STP Project Ethical Approval Process

Introduction

This document has been produced specifically for STP trainees who will undertake their University of Manchester Masters research project within the NHS. The aim is to guide students through the process of obtaining regulatory approvals for their study.

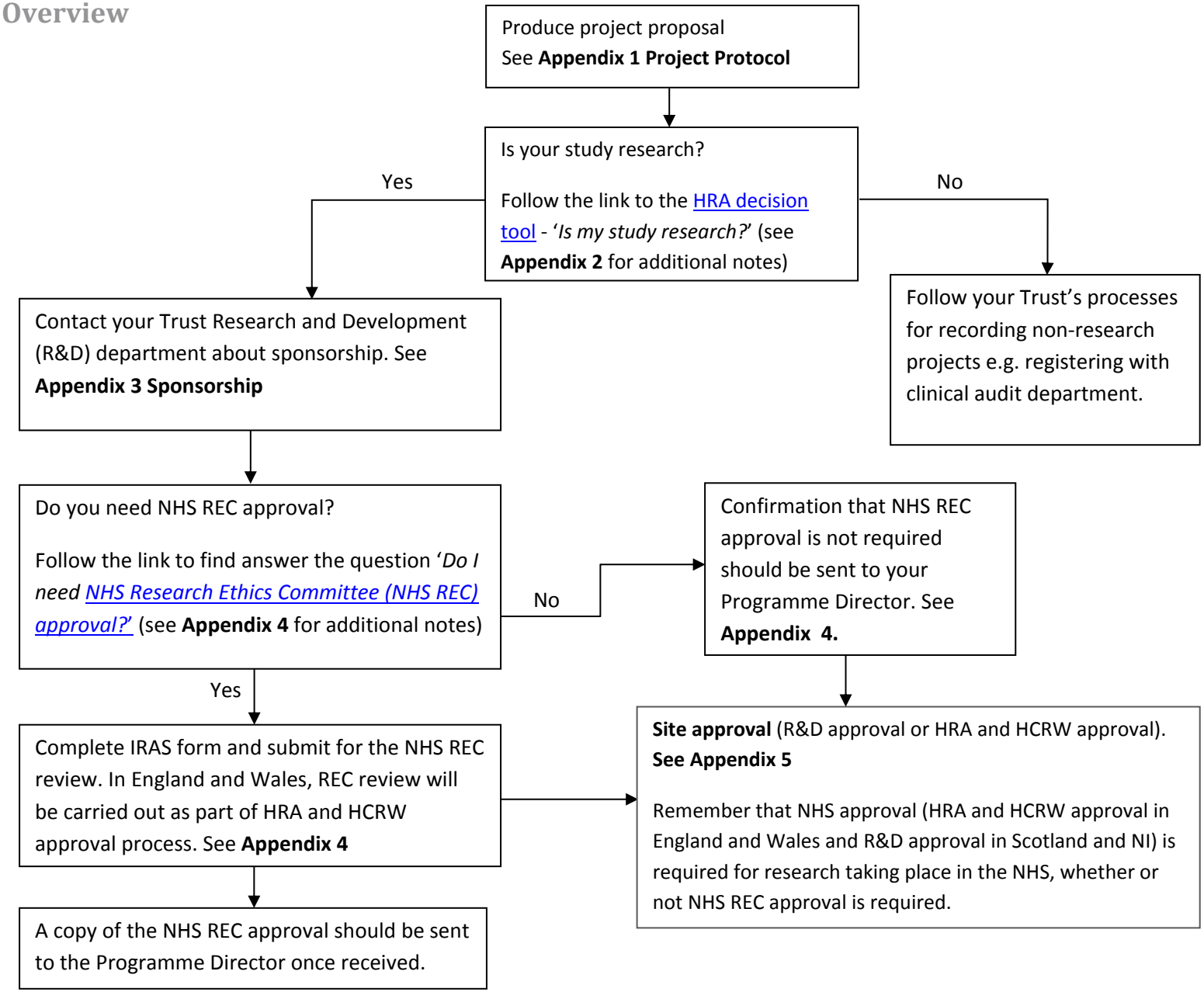
Health-related research is highly regulated, protecting participants and ensuring that any work undertaken is ethically sound, of high quality, and is safe. There are numerous regulatory bodies in the UK which each have roles associated with different areas of health-related research, and have responsibilities to review and approve research activity.

