Integrated Research Application System (IRAS)

Project filter – collated guidance

The following document collates all guidance on questions in the IRAS Project Filter.

Contents

Question 1 Audit and service evaluation

Where audit or service evaluation is selected:

You have selected "No" so your project is assumed to be audit or service evaluation.

All potential applications under IRAS have therefore been disabled except those to the National Information Governance Board (see below) and the Ministry of Justice. Applications to RECs, NHS R&D offices and other bodies are required only where a project is considered to be research.

For guidance on differentiating between research, audit and service evaluation, please consult the detailed guidance notes next to question 1.

National Information Governance Board for Health and Social Care (NIGB)

If you are conducting an audit, service evaluation or other non-research project with a medical purpose and you plan to access or use identifiable patient data without explicit consent, you may need to apply to the NIGB for approval under Section 251 of the NHS Act 2006. Please select NIGB under Question 4 below in the Project Filter and continue with the application.

Please see http://www.nigb.nhs.uk for further guidance.

Detailed guidance from information button:

Research or audit/ service evaluation

Where a project is not classified as research, all potential applications in IRAS are disabled except those to the National Information Governance Board (see below) and Ministry of Justice. Applications to other bodies are required only where a project is considered to be research.

The Research Governance Frameworks for Health and Social Care set out the responsibilities and standards that apply to work managed within the formal research context. For the purposes of Research Governance, 'research' means the attempt to derive generalisable new knowledge by addressing clearly defined questions with systematic and rigorous methods. Although some research projects include evaluation, where a project is considered to be ***solely*** audit or

service/therapy evaluation, it will not be managed as research within the NHS or social care. **Such projects do not require ethical review by a NHS or Social Care Research Ethics Committee or management permission through the NHS R&D office.** There is no need to submit applications in IRAS either to the REC or R&D office.

Differentiating research, audit and service evaluation

NRES has prepared some simple guidance for researchers in its leaflet "Defining Research", which is available at http://www.nres.npsa.nhs.uk/rec-community/guidance/#Researchoraudit. The NHS R&D Forum has published more detailed guidance aimed primarily at NHS R&D offices, which is available at http://www.rdforum.nhs.uk/docs/categorising_projects_guidance.doc.

If in doubt, you may consult the Chair of your local REC or your R&D office, or email the NRES Queries Line at queries@nres.npsa.nhs.uk. Please send a summary of your project proposal (maximum two pages). Confirmation will be provided in writing. If you plan to publish your findings, this may be provided to the Journal as evidence that ethical approval is not required under NHS research governance arrangements.

Additional guidance on the characteristics of research in the social care setting is available in the Research Governance Framework Resource Pack for social care available at http://www.ssrg.org.uk/governance/index.asp. You can also seek advice from the Social Care REC coordinator (0207 089 6840).

If after discussion the project is considered to be research, reply "Yes" to sieve question 1 and proceed with applications to a REC and R&D office.

If the project is solely audit or service evaluation, or some other type of non-research activity such as case study, system/equipment testing or satisfaction survey, you should check with the NHS clinical governance office or local authority what other review arrangements or sources of advice apply to the project. For example, there may be standard guidelines on the conduct of clinical audit. The Caldicott Guardian of Local Authority Information Governance Lead will be a source of advice on the use of patient or service user data.

National Information Governance Board for Health and Social Care (NIGB)

If you are conducting an audit, service evaluation or other non-research project with a medical purpose and you plan to access or use identifiable patient data without explicit consent, you may need to apply to the NIGB for approval under Section 251 of the NHS Act 2006. Please select NIGB under Question 4 below in the Project Filter and continue with the application.

Please see http://www.nigb.nhs.uk for further guidance.

Question 2 Type of research

Clinical trials of investigational medicinal products

Select this option for medicinal trials falling within the scope of the EU Clinical Trials Directive and the Medicines for Human Use (Clinical Trials) Regulations 2004.

Medicinal products are substances or combinations of substances which either prevent or treat disease in human beings or are administered to human beings with a view to making a medical diagnosis or to restore, correct or modify physiological functions in humans.

A clinical trial is an investigation in human subjects which is intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal products, identify any adverse reactions or study the absorption, distribution, metabolism and excretion, with the object of ascertaining the safety and/or efficacy of those products. This definition includes pharmacokinetic studies.

Clinical studies involving only medical devices, food supplements or other non-medicinal therapies (such as surgical interventions) are not covered by the Directive. The Regulations do not apply to non-interventional trials. In such trials, no additional diagnostic or monitoring procedure should be applied. Epidemiological methods should be used for the data analysis.

The Medicines and Healthcare products Regulatory Agency (MHRA) is responsible for advising on the Regulations and requirements for clinical trial authorisation (CTA). More detailed guidance is available at:

http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Isaclinicaltrialauthorisationrequired/index.htm

Section 2 of the guidance links to an algorithm to help you decide whether or not your research is a clinical trial of an investigational medicinal product (CTIMP).

If you remain unsure after checking the algorithm, please contact the MHRA Clinical Trials Helpline for advice by writing to clinicaltrialhelpline@mhra.gsi.gov.uk.

It is a criminal offence to conduct a CTIMP anywhere in the UK without CTA from the MHRA. This applies both to commercial and non-commercial research, and both to phase 1 drug development and later phase research.

Non-interventional trials of licensed medicines

Regulation 2 of the Clinical Trials Regulations defines a “non-interventional trial” as a study of one or more medicinal products with a marketing authorisation meeting all of the following conditions:

(a) the products are prescribed in the usual manner in accordance with the terms of that authorisation
(b) the assignment of any patient involved in the study to a particular therapeutic strategy is not decided in advance by a clinical trial protocol
(c) the decision to prescribe a particular medicinal product is clearly separated from the decision to include the patient in the study
(d) no diagnostic or monitoring procedures are applied to the patients included in the study, other than those which are ordinarily applied in the course of the particular therapeutic strategy in question
(e) epidemiological methods are to be used for the analysis of the data arising from the study.

If your study is a non-interventional trial of a licensed medicine according to the Regulations, please select another option in sieve question 2. Where no additional research procedures are involved (e.g. questionnaires), the most appropriate category will usually be "Study limited to working with human tissue samples and/or data". If the research will also involve questionnaires, please select "Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology".

Post-marketing surveillance by the pharmaceutical industry not involving any additional research procedures will generally fall within the classification of service/therapy evaluation rather than research. Under NHS research governance arrangements, service/therapy evaluation does not require either ethical review or management permission from R&D offices. For further guidance on differentiating between research, audit and service/therapy evaluation, please refer to the NRES leaflet "Defining Research", which is available at http://www.nres.npsa.nhs.uk/rec-community/guidance/#Researchoraudit

Trials subject to EAG/CHM assessment

Introduction

For certain types of clinical trial the MHRA will seek advice from the Expert Advisory Group on Clinical Trials (EAG) and the Commission on Human Medicine (CHM) before giving approval.

Applicants should indicate in answer to Question 2a whether the proposed trial falls within the scope of the expert advice arrangements.

Sponsors are requested to make contact with the Agency before making the application for Clinical Trial Authorisation (CTA) for such trials and to make available a data package allowing that advice to be obtained. The normal CTA application timeline will follow receipt of a valid application.

Scope of the EAG/CHM arrangements

The arrangements apply to certain types of First in Human (FIH) trial with novel compounds, and to trials with integrin antagonists targeting leucocyte trafficking.

The decision to refer applications for expert advice will be based on assessment of risk factors and the proposed mitigation strategy. Areas for consideration when determining risk factors include mode of action, nature of the target and the relevance of animal species and models.

