that will apply. A copy of the relevant policy must be provided.

Question A77  Compensation for harm where liability does not arise

- This question addresses the possibility of compensation where no legal liability arises for any person, e.g. a participant has suffered harm as a result of taking part in the research but there has been no negligence in its management, design or conduct and no other liability arises such as product liability. This compensation is commonly known as “no fault compensation”.

- Sponsors are not obliged to offer no fault compensation in all cases. The REC will inform you if they consider that provision for no fault compensation is needed.

Commercially sponsored trials

- In the case of commercially sponsored CTIMPs or medical device studies, arrangements for no fault compensation will normally be provided in accordance with the Association of British Pharmaceutical Industry (ABPI) or Association of British Healthcare Industry (ABHI) schemes. Tick the response to indicate that arrangements for compensation have been made, and confirm that the ABPI/ABHI guidelines will be followed. A copy of the form of indemnity (unsigned) to be used should be enclosed with the application.

Non-commercial research

- In the case of non-commercial research, arrangements for no fault compensation cannot be made in advance by the NHS or other public bodies (e.g. MRC). Such organisations, although not accepting liability, may consider making an *ex gratia* payment on a voluntary basis in the event of a claim.

- Some Higher Education Institutions may choose to provide no fault compensation for research involving their employees. If this is the case, tick the response to indicate that arrangements for compensation have been made. A copy of the policy should be provided.

- Where no organisation has arranged or is able to provide no fault compensation, tick the response to indicate that no arrangements for compensation have been made.

Information for participants

- Before agreeing to take part, participants should be made aware of any provision (or lack of provision) for no fault compensation. If no such provision is available, participants should be aware that in the unlikely event of a claim, for which negligence could not be demonstrated, they might need to take legal action for which they would need to pay.


REC responsibilities
• For non-commercial research, there are no guidelines on whether provision for no-fault compensation should be in place. It is an ethical issue for the sponsor and the REC to consider on a case by case basis, taking into account the potential risk to participants. In most studies this will not be necessary.

• The REC may decide that participants should be protected by no fault compensation arrangements. If so, the research could go ahead only if a body was willing and able to make provision for compensation, backed by adequate insurance or indemnity arrangements.

Question A78 Intellectual property

• Intellectual Property is the tangible output of any intellectual activity that is new or previously un-described. It has an owner; it can be bought, sold or licensed and must be adequately protected. It can include inventions, industrial processes, software, data, written work, designs and images.

• Any research which could potentially lead to intellectual property rights for you or your employer should be discussed with your employer and the lead NHS R&D office as early as possible in the planning of the research.