The review processes required for each study will depend on the nature of the study and where it is being carried out. The two main areas for consideration when it comes to the study approvals are (1) making sure that the studies have been through an appropriate ethical review process and (2) approval is sought for the sites hosting the research.

This document focuses on the process for getting ethical approval from an NHS ethics committee, where required. There is also a description of the process for getting approval at the Trusts and details about the role of research governance sponsor.

The overall process is summarised in an initial flowchart and associated information and guidance is contained in a series of the appendices.

Process Overview



Appendix 1 Project protocol

A protocol outlines the background to the research, giving justification for the specific research proposed (all research carries some risk and/or inconvenience for the participant and must be justified).

The protocol also outlines the proposed methodology, including how potential participants are to be identified, approached and recruited. The methodology will also explain what the participant will be asked to do, such as how contact is made, how often (e.g in case of reminder mailings); what questionnaire instruments they will have to complete, how long this will take etc;

Suggested sections include

- title;
- abstract/summary;
- justification for the proposed research;
- aims / objectives;
- experimental design and methods (including statistical analysis);
- ethical considerations;
- safety considerations/reporting
- benefits of the study; and
- resources and costs.

This is the document that sets out what you propose to do and how and, once this has been given a positive ethical opinion, you are bound by it. Any changes/deviations from the 'approved protocol' are considered breach of protocol and constitute research misconduct as defined by the University's Code of Practice for Dealing with Complaints of Misconduct in Research.

If you wish to alter your protocol substantially (this is termed a substantial amendment), you will need to submit any proposed changes to the relevant ethics committee as a substantial amendment. You must have received approval for this new version of the protocol before you can change the way you conduct the research.

Your protocol should be dated and contain a version number so that you are clear which version you are working to.

For guidance on research involving human tissue and data see Data and Tissues Tool Kit.

Appendix 2 Is my study research?

This can be a difficult question to answer but, whether your study is or isn't research has implications for the approval that may be required before your study starts.

How is research defined?
The UK Policy Framework for Health and Social Care Research 2018 defines research as:

For the purpose of this policy framework, research is defined as the attempt to derive generalisable or transferable[10] new[11] knowledge to answer or refine relevant questions with scientifically sound methods[12]. This excludes audits of practice and service evaluations. It includes activities that are carried out in preparation for or as a consequence of the interventional part[13] of the research, such as screening potential participants for eligibility, obtaining participants' consent and publishing results. It also includes non-interventional health and social care research (i.e. projects that do not involve any change in standard treatment, care or other services), projects that aim to generate hypotheses, methodological research and descriptive research. Projects whose primary purpose is educational to the researcher, either in obtaining an educational qualification or in otherwise acquiring research skills, but which also fall into the definition of research, are in scope of this policy framework. Activities that are not research according to this definition should not be presented as research and need not be conducted or managed in accordance with this framework. A decision tool that provides a definitive answer about whether a project counts as research under this policy framework is available at www.hra-decisiontools.org.uk/research.

[10] NB This definition involves an *attempt* at generalisability or transferability, i.e. the project deliberately uses methods intended to achieve quantitative or qualitative findings that can be applied to settings or contexts other than those in which they were tested. The *actual* generalisability or transferability of some research findings may only become apparent once the project has been completed.
[11] Including new knowledge about existing treatments or care.
[12] Projects that are not designed well enough to meet this definition are not exempt from this policy framework – see paragraph 9.10.a.
[13] This means the part of the research where a change in treatment, care or other services is made for the purpose of the research. It does not refer to other methodological 'interventions', e.g. issuing a postal survey.