First in human (FIH) trials with novel compounds

Sponsors of all FIH trials should take account of the *Guideline on Strategies to Identify and Mitigate Risks for First-in-Human Clinical Trials with Investigative Medicinal Products*, issued by the Committee for Medicinal Products for Human Use in July 2007 at:

http://www.emea.europa.eu/pdfs/human/swp/2836707enfin.pdf

MHRA may seek expert advice on FIH trials with novel compounds where:

- where the mode of action involves a target that is connected to multiple signalling pathways (target with pleiotropic effects), e.g. leading to various psychological effects or targets that are ubiquitously expressed

- acting (directly or indirectly) via a cascade system where there may be an amplification effect which might not be sufficiently controlled by a physiological feedback mechanism

- acting (directly or indirectly) via the immune system with a target or mechanism of action which is novel or currently not well characterised

- where there is novelty in the structure of the active substance, e.g. a new type of engineered structural format such as those with enhanced receptor interaction as compared with the parent compound

- where the level of expression ad biological function of the target receptor may differ between healthy individuals and patients with the relevant disease

- where there is insufficient available knowledge of the structure, tissue distribution, cell specificity, disease specificity, regulation, level of expression and biological function of the human target, including down-stream effects

- acting via a possible or likely species specific mechanism or where animal data are unlikely to be predictive of activity in humans.

Trials with integrin antagonists targeting leucocyte trafficking

MHRA will seek expert advice from EAG/CHM in the case of trials with compounds which modulate leucocyte trafficking, except Phase 1 studies in subjects with no previous immunosuppression.

1. The following applications will not routinely require referral:

   (a) Compounds which modulate angiogenesis but no leucocyte trafficking nor have any cross-reactivity to integrins that modulate leucocyte trafficking

   (b) Phase 1 healthy volunteer studies and patient studies in subjects with no previous immunosuppression using compounds which modulate leucocyte trafficking, provided that all the following conditions are met in the protocol:

   - A minimum of 3 months follow-up
   - Sbject Alert Card
   - Neurological monitoring during the trial
   - MRI scanning where the patient population has a neurological condition *(patient studies only)*
   - PML Management Algorithm.

2. Applications will require referral if they are:

(a) Phase 1 patient studies with compounds which modulate leucocyte trafficking
(b) Tials in previously immunosuppressed subjects or where subjects will receive concomitant immunosuppressant therapy
(c) All Phase 2 and 3 studies with compounds which modulate leucocyte trafficking
(d) Any application falling into (1) above where there is an area of concern.

EAG/CHM procedures and required areas of discussion

Guidance on procedures for seeking advice from EAG/CHM and applying for CTA have been published by the MHRA at:
http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=986
The guidance includes a list of required areas of discussion by EAG/CHM and the contents of the data package to be submitted to MHRA.

Implications for REC applications

Applicants should indicate in answer to Question 2a whether the proposed trial falls within the scope of the EAG/CHM arrangements.

If so, please explain the current status of the application for CTA in answer to Question A55 in IRAS. Further guidance is available from the information button next to this question. A copy of any relevant correspondence with MHRA should be enclosed with the REC application.

The sponsor is responsible for ensuring that the main REC is kept informed about the progress of the CTA application and any changes made to the trial as a result of the expert advice from EAG/CHM. The REC should be fully informed about this either as part of the initial application or through further information provided in the course of the ethical review.

Sequential or parallel processing?

Sponsors may opt to apply either sequentially or in parallel to the MHRA and the REC.

This decision may be influenced by a number of considerations. A sequential process may be preferable where, despite pre-submission advice from MHRA, 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. A sequential process would allow the ethics committee to receive the final version of the protocol and be fully informed about the outcome of the CTA application when undertaking its review.

However, in other cases the sponsor may be confident that the protocol is unlikely to change and may wish to apply in parallel.

Guidance for ethics committees

Detailed guidance for ethics committees on the review of trials subject to EAG/CHM advice has been issued by NRES in an open letter dated 14 August 2007. A copy of

this letter is available on the NRES website at: http://www.nres.npsa.nhs.uk/rec-community/guidance/#phase1

Gene therapy medicinal products

Gene therapy medicinal products are defined in Part IV of Directive 2003/63/EC (amending Directive 2001/83/EC) as follows:

> "… [a] gene therapy medicinal product means a product obtained through a set of manufacturing processes aimed at the transfer, to be performed either in vivo or ex vivo, of a prophylactic, diagnostic or therapeutic gene (i.e. a piece of nucleic acid), to human/animal cells and its subsequent expression in vivo. The gene transfer involves an expression system contained in a delivery system known as a vector, which can be of viral, as well as non-viral origin. The vector can also be included in a human or animal cell."

For a list of examples of gene therapy products, please see the Gene Therapy Advisory Committee website at: http://www.advisorybodies.doh.gov.uk/genetics/gtac. Further guidance may be sought from the GTAC Secretariat.

If you select Yes in answer to this question, the main application for ethical review must be submitted to GTAC. Further guidance about applications is available next to the GTAC option in Question 4 of the Project Filter.

Clinical investigations or other studies of medical devices

This option should be selected for any clinical investigation or other research study of a medical device. Further questions will appear to identify the type of study and generate the appropriate version of the form.

Do not select this option where the research protocol involves use of a CE marked device within its intended purpose *but is not designed to investigate the device itself*.

Sub-classifications of medical device studies:

Clinical investigation of a medical device

This option should be selected for any of the following:

- Clinical investigation undertaken by the manufacturer for CE marking purposes, involving:
  - A non-CE marked medical device;
  - A CE marked device which has been modified; or
  - A CE marked device, which is being used outside its intended purpose.
- Clinical investigation of a non-CE marked medical device, which has been manufactured "in-house" in a healthcare establishment.
- Clinical investigation of "off-label" use of a medical device by a clinician.

Clinical investigations apply only to medical devices and active implantable medical devices. For in-vitro diagnostic devices, select the specific option for performance evaluation of IVDDs.

Further guidance is available in the document "Approval for Medical Devices Research" at:

http://www.nres.npsa.nhs.uk/applicants/guidance/

Guidance on requirements for approval of clinical investigations by MHRA Devices is available on the MHRA website:

http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=194

For specific advice, please contact MHRA Devices (see contact details at the foot of the web page above).

Performance evaluation of an In Vitro Diagnostic Device

This option should be selected for a performance evaluation of an in vitro diagnostic device (PEIVDD). This means a device intended by the manufacturer to be subject to one or more performance evaluation studies in laboratories for medical analyses or in other appropriate environments outside his own premises.

PEIVDDs do not require a Notice of No Objection from the Competent Authority. Applicants are not required to apply to MHRA Devices using IRAS. However, notification is required under the In Vitro Diagnostic Medical Devices Directive and the Medical Devices Regulations 2002 where the manufacturer or its authorised representative is based in the UK. The MHRA must be provided with details of the manufacturer and the IVDDs being placed on the market using Registration Form RG3. Guidance is available on the MHRA website at:

http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=196

Where PEIVDDs are conducted at NHS sites, ethical approval should be sought from a NHS Research Ethics Committee and permission obtained to conduct the research from relevant NHS R&D offices.

Clinical trial of a drug/device combination

Select this option only where the trial involves the use of *both* an investigational medicinal product *and* an investigational medical device (either a non-CE marked device or a device which has been modified or is being used for a purpose not covered by the CE mark).

In these circumstances, the trial would exceptionally require *both*:

- Notice of No Objection under the Medical Devices Regulations 2002, *and*
- Clinical trial authorisation under the Medicines for Human Use (Clinical Trials) Regulations 2004.

Applicants are advised to seek expert advice from either branch of MHRA on the regulatory requirements for combined drug/device trials. Contact either of the following:

- Clinical Trials Helpline (for medicinal trials) at clinicaltrialhelpline@mhra.gsi.gov.uk or 0207 084 2327

- MHRA Devices (for devices investigations), using the contact details at http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=194 (see foot of the page).

Where MHRA advise that the trial will be regulated under only the Medicines or Devices Regulations, please untick the combined drug/device option and proceed as follows:

- If regulated only as a medicinal trial, select "Clinical trial of an investigational medicinal product".

- If regulated only as a devices investigation, select "Clinical investigation of a medical device".

Research study of a CE marked device

Select this option for research studies of CE marked devices, which have not been modified and are being used in accordance with their intended purpose.