What guidance is there?
The HRA has developed an online tool to assist with the decision making; the tool can be accessed here: http://www.hra-decisiontools.org.uk/research/. The tool asks a series of 'Yes/No' questions and based on the responses will indicate whether the study is research. You need to be sure that the responses you give to the questions are accurate. If you are not sure about any of the questions or the outcome of the tool then make sure you get further advice from your supervisor, the Trust or the HRA (hra.queries@nhs.net).

If the tool confirms that the study is not research then you will not need to apply for NHS REC approval or NHS approval (HRA and HCRW approval or R&D approval). You should send a copy of the outcome of the tool(s) to your University supervisor as confirmation that ethical approval is not required.

The HRA has published a table which can provide some more information about the difference between research, service evaluation (including the service development and quality improvement), clinical audit, surveillance, usual practice (in public health). The table can be accessed from within

the decision tool or directly from: http://www.hra-decisiontools.org.uk/research/docs/DefiningResearchTable_Oct2017-1.pdf.

If my study is not research does this mean I don't need any approvals?

You may not need regulatory approvals but, even if your study is considered to be a service evaluation (including service development) or clinical audit, most Trusts would still expect it to be registered with them. Some Trusts have a clinical audit department or equivalent that should be informed about your study. If you are not sure of the process for registering your study then you can contact the R&D office for the Trust and ask them to advise. The R&D contacts for all NHS Trusts can be found using the National Directory of NHS Research Offices: http://www.rdforum.nhs.uk/content/contact-details/.

Appendix 3 Sponsorship

All research that is undertaken in the NHS needs to have a research governance sponsor i.e. an organisation that takes overall responsibility for the study. The sponsor is responsible for making sure that everything is place before the study starts and has oversight of the study from beginning to end. The sponsor also needs to sign off NHS REC and HRA and HCRW approval/R&D applications.

In most cases the University of Manchester would expect to take on the role of research governance sponsor for research being carried out by registered students. However, in the case of some student projects, it is more appropriate for the host Trust to take on this role e.g. where the student is employed by a Trust.

As a University, we expect that the Trust takes on the responsibility of sponsorship for STP MSc student projects on the basis that:

- The research is generally limited to a single host Trust
- The students carrying out the research are employed by the host Trust
- The supervisors overseeing the research are employed by the host Trust
- The host Trust has a duty of care to the patients (or tissue or data) that are recruited/accessed as part of the study
- The Trust is the data custodian and no data will transfer to the University
- The approval processes are more streamlined when the organisation hosting the research also acts as sponsor; the study will not need to go through the UoM sponsor review process and there are less documents required as part of the HRA AND HCRW approval/R&D approval process. These additional steps associated with University sponsorship have been seen in the past as adding to the delay in getting the approvals in place.

This approach is falls under the UK Policy Framework caveat for sponsorship of student research:
9.12. Universities and colleges should accept the role of sponsor for all educational research conducted by their own students, ***unless the student is employed by a health or social care provider that prefers to take on this role.*** *Sponsors of educational research should ensure that supervisors can and do carry out the activities involved in fulfilling this role. Where the academic supervisor cannot adequately satisfy the sponsor's oversight responsibilities due to location or expertise, the sponsor should agree co-supervision arrangements with a local care practitioner.*
UK Policy Framework for Health and Social Care Research 2017

In order to discuss sponsorship with the Trust, you should contact the R&D office within the Trust. It is important to make it clear during these discussions that you a Trust member of staff undertaking an MSc as part of your training. The R&D contacts for all NHS Trusts can be found using the National Directory of NHS Research Offices: http://www.rdforum.nhs.uk/content/contact-details/.

If the Trust is not in a position to act as sponsor then you need to contact the Programme Director to discuss what options are available.