This category will normally apply to clinician-led medical devices research, i.e. research other than clinical investigations undertaken for CE marking purposes by the manufacturer.

Further guidance is available in the document "Approval for Medical Devices Research" at:

http://www.nres.npsa.nhs.uk/applicants/guidance/

Guidance on the regulation of medical devices is available on the MHRA website:

http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=194

For specific advice, please contact MHRA Devices (see contact details at the foot of the web page above).

Post market surveillance study of a CE marked device

In general, Post Market Surveillance (PMS) studies of CE marked devices are classified as service evaluation and do not require ethical review or management permission from NHS R&D offices. If you select this option, all applications in IRAS will be disabled.

PMS studies are regarded as service evaluation where they meet all the following criteria:

(i) The product is used within its intended purpose;
(ii) The assignment of any patient involved in the study to a particular therapeutic strategy or diagnostic procedure is not decided in advance by a protocol but falls within current clinical practice;

(iii) The decision to use the product is clearly separated from the decision to include the patient in the study;
(iv) No diagnostic or monitoring procedures are applied to the patients included in the study, other than those which are ordinarily applied in the course of current clinical practice; and
(v) Epidemiological methods are to be used for the analysis of the data arising from the study.

If the study does not meet all of these criteria, it should be regarded as research. In particular, *randomised controlled trials* and any case series study involving *additional research procedures* (e.g. scans, questionnaires) should be regarded as research and will require ethical review and R&D approval if conducted within the NHS.

Where this applies, please select the option "Research study on a CE marked device".

Further guidance is available in the document "Approval for Medical Devices Research" at:

http://www.nres.npsa.nhs.uk/applicants/guidance/

Guidance on the regulation of medical devices is available on the MHRA website:

http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=194

For specific advice, please contact MHRA Devices (see contact details at the foot of the web page above).

Other clinical trials or clinical investigations

This option should be selected for clinical research not involving investigational medicinal products or medical devices.

For example, this option would be appropriate for research involving:

- Surgery
- Radiotherapy
- Imaging investigations
- Mental health investigations or therapies
- Physiological investigations
- Trials of products not defined as medicines or medical devices (e.g. nutritional)
- Complementary or alternative therapies

Medicinal research

If you are unsure whether your research is subject to the Medicines for Human Use (Clinical Trials) Regulations 2004, please consult the detailed guidance on the MHRA website at:

http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Isaclinicaltrialauthorisationrequired/index.htm

Section 2 of the guidance links to an algorithm to help you decide whether or not your research is a clinical trial of an investigational medicinal product (CTIMP). Specific advice may be sought by emailing clintrialhelpline@mhra.gsi.gov.uk. If the research is a CTIMP, you must select the first option in answer to Question 2 on the sieve.

Devices research

If your research is a study of a medical device, please select the appropriate option on the sieve rather than "Other clinical trials or investigations".

Guidance on medical devices research is available in the document "Medical Devices Guidance for Applicants and RECs" at:

http://www.nres.npsa.nhs.uk/applicants/guidance/

Guidance on requirements for approval of clinical investigations by MHRA Devices is available on the MHRA website:

http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=194

For specific advice on devices research, please contact MHRA Devices (see contact details at the foot of the web page above).

Study administering questionnaires/interviews for quantitative or mixed quantitative/qualitative analysis

Please select this option if your research:

- Involves no clinical interventions or procedures (otherwise please select one of the clinical research categories);
- Involves administering a questionnaire, or conducting interviews or focus groups with participants; and
- Will use quantitative analysis, or a mix of quantitative and qualitative analysis methods.

Study involving qualitative methods only

Please select this option if your research:

- Involves no clinical interventions or procedures (otherwise please select one of the clinical research categories)
- Involves no use of human tissue samples or other human biological materials
- Will use only qualitative analysis methods.

If you select this option, questions in IRAS relating to statistical analysis will be disabled.

Study limited to working with human tissue samples and/or analysis of data

Research in this category is based entirely on the analysis data and/or use of human tissue samples or other human biological material. It must involve no change to the normal clinical care or treatment of participants. There will be no participant contact or observation other than to collect samples and seek informed consent where appropriate.

This category applies to *specific research projects* using samples and/or data. Where a favourable ethical opinion is given, this will apply for the duration of this project only. To apply for ethical review of a licensed research tissue bank or a research database, please select the appropriate category.

If you select this option, supplementary questions will appear about the proposed use of data or human tissue samples in your study. The version of the form applicable to your project will depend on your answers to these questions. Tick all options that apply.

Research involving data collection through questionnaires or other intervention with participants should select another option.

Research taking new human tissue samples

This option should be selected for research in which samples are collected prospectively from participants primarily for research purposes.

Research using surplus or existing samples identifiable to the researcher

Select this option for research using residual tissue left over from routine clinical or diagnostic procedures, or existing stored samples from an archived collection or tissue bank, where the samples will be identifiable to the researcher.

Research involving surplus or existing samples not identifiable to the researcher

Select this option for research using residual tissue left over from routine clinical or diagnostic procedures using existing samples from an archived collection or tissue bank, where *all* the samples will be anonymised or pseudonymised and there is no possibility of the researcher being able to identify any donor.

Research involving identifiable data

This option should be selected for research:

- Using non-anonymised patient or service user data from databases or records, or
- Observing treatment or care with *no intervention*.

Research involving data collection through questionnaires or other intervention with participants should select another option.

Research using anonymised or pseudonymised data

This option should be selected for research using *only* non-identifiable data, i.e. data that are "anonymised" or "pseudonymised" at the point of access by researchers.

Anonymised data means data prepared from personal information but from which all identifiers have been removed so that it is no longer possible to identify the person concerned.

"Pseudonymised data is like anonymised data in that in the possession of the holder it cannot reasonably be used by the holder to identify an individual. However it differs in that the original provider of the information may retain a means of identifying individuals. This will often be achieved by attaching codes or other unique references to information so that the data will only be identifiable to those who have access to the key or index. Pseudonymisation allows information about the same individual to be linked in a way that true anonymisation does not." [Patient Information Advisory Group]

Tissue/data supplied by approved tissue banks and databases

NHS researchers undertaking specific research projects using tissue/data supplied by a Research Tissue Bank or Research Database must still apply for permission to R&D offices at all organisations where the research is conducted, whether or not the bank/database has ethical approval. Where the tissue/data is received in non-identifiable form and the research is covered by the terms of generic ethical approval, no further REC application is required but the bank/database should list the project in its annual report to the REC.

Other research

Select this option if your research does not appear to fit any other category.

Research tissue bank

Organisations responsible for the management of research tissue banks (RTB) anywhere in the UK may apply for ethical review of their arrangements for collection, storage, use and distribution of tissue. A "research tissue bank" (or "biobank") is defined as:

A collection of human tissue or other biological material, which is stored for potential research use beyond the life of a specific project with ethical approval or for which ethical approval is pending.

Applications are not restricted to collections of human tissue within the definition of "relevant material" under the Human Tissue Act 2004.

If your research is a specific research project involving human tissue you should select another option on the sieve.

Licensing requirements

Under the Human Tissue Act, tissue banks in England, Wales and Northern Ireland storing relevant material for use in as yet unspecified research must obtain a licence from the Human Tissue Authority (HTA).

Applicants for ethical review of RTBs will be expected to provide the REC with a copy of the licence as a condition of ethical approval except where:

- The RTB is established in Scotland
- The biological material to be stored for use in research is outside the definition of "relevant material" under the Human Tissue Act, e.g. DNA, plasma, serum, cell lines.

Detailed guidance on licensing is available from the HTA at http://www.hta.gov.uk/licensing.cfm

Application for ethical review is voluntary

There is no formal requirement for tissue banks to obtain ethical approval under the Human Tissue Act or NHS research governance systems. Applications for ethical review will therefore be made on a voluntary basis.

However, ethical approval for a bank may have benefits by facilitating programmes of research without a need for individual project-based ethical approval. The RTB application form has an option for the applicant to seek generic ethical approval prospectively for a range of research to be carried out by the establishment responsible for the bank and/or by other researchers to whom tissue is released by the bank within the conditions of the ethical approval. Such approval may be given for a period of up to 5 years and will be renewable.

Further guidance on RTB applications is available in the FAQs on the Human Tissue Act on the NRES website at http://www.nres.npsa.nhs.uk/applicants/help/faq/

Booking applications

NRES recommends that applications for ethical review of RTBs are booked for review via the Central Allocation System (CAS) by telephoning 0845 270 4400. When speaking to CAS staff it is helpful to begin by saying that the application is for a RTB rather than a specific project. For further guidance on booking, see http://www.nres.npsa.nhs.uk/applicants/apply/applying-for-ethical-review/.

Applications will normally be allocated by CAS to one of a panel of "flagged RECs", which have been assigned to review RTB applications and have received additional training.

However, applicants may opt to apply to another committee within their geographical domain if they prefer.

NHS management permission

Under the Research Governance Framework (RGF), there is no requirement for NHS research permission for the establishment of research tissue banks in the NHS. Applications to NHS R&D offices through IRAS are not required as all NHS organisations are expected to have included management review in the process of establishing the tissue bank and, where applicable, applying for licensing.

Research permission is also not required by collaborators at tissue collection centres (TCCs) who provide tissue samples or other biological material to a RTB under the terms of a supply agreement between the care organisation and the bank. TCCs are not research sites for the purposes of the RGF.

RTB managers are advised to provide R&D offices at all TCCs with a copy of the REC application for information, together with a copy of the favourable opinion letter when available. All TCCs should be listed in Part C of the REC application.

NHS researchers undertaking specific research projects using tissue/data supplied by a RTB must apply for permission to R&D offices at all organisations where the research is conducted, whether or not the bank has ethical approval. Where the tissue/data is received in non-identifiable form and the research is covered by the terms of generic ethical approval for the RTB, no further REC application is required but the RTB should list the project in its annual report to the REC.

Research database

Organisations responsible for the management of research databases anywhere in the UK may apply for ethical review of their arrangements for collection, storage and use of data, including arrangements of release of data to researchers.

A "research database" is defined as:

> *A collection of data, which is stored for potential research use beyond the life of a specific project with ethical approval or for which ethical approval is pending.*

Application for ethical review is voluntary

There is no formal requirement for databases to apply for ethical review under NHS research governance systems, and ethical approval would only be required by legislation if processing identifiable data without consent. Applications for ethical review will therefore normally be made on a voluntary basis.

However, ethical approval for a database may have benefits by facilitating programmes of research without a need for individual project-based ethical approval. The database application form has an option for the applicant to seek generic ethical approval prospectively for a range of research to be carried out by the establishment responsible for the database and/or by other researchers to whom data is released within the conditions of the ethical approval. Such approval may be given for a period of up to 5 years and will be renewable.

Booking applications

NRES recommends that applications for ethical review of research databases are booked for review via the Central Allocation System (CAS) by telephoning 0845 270 4400. When speaking to CAS staff it is helpful to begin by saying that the application is for a database rather than a specific project. For further guidance on booking, see http://www.nres.npsa.nhs.uk/applicants/apply/applying-for-ethical-review/.

Applications will normally be allocated by CAS to one of a panel of "flagged RECs", which have been assigned to review database applications.

However, applicants may opt to apply to another committee within their geographical domain if they prefer.

NHS management permission

Under the Research Governance Framework (RGF), there is no requirement for NHS research permission for the establishment of research databases in the NHS. Applications to NHS R&D offices through IRAS are not required as all NHS organisations are expected to have included management review in the process of establishing the database.

Research permission is also not required by collaborators at data collection centres (DCCs) who provide data under the terms of a supply agreement between the organisation and the database. DCCs are not research sites for the purposes of the RGF.

Database managers are advised to provide R&D offices at all DCCs with a copy of the REC application for information, together with a copy of the favourable opinion letter when available. All DCCs should be listed in Part C of the REC application.

NHS researchers undertaking specific research projects using data supplied by a database must apply for permission to R&D offices at all organisations where the research is conducted, whether or not the database has ethical approval. Where the data is received in non-identifiable form and the research is covered by the terms of generic ethical approval for the database, no further REC application is required but the database should list the project in its annual report to the REC.

Question 2a Ionising radiation

You should answer Yes to this question if the research protocol includes any procedure involving exposure to diagnostic or therapeutic ionising radiation as defined in the Ionising Radiation (Medical Exposure) Regulations 2000 ("IRMER").

For all studies where the answer to this question is Yes, Part B Section 3 of IRAS will be enabled. This section should be completed with input from a lead Medical Physics Expert (MPE) and lead Clinical Radiation Expert (CRE). Detailed guidance is available by clicking on the links in this section of IRAS.

If the research involves (or might involve) ionising radiation at any stage, you should seek early a MPE on completion of Part B Section 3 and compliance with IRMER.

Procedures involving ionising radiation include:

- Diagnostic X-rays, CT scans or DXA scans
- Radiotherapy (including brachytherapy and therapy using unsealed sources)
- Radionuclide imaging (including diagnostic imaging and in vitro measurements).

Magnetic Resonance Imaging (MRI) or ultrasound investigations do not involve ionising radiation.

You should answer "Yes" even where the exposures to be received under the protocol would be in accordance with normal clinical care outside the research setting.

You should answer "Yes" where imaging investigations involving ionising radiation are required by the *screening procedures* for the study, for example where the protocol requires a diagnostic X-ray to confirm suitability for inclusion.

However, you may answer "No" if the *selection criteria* include normal clinical exposures received outside the study but the study itself does not involve radiation exposure. This would apply where both the following criteria are met:

- The exposures are authorised and undertaken in the course of normal clinical management, not for research purposes; and
- The decision to authorise the exposures is clearly separated from the decision to include the participant in the research and is not decided in advance by the research protocol.

For example, an epidemiological study of the long-term effects of radiotherapy might require that the participant had received radiotherapy of a particular type or within a particular period prior to inclusion in the research. The radiotherapy would have needed to comply with the provisions of IRMER relating to clinical exposures. However, it is not a research exposure for the purposes of IRMER and does not require approval as part of the ethical opinion.

Question 2b New human tissue samples (or other human biological samples)

Please answer Yes if the research will involve collecting samples prospectively from participants primarily for research purposes.

Question 2c Existing human tissue samples (or other human biological samples)

Please answer Yes if the research will involve the use of residual material left over from routine clinical or diagnostic procedures, or existing stored samples from an archived collection or tissue bank.

Question 3 Countries of the UK

Please tick all the countries in the UK in which research sites will be located.

A research site is defined as the single organisation responsible for conducting the research at a particular locality.

The *research site* is not necessarily the *location* where research activities will actually take place. For example, in a research project by practice nurses from GP practices, interviews with participants may take place in the participant's home, but the research site would be the GP practice, because the GP practice would be responsible for the research activity.

Organisations where clinicians or clinical units refer potential participants to the research team for assessment and possible recruitment are not considered to be research sites.

For research tissue banks:

In Question 3a please indicate in which country the research tissue bank is physically located.

In Question 3b please tick all the countries where centres will be providing tissue and data to the research tissue bank.

For research databases:

In Question 3a please indicate in which country the research database is physically located.

In Question 3b please tick all the countries where centres will be providing data to the research database.

National Information Governance Board for Health and Social Care (NIGB)

If the database will be processing identifiable patient information relating to people in England and Wales, *either without their consent or to identify people in order to seek their consent*, then application may need to be made to the National Information Governance Board (NIGB) for approval.

The remit of the National Information Governance Board for Health and Social Care (NIGB) covers data about patients living in or receiving care or treatment in England and Wales, *whether it is processed in England and Wales or in other countries*. Where NIGB approves an exemption under Section 251 of the NHS Act 2006 this lifts the common law duty of confidentiality and provides protection to organisations in England and Wales owing that duty.