Appendix 4 Is NHS REC review required?

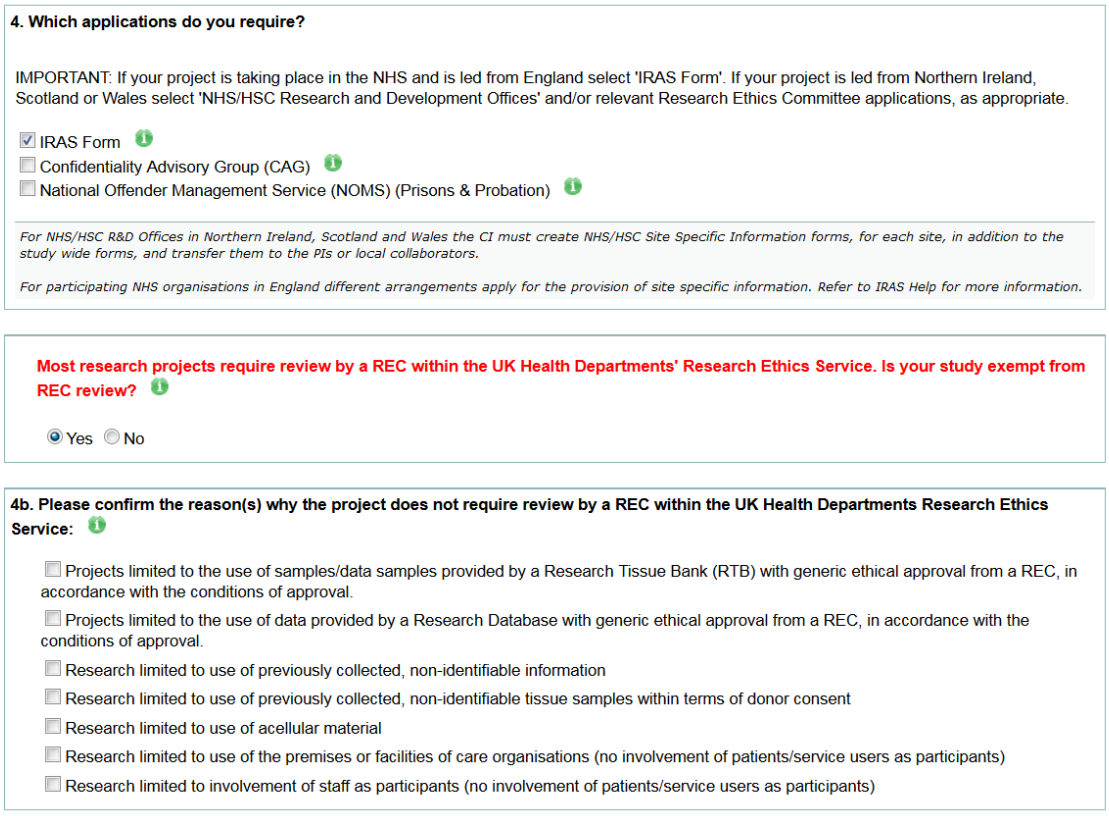
There are a number of legal and policy requirements for NHS REC review. In most cases the involvement of any NHS or adult social care service users or their family/ carers either in terms of their active involvement or the use of their data or tissue, would require NHS REC review. There are also other requirements for NHS REC review which mean some studies that don't involve service users still need NHS REC review e.g. the involvement of any individual that lacks capacity consent would mean a study would have to be reviewed by an NHS REC.

The HRA has developed an online tool which can be used as a guide as to whether NHS REC review is required. The tool is available here: http://www.hra-decisiontools.org.uk/ethics/. The tool is completed by answering a number of 'Yes/No' questions at the end of which the tool will generate a report indicating whether NHS REC review is required or not. You will be able to print a summary report of the outcome.