Detailed guidance about applications to NIGB is available next to the NIGB option in Question 4.

Question 4 Which bodies are you applying to?

Application to the Social Care Research Ethics Committee

As the Social Care Research Ethics Committee was established in April 2009, its remit is still under development. It is expected that the Social Care Research Ethics Committee will review applications involving the social care sector (eg local authority, private and voluntary care settings) that would not otherwise have access to ethical review, or which cross sector boundaries. The Committee will also review research initiated in England or Wales which crosses national boundaries to Northern Ireland or Scotland. The Social Care REC will complement rather than replace the University REC system, but will review social care studies directly funded by Dept of Health and is approved to review social care research where participants lack mental capacity. Social Care REC has an interest in facilitating user-controlled research...

The Committee cannot review proposals to conduct research with children, as children's services involving healthcare are either within the remit of the other, NHS-focussed RECs under NRES, or are the responsibility of Dept for Children, Schools and Families. The Committee will not be flagged to consider prison or offender research.

The Committee will not consider any research involving clinical interventions, as this will need review by a healthcare REC.

Applications to the Social Care Research Ethics Committee are expected to fall into one of the categories below:

- Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- Study involving qualitative methods only
- Study limited to working with data and/or human tissue samples or other human biological samples (*specific project only*)

It should be noted, though, that in the last category only research limited to working with data will be permitted.

If you selected "Other Study" at question 2, this option will be disabled if Social Care REC is selected here, to avoid the risk of inappropriate applications to the Social Care REC. Please go back to question 2 and select one of the other options that are still available.

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 SCIE (0207 089 6840).

Application to Research Ethics Committee

Application for ethical review may be required under either NHS research governance systems or legislation. (In this guidance, the term NHS includes Health and Social Care in Northern Ireland.)

NHS research

Under the Governance Arrangements for NHS Research Ethics Committees (published by DH, July 2001), application to a NHS REC in England and Wales is required for research involving:

(a) Patients and users of the NHS. This includes all potential research participants recruited by virtue of the patient's or user's past or present treatment by, or use of, the NHS. It includes NHS patients treated under contract with private institutions.

(b) Individuals identified as potential research participants because of their status as relatives or carers of patients and users of the NHS.

(c) Access to the personal data or bodily material of past and present NHS patients.

(d) Fetal material and IVF involving NHS patients.

(e) The recently dead in NHS premises.

(f) NHS staff recruited as research participants by virtue of their professional role.

(g) The use of, or potential access to, NHS premises or facilities in addition to one of the other categories above.

Similar policies apply to NHS REC review in the rest of the UK.

In addition to the categories listed in GAfREC:

- In Northern Ireland the remit of Health and Social Care RECs formally extends to research in social care.

- In England and Wales, the remit of NHS RECs includes any health-related research involving prisoners or young offenders in the custody of HM Prison Service.

NHS RECs have the discretion to accept applications for review of health or social care research not involving one of the categories listed above. Except where application is required under legislation (see below), it is advisable to check with a REC office before submission whether the REC would be willing to accept the application. Further guidance may be sought from NRES operational management where necessary.

Statutory requirements for ethical review

Application for ethical review is required by legislation in the circumstances listed in the table below. Legislation may apply only to certain UK countries or be UK-wide.

Where a statutory requirement for ethical review applies, the application will always be accepted for review by the NHS REC system, whether or not the research involves the NHS. In some cases, only RECs in certain countries or with appropriate recognition are able to review the application. Please refer to the NRES website for further guidance:

http://www.nres.npsa.nhs.uk/applicants/apply/applying-for-ethical-review/

Legislation	*Extent*	*Type of research*	*Apply to*
Medicines for Human Use (Clinical Trials) Regulations 2004	UK-wide	Clinical trials of investigational medicinal products (CTIMPs)	A REC with appropriate recognition from UKECA. Most recognised RECs are NHS RECs, but some ethics committees outside the NHS are recognised to review Phase 1 CTIMPs in healthy volunteers only.
Medical Devices Regulations 2002	UK-wide	Clinical investigations of medical devices for CE	Legislation does not specify what type of ethics

		marking purposes	committee. Application to a NHS REC is recommended.
Mental Capacity Act 2005	England and Wales	Research including adults unable to consent for themselves.	All NHS RECs in England or Wales are legally recognised, but NRES requires application to a flagged REC for this type of research.
Adults with Incapacity (Scotland) Act 2000	Scotland	Research including adults unable to consent for themselves.	Scotland A REC (in all cases).
Human Tissue Act 2004 Human Tissue Act 2004 (Ethical Approval, Exceptions from Licensing and Supply of Information about Transplants) Regulations 2006	England, Wales and Northern Ireland	Research to which any of the following applies: (i) The research involves storage of relevant material (including temporary storage) and the establishment does not hold a storage licence from the Human Tissue Authority. (ii) The research involves relevant material from the living and no consent has been given to store/use the material for research. (iii) The research involves analysis of DNA in bodily material from the living and no consent has been given for DNA analysis. (ii) and (iii) do not apply to "existing holdings" stored prior to 1 September 2006.	Any NHS REC in the UK.
Ionising Radiation (Medical Exposure) Regulations 2000	UK-wide	Research involving administration of ionising radiation as part of the protocol.	Any NHS REC in the UK.
Health Service (Control of Patient Information) Regulations 2002	England and Wales	Research, audit or service/therapy evaluation involving use of patient identifiable information without consent.	Any NHS REC in the UK.

(Note: These Regulations were originally made under section 60 of the Health and Social Care Act 2001 and were re-enacted by section 251 of the NHS Act 2006.)			

Application for NHS/ HSC management permission

Researchers wishing to conduct research in the NHS (or Health and Social Care in Northern Ireland) must obtain NHS or HSC management permission (also referred to as R&D approval) for each NHS/ HSC research site.

Where the research site is a primary care site, e.g. GP practice, the host organisation is the Primary Care Trust (England), Health Board (Scotland), Local Health Board (Wales) or primary care site (Northern Ireland). For other NHS research sites the host organisation is the NHS Trust (England and Wales), Health Board (Scotland) or Health and Social Care Trust (Northern Ireland). Permission to conduct the research will be confirmed by the R&D office to the PI directly

Chief Investigators are responsible for transferring SSI Forms to each Principal Investigator (PI) for completion. Each PI should also be provided with the R&D Form and the full set of documents in the R&D Form checklist.

The process for applying for NHS/ HSC permission varies across the UK. The appropriate instructions for the CI are provided in the submission tab for the R&D Form, and the content of the tab is determined by the location of the lead R&D office as indicated in the project filter. The appropriate instructions for each PI are provided in the submission tab for the SSI Form, and the content of the tab is determined by the location of the lead R&D office selected by the CI and the location of the research site as indicated in the SSI Form.

Where the research includes NHS sites in England and has a lead R&D office in England, please also review the guidance to question 5a of the project filter on whether you wish your R&D applications to be processed through the NIHR Co-ordinated System for gaining NHS Permission.

Further guidance on applying for NHS/ HSC management permission is available on the website of the NHS R&D Forum at http://www.rdforum.nhs.uk/rdform.htm. Contact details for R&D offices can be obtained via the links at http://www.rdforum.nhs.uk/links/rdlinks.htm.

Applying for Clinical Trial Authorisation (MHRA)

Clinical trial authorisation (CTA) from the licensing authority (MHRA Medicines) is required for any clinical trial of an investigational medicinal product (CTIMP) to be conducted in the UK.

Please refer to the QSG on the CTIMP option in Question 2 for guidance on how to determine whether your project is a CTIMP.

Applications to MHRA may be made through IRAS. For further details see the guidance on applying to the MHRA on the Help Page.

Application to MHRA Devices

This option should be selected for a clinical investigation of a medical device undertaken by the manufacturer for CE marking purposes. This will be either an investigation of a non-CE marked product, or an investigation of a CE marked product that has been modified or is to be used outside its intended purpose. Notice of No Objection for such investigations must be obtained from MHRA Devices. The forms required to apply to MHRA (PCA1, PCA2 and the sterilisation annex) can be generated from IRAS.

MHRA approval is not always required in the case of:

- Medical devices manufactured "in-house" in a healthcare establishment
- Clinician led off-label use of a medical device.

The need for MHRA approval will depend on the purpose of the investigation. Guidance on whether MHRA approval is required can be found on the MHRA website at:

http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=194

(See the information at the foot of the web page and in Bulletin 18, which is also available via the link above.)

Where research involves in-house devices or clinician-led off-label use, applicants are advised to contact MHRA Devices to discuss the purpose of the investigation and determine whether MHRA approval is required. Contact details for MHRA Devices are on the website (see link above).

Application to Gene Therapy Advisory Committee

If your application is for ethical approval of a **gene therapy clinical trial** you must apply to the Gene Therapy Advisory Committee (GTAC). GTAC is the UK national REC for gene therapy clinical research according to regulation 14(5) of The Medicines for Human Use (Clinical Trials) Regulations 2004. This means that GTAC is the main REC for gene therapy clinical trials.

If you select GTAC in Question 4, do not select the option to apply to another Research Ethics Committee.

The option to apply to GTAC is only available where Question 2 indicates that the study is a clinical trial of an investigational medicinal product.

Gene therapy medicinal products

Gene therapy medicinal products are defined in Part IV of Directive 2003/63/EC (amending Directive 2001/83/EC) as follows:

> *"… [a] gene therapy medicinal product means a product obtained through a set of manufacturing processes aimed at the transfer, to be performed either in vivo or ex vivo, of a prophylactic, diagnostic or therapeutic gene (i.e. a piece of nucleic acid), to human/animal cells and its subsequent expression in vivo. The gene transfer involves an expression system contained in a delivery system known as a vector, which can be of viral, as well as non-viral origin. The vector can also be included in a human or animal cell."*

For a list of examples of gene therapy products, please see the GTAC website at: http://www.advisorybodies.doh.gov.uk/genetics/gtac.

Applying to GTAC

GTAC meeting dates are given on the GTAC website at: http://www.advisorybodies.doh.gov.uk/genetics/gtac/meetings.htm.

Applications should usually be submitted at least 60 days before the GTAC Committee meeting at which it will be considered. Before making a submission, please inform the GTAC Secretariat when you are planning to submit, and before making a formal submission, please call the Secretariat for a reference number. Contact details can be found here: http://www.advisorybodies.doh.gov.uk/genetics/gtac/contact.htm.

The application form for GTAC in IRAS is identical to that for any other CTIMP submitted to a recognised REC. There are however some differences in submission procedures:

- There is an extended time period of 90 days for ethical approval.
- Electronic submission of **all** documents is required.
- Applicants should also submit one unbound hard copy and five bound copies of all documents.

Please see the GTAC website for further guidance on applications.

Application to the National Information Governance Board (NIGB)

Introduction

From 1 January 2009, the National Information Governance Board for Health and Social Care (NIGB) took over responsibility from the former Patient Information Advisory Group (PIAG) for administering powers under Section 251 of the NHS Act 2006[1] on behalf of the Secretary of State for Health.

When should you apply to the NIGB?

You should apply to the NIGB if you need to access:

[1] Originally enacted under Section 60 of the Health and Social Care Act 2001.

- Identifiable patient information relating to people living in, or receiving healthcare in, England and Wales without explicit consent, prior to the disclosure of confidential information or

- Central Register (formerly NHSCR) information (either with or without consent), or

- Hospital Episode Statistics / Secondary Uses Service (HES/SUS) for either identifiable or sensitive data (either with or without consent).

Section 251 applications

Section 251 of the NHS Act 2006 re-enacted Section 60 of the Health and Social Care Act 2001. The terms Section 60 and Section 251, when used in relation to use of patient information, therefore refer to the same powers. These powers allow the Secretary of State for Health to make regulations to set aside the common law duty of confidentiality for medical purposes where it is not possible to use anonymised information and where seeking individual consent is not practicable. Approval of applications under Section 251 will only be considered where anonymised data will not suffice and consent is genuinely not practicable.

Section 251 applications should be submitted to the NIGB Secretariat.

Applications for HES/SUS data

Details of how to apply for HES/SUS data, what application forms you need to complete and where they need to be sent can be found on the HES On-line website www.hesonline.nhs.uk along with details of what data items in HES are deemed sensitive and what are deemed identifiable. The HES forms are also included in IRAS as appendices to the NIGB's Section 251 form.

- For **all** requests for HES data, IRAS should generate the relevant section of the NIGB form and the HES Appendices for you to complete. These will be generated based on which fields of HES data are requested (i.e. identifiable, potentially identifiable or non-identifiable).

- Where the data being requested is identifiable AND valid consent has not been obtained, then the NIGB application form for Section 251 approval needs to be completed in full. IRAS generates this form for applicants.

The Section 251 form should be submitted to the NIGB Secretariat along with the HES Appendices and other with supporting documents.

The HES appendices or HES online form also need to be submitted to the Information Centre to enable them to process the requested data.

Applications for Central Register data

The Application form for Central Register data has not yet been incorporated into IRAS. Applications should be made using the MRIS application form and *submitted to the NHS Information Centre for Health and Social Care*. Please see www.ic.nhs.uk/mris for more information.

The application form for Section 251 approval will not generally need to be completed for Central Register applications (other than where approval is needed under Section 251 for *other aspects* of a study). However, additional Data Security information will need to be provided.

MRIS applicants should ensure that patient information leaflets and consent forms include reference to data-sharing with the Central Register, please see MRIS website for more details.

The MRIS form is currently under review and it is planned in future to integrate a revised MRIS form into IRAS.

Further information

Further details about the legal and organisational changes and the applications process can be found on the NIGB website: www.nigb.nhs.uk

For application enquiries:
Email: ECCapplications@nhs.net
Tel: 020 7633 7011

For general information governance enquiries:
Email: nigb@nhs.net
Tel: 020 7633 7052

The NIGB Secretariat is located at:
New Kings Beam House, 7th Floor, 22 Upper Ground, London SE1 9BW.

For historical information the PIAG website will also remain live during 2009: www.advisorybodies.doh.gov.uk/PIAG.

Application to the Ministry of Justice

Select this option for projects subject to the Research Quality Assurance (RQA) process within the Ministry of Justice.

RQA applies to projects taking place within the National Offender Management Service (HM Prison Service and HM Probation Service), HM Courts Service or any other agency within the responsibility of the Ministry of Justice for England and Wales **and** meeting any of the following criteria:

- National in scope;
- Intended to be published;
- Results to be sent to Ministers; or
- A study of outcomes of policy or operational changes.

Projects defined as audit or service evaluation rather than research will still be subject to RQA if they meet any of the above criteria.

Most of the information required in the MoJ application form is common to other applications (such as the application for ethical review) and is generated from Part A of IRAS. Additional information required only by MoJ is generated by completion of Part B Section 10.

Further advice

For advice on the Research Quality Assurance process at the Ministry of Justice, please contact Analytical Services (Offender Management and Sentencing) in MoJ. The main contact point is David Brown at David.brown@cjs.gsi.gov.uk

Submission procedure

The completed MoJ application form should be submitted electronically by sending as a file attachment to David Brown at the above email address. Hard copy is not required and the form does not need to be signed. No additional documentation is required unless requested.

Applications to the National Offender Management Service

Please note that if you will be conducting your research in prisons or probation services in England and Wales, you will also require approval from the National Offender Management Service (NOMS). Discussions are taking place with NOMS about adoption of IRAS but applications cannot be made using IRAS at present. For further guidance about current application procedures, see the Offender Health Research Network website at http://www.ohrn.nhs.uk.

Question 4b Research requiring NHS permission but not ethical review

The following types of research project do not require application for ethical review but still require NHS management permission through the R&D office:

(i) Projects limited to the use of samples/data samples provided by a Research Tissue Bank (RTB) with generic ethical approval from a REC, in accordance with the conditions of approval. Samples/data must be non-identifiable to the researcher at point of access, otherwise further ethical review of the project is required.

(ii) Projects limited to the use of data provided by a Research Database with generic ethical approval from a REC, in accordance with the conditions of approval. Data must be non-identifiable to the researcher at point of access, otherwise further ethical review of the project is required.

(iii) Projects involving the use of NHS premises or resources but with no human participants or use of any samples/data from human participants.

Please indicate in question 4b whether any of the above apply to your project. If not, please return to question 4 and select the option to apply for ethical review.

Question 5 NHS or non-NHS site?

A research site is defined as the single organisation *responsible* for conducting the research at a particular locality.

NHS research sites would typically be:

- A NHS Trust (in England or Wales)
- A NHS Health Board (in Scotland)
- A Health and Social Care Trust (in Northern Ireland)
- A GP practice
- A Strategic Health Authority in England (for public health, epidemiology or
- needs assessment studies)
- A prison establishment in England or Wales.

The *research site* is not necessarily the *location* where research activities will actually take place. For example, in a research project by practice nurses from GP practices, interviews with participants may take place in the participant's home, but the research site would be the GP practice, because the GP practice would be responsible for the research activity.

Organisations where clinicians or clinical units refer potential participants to the research team for assessment and possible recruitment are not considered to be research sites.

NHS management permission (also termed "R&D approval") must be obtained for all NHS research sites.

Question 5a **NIHR Co-ordinated System for gaining NHS Permissions (NIHR CSP)**

What is NIHR CSP?

The National Institute for Health Research (NIHR) Coordinated System for gaining NHS Permission (CSP) is a new system designed to support the application and approvals process for NHS permissions for NIHR Clinical Research Network Portfolio studies.

Initially CSP will be available only to multi-site and single-site studies which are eligible for the NIHR Clinical Research Network Portfolio. This includes studies which are *automatically eligible* for the NIHR Clinical Research Network Portfolio, and those which are actively *adopted* into the NIHR Clinical Research Network Portfolio (including commercially sponsored studies).

Is my study eligible for NIHR Clinical Research Network Portfolio?

Please refer to the full eligibility criteria for details on the inclusion of studies in the NIHR Clinical Research Network Portfolio:
http://www.ukcrn.org.uk/index/clinical/portfolio_new/P_eligibility/mainColumnParagraphs/00/document/Eligibility.pdf

How do I submit my study to CSP?

If your study is potentially eligible for NIHR Clinical Research Network Portfolio, select **Yes** to question 5a, "Do you want your application to be processed through the NIHR Coordinated System for gaining NHS Permission?" to use CSP for obtaining NHS permissions for your study. You will be required to complete a short

Portfolio Adoption Form (PAF), to provide basic details about your study to the NIHR Clinical Research Network Coordinating Centre.

How will I know if my study has been registered with CSP?

- For Non-commercially sponsored studies – The CSP Application Team at the NIHR Clinical Research Network Coordinating Centre will review your PAF to assess whether your study may be eligible for the NIHR Clinical Research Network Portfolio. You will be notified of the decision by email within 2 working days.. Queries about the eligibility of non-commercial research should be made to cspapplication@ukcrn.org.uk

- Commercially sponsored studies – The Industry team at the NIHR Clinical Research Network Coordinating Centre will review your PAF to determine whether your study is already adopted by an NIHR Clinical Research Network. If not, the Industry team will contact the commercial sponsor to initiate the Industry Adoption process for the NIHR Clinical Research Network Portfolio. Queries about the eligibility of commercial research should be made to industry@ukcrn.org.uk

How is confidentiality maintained?

NIHR CSP will replace existing application and approval processes for NHS permissions for NIHR Clinical Research Network Portfolio studies. All information and documentation submitted through IRAS to NIHR CSP will be held in the strictest confidence at all times and managed under a duty of confidence.
If adoption of a commercially sponsored study is required, the NIHR Clinical Research Network Coordinating Centre will ensure that the UKCRN model Confidentiality Disclosure Agreement is in place before commencing the Industry feasibility and adoption process.

Question 6 Children

Please answer Yes if the research will include participants aged under 16, or use of their samples or data.

You should still answer Yes if some or all of the participants will be able to consent for themselves under the Gillick principles. Further guidance about this is available in Part B Section 7 of IRAS, which covers issues in the inclusion of children in research.

Question 7 Adults unable to consent for themselves

Please answer Yes if it is possible that the research could *at any stage* include adults (aged 16 or over) who are unable to consent for themselves due to physical or mental incapacity.

You should still answer Yes if participants will be able to give consent initially but you plan to undertake further research procedures on or in relation to such participants (including collection of new samples or data) following loss of capacity to consent during the study. If participants would be withdrawn from the study following loss of capacity, you may answer No. For guidance on retaining samples or data already

collected at the point capacity is lost, please refer to the guidance on Question A35 in IRAS.

Where research involves adults unable to consent for themselves, the application and approval requirements differ according to:

- Whether your research is a clinical trial of an investigational medicinal product (CTIMP) or a non-CTIMP, and
- In which countries of the UK the research sites will be located.

Please indicate, in answer to the supplementary question, which countries you expect the research sites to be located in.

Guidance

Detailed guidance on ethical review of applications involving adults unable to consent for themselves is available on the NRES website at:
http://www.nres.npsa.nhs.uk/docs/guidance/AWI_Guidance.pdf

A summary of key points is below.

Booking the ethics application

All ethics applications potentially including adults unable to consent for themselves should be booked for review through the NRES Central Allocation System (CAS) by calling 0845 270 4400. This includes both single- and multi-site studies and applications to the Social Care REC.

Please notify CAS that the research may include adults unable to consent for themselves and indicate which UK countries are involved.

The application will be allocated to review by a "flagged REC" (see below). Applicants for research in England and Wales may indicate a preference for a particular flagged REC when booking the application with CAS.

Further information about booking is available at
http://www.nres.npsa.nhs.uk/applicants/review/apply/apply.htm#book

Flagged RECs

NRES has appointed a panel of flagged RECs to review all new research potentially including adults unable to consent for themselves. The list of flagged RECs is available in Annex B to the guidance on the NRES website, available at
http://www.nres.npsa.nhs.uk/docs/guidance/AWI_Guidance.pdf

Where the research is a CTIMP, the application will be allocated to a committee which is *both* recognised by UKECA for review of CTIMPs *and* flagged for review of research involving adults unable to consent for themselves.

Where the research is a CTIMP to be conducted at one or more sites in Scotland and the Chief Investigator is professionally based in Scotland, it must be reviewed by the Scotland A REC.

Approval requirements (CTIMPs)

The inclusion of adults unable to consent for themselves in any part of the UK is governed by the Medicines for Human Use (Clinical Trials) Regulations 2004. *The Mental Capacity Act 2005 has no application to CTIMPs*.

The ethical review must consider whether the trial is justified having regard to the conditions and principles specified in Part 5 of Schedule 1 to the Regulations. These include provisions for informed consent to be given by the subject's legal representative. A definition of "legal representative" for this purpose is given in Part 1 of Schedule 1.

NRES has issued an information paper on "Informed Consent in Clinical Trials of Investigational Medicinal Products", outlining the relevant provisions of Schedule 1. This is available at:
http://www.nres.npsa.nhs.uk/recs/guidance/guidance.htm#consent

Applicants should give information about the inclusion of adults unable to consent in Part B Section 6 of the application form.

Approval requirements (all other NHS and non-NHS research)

Approval requirements for non-CTIMPs differ across the UK as follows:

England and Wales:

- In England and Wales, approval is required by an "appropriate body" under section 30 of the Mental Capacity Act 2005 (MCA) for any research, whether NHS or non-NHS research.

- This approval must be given by a NHS REC in England or Wales, even where the research does not involve NHS patients.

- For guidance on the research provisions of the MCA, see chapter 11 of the Code of Practice, available at http://www.opsi.gov.uk/acts/en2005/ukpgaen_20050009_en_cop.pdf

Scotland:

- In Scotland, approval is required under section 51 of the Adults with Incapacity (Scotland) Act 2000. *This approval must be given by the Scotland A REC*.

Northern Ireland:

- In Northern Ireland, there is no equivalent legislation. Inclusion in research of adults unable to consent for themselves is governed by the common law.

- Where the research will be taking place in Northern Ireland only, it should be reviewed by a Health and Social Care (HSC) REC in Northern Ireland.

Where the research will be taking place in another UK country as well, the research should be reviewed by a REC on the mainland in consultation with a HSC REC in Northern Ireland.

The table below summarises the process for non-CTIMPs taking place in different UK countries.

Countries where sites located	*Application process*
England and/or Wales only	Apply to any flagged REC in England or Wales.
Scotland only	Apply to Scotland A REC.
Northern Ireland only	Apply to any HSC REC in Northern Ireland.
England and Wales	Apply to any flagged REC in England or Wales.
England/Wales and Scotland	Two applications should be made: 1. The England/Wales application should be made to a flagged REC in England or Wales. 2. The Scotland application should be made to the Scotland A REC. Separate application forms should be submitted with separate REC reference numbers. The application form can be duplicated to minimise form-filling. The applications will be reviewed separately having regard to the relevant legislation. Any favourable opinion will apply only to England/Wales or Scotland respectively. Different opinions may be given.
England/Wales and Northern Ireland	Apply to any flagged REC in England or Wales. Only one application is required. The main REC will seek advice from a HSC REC on issues relating specifically to participants in Northern Ireland. Any advice will be incorporated in the main review.
Scotland and Northern Ireland	Apply to Scotland A REC. Only one application is required. The main REC will seek advice from a HSC REC on issues relating specifically to participants in Northern Ireland. Any advice will be incorporated in the main review.
England/Wales, Scotland and	Two applications should be made:

Northern Ireland	1. Application for England/Wales/Northern Ireland should be made to a flagged REC in England or Wales. 2. Application for Scotland should be made to the Scotland A REC. Separate application forms should be submitted with separate REC reference numbers. The application form can be duplicated to minimise form-filling. The applications will be reviewed separately having regard to the relevant legislation. Any favourable opinion will apply only to England/Wales/Northern Ireland or Scotland respectively. Different opinions may be given.

Question 8 Prisoners

For this purpose, a prisoner or young offender is defined as any inmate of the prison systems of England and Wales, Scotland or Northern Ireland. It does not include patients detained under the Mental Health Act at special hospitals or other psychiatric secure units, or juvenile offenders detained in local authority secure accommodation or secure training centres.

The Offender Health Research Network (OHRN) publishes guidance on the various approvals and permissions required to conduct research involving prisoners in England and Wales, and may be able to assist with specific queries. Further information is at http://www.ohrn.nhs.uk.

Except in Scotland, ethics applications involving prisoners should be booked with the NRES Central Allocation System (CAS), which will arrange allocation to one of the RECs designated by NRES to review such research. In Scotland the application may be made direct to the relevant REC if it is within a single domain; if it is multi-domain, it should be allocated through CAS.

Health research involving prisoners or young offenders should relate directly to their health care and be of such a nature that it could only be conducted in this population.

Question 9 Educational projects

An educational project means any study undertaken for the purposes of obtaining an academic award, i.e. it is a required piece of assessed work in part fulfilment of the award. This includes doctoral research.

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 SCIE (0207 089 6840).

If the project is undertaken as part of a PhD or other doctorate, answer Yes to Question 9a. If this is the case, the student should normally be named as the Chief Investigator.

If the project is undertaken as part of an undergraduate or Masters level award, answer No to Question 9a. The student should complete the application, but should generally not be named as the Chief Investigator. Normally the student's academic supervisor should be named as the Chief Investigator and should complete both the CI and supervisor declarations in Part D.

Further guidance on student research is available on the Help page.

Question 10 Research funded by the US DHHS

Applicants for ethical review should note special arrangements for review of research with funding support from the US Department of Health and Human Services (DHHS).

1. Applying to a REC with OHRP registration

All such applications should be booked for review with the NRES Central Allocation System (CAS) on 0845 270 4400 and allocated to a REC which is flagged for this purpose (see table below).

All flagged RECs are registered with the US Office for Human Research Protections (OHRP) as an Institutional Review Board (IRB) / Independent Ethics Committee (IEC).

CAS staff can also advise on booking with a REC that is flagged for the appropriate *type of study* (where applicable). For example, a clinical trial of an investigational medicinal product (CTIMP) with funding support from the DHHS must be reviewed by a committee that is *both* recognised to review the relevant type of CTIMP *and* registered with the OHRP.

Where a DHHS-funded study is in a category that does not require review by a flagged REC by study type (e.g. a clinical trial not involving medicines or devices), it may be reviewed by any flagged REC for DHHS-funded research.

2. Requirements for Federal Wide Assurance at research sites

Each Trust or other host organisation participating in the study must have Federal Wide Assurance (FWA) in place with the OHRP.

Guidance on how to register for FWA at a non-US research site is available at:

http://www.hhs.gov/ohrp/assurances/assurances_index.html#international

Sponsors and Chief Investigators are strongly encouraged to make early contact with R&D offices at each planned research site to discuss preparations for the study. Section 5 of the FWA registration form must give details of the IRB/IEC(s) undertaking ethical review of DHHS-funded research to be conducted at the site. Therefore the FWA at each site must list the Research Ethics Committee responsible for reviewing the current study and this REC must be registered with the OHRP.

It is open to R&D offices to list **all** the RECs flagged by NRES on their FWA. This can be done in advance of submitting the REC application and allocation to a particular REC for review, and may reduce start-up time.

Trusts with an existing FWA may update their FWA at any time to include additional IRB/IECs. To update FWA, a revised version of the form should be submitted to OHRP.

3. List of flagged RECs

The table below lists all flagged RECs for DHHS-funded research:

REC	**Types of study** [(1)]	**HHS IRB registration no.**
Berkshire REC	Type 1 CTIMPs Type III CTIMPs Research involving children Research involving adults lacking capacity to consent for themselves	IRB00009040
Charing Cross REC	Type III CTIMPs Research involving children	IRB00006641
Leeds East REC	Type III CTIMPs Research involving children Research tissue banks	IRB00006622
Leicestershire, Northamptonshire and Rutland 1 REC	Type II CTIMPs	IRB00006669
North Sheffield REC	Type II CTIMPs Research involving medical devices Research involving children Research tissue banks	IRB00006578
North Somerset & Bristol REC	Type III CTIMPs Research tissue banks Research involving children Research databases	IRB00006654
Oxfordshire B REC	Type 1 CTIMPs Type III CTIMPs (including Phase 1 trials in patients)	To be advised
South Manchester REC	Type II CTIMPs Research involving medical devices Research involving adults lacking capacity to consent for themselves	IRB00003481
Wandsworth REC	Type I CTIMPs Type III CTIMPs Research involving children	To be advised

[1] Where the type of study is not subject to flagging arrangements by NRES, any of the RECs listed may review the application. For example, a clinical trial not involving an investigational medicinal product or an investigational device may be reviewed by any REC.

4. Further advice

For further advice about the requirements of the DHHS or the process of registration for FWA, please contact the OHRP directly:

http://www.hhs.gov/ohrp/about/index.html#contact

For questions relating to the allocation of your REC application, please contact the NRES Central Allocation System on 0845 270 4400 once you are ready to submit the application.

Question 11 Processing identifiable information without consent

If your project involves access to identifiable patient information relating to people living or receiving care and treatment in England and Wales without explicit consent, you may need to apply to the National Information Governance Board for approval.

For details of Section 251 of the NHS Act 2006, how it regulates the control of identifiable patient information and how it may impact on your research, see www.nigb.nhs.uk. Further guidance is available from the information button next to the option on applying to NIGB in Question 4 of the Project Filter.

Approval by NIGB does not negate the need for a favourable opinion from a REC or approval/permission from the host organisation.