It is important to make sure that you answer the questions accurately. If you are not sure about the questions or the decision then you can contact the HRA (HRA.Queries@nhs.net) or speak to your Trust's R&D office.

Are there any exemptions to NHS REC review?

There are a small number of exemptions from NHS REC review. There is an option on the filter question in IRAS (Q4) which allows you to indicate that the study is exempt from NHS REC review. This brings up a list for exemptions:



4. Which applications do you require?

IMPORTANT: If your project is taking place in the NHS and is led from England select 'IRAS Form'. If your project is led from Northern Ireland, Scotland or Wales select 'NHS/HSC Research and Development Offices' and/or relevant Research Ethics Committee applications, as appropriate.

- [x] IRAS Form
- [ ] Confidentiality Advisory Group (CAG)
- [ ] National Offender Management Service (NOMS) (Prisons & Probation)

For NHS/HSC R&D Offices in Northern Ireland, Scotland and Wales the CI must create NHS/HSC Site Specific Information forms, for each site, in addition to the study wide forms, and transfer them to the PIs or local collaborators.

For participating NHS organisations in England different arrangements apply for the provision of site specific information. Refer to IRAS Help for more information.

Most research projects require review by a REC within the UK Health Departments' Research Ethics Service. Is your study exempt from REC review?

- (•) Yes
- ( ) No

4b. Please confirm the reason(s) why the project does not require review by a REC within the UK Health Departments Research Ethics Service:

- [ ] 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.
- [ ] 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.
- [ ] Research limited to use of previously collected, non-identifiable information
- [ ] Research limited to use of previously collected, non-identifiable tissue samples within terms of donor consent
- [ ] Research limited to use of acellular material
- [ ] Research limited to use of the premises or facilities of care organisations (no involvement of patients/service users as participants)
- [ ] Research limited to involvement of staff as participants (no involvement of patients/service users as participants)

The following list is taken from the IRAS guidance for Filter question 4b. It is important to note that even though such research may be exempt from NHS REC review, such studies may need NHS permission/approval i.e. HRA and HCRW or R&D approval.

- **Projects limited to the use of non-identifiable samples/data samples provided by a Research Tissue Bank (RTB) with generic ethical approval from a REC, in accordance with the conditions of approval.**

- **Projects limited to the use of non-identifiable data provided by a Research Database with generic ethical approval from a REC, in accordance with the conditions of approval.**

- **Research involving previously collected, non-identifiable information.** Research limited to secondary use of information previously collected in the course of normal care (without an intention to use it for research at the time of collection) is generally excluded from REC review, provided that the patients or service users are not identifiable to the research team in carrying out the research. This exception also applies to research undertaken by staff within a care team using information previously collected in the course of care for their own patients or clients, provided that data is anonymised or pseudonymised in conducting the research.

- **Research involving previously collected, non-identifiable tissue samples.** Research limited to use of previously collected, non-identifiable material consisting of or including cells in accordance with the terms of donor consent is generally excluded from REC review. However, REC review would be required if any of the following applied:

  (a) Consent for research has not been given, or the research is not within the terms of the consent
  (b) The samples will be held on premises in England, Wales or Northern Ireland without a licence from the Human Tissue Authority to store relevant material for scheduled purposes
  (c) The research also involves removal, storage or use of new samples from the living or the deceased
  (d) The research also involves use of identifiable information held with the samples.

- **Research involving acellular material.** Research limited to acellular material (e.g. plasma, serum, DNA*) extracted from tissue previously collected in the course of normal care is generally excluded from REC review, provided that the patients or service users are not identifiable to the research team in carrying out the research. This exception applies to research undertaken by staff within a care team using samples previously collected for clinical purposes from their own patients or clients, provided that the samples/data are anonymised or pseudonymised in conducting the research. However, REC review would be required if the research involved:

  (a) Collection of tissue samples from patients in order to extract acellular material for the research
  (b) Collection of information from patients
  (c) Use of previously collected information from which patients could be identified by the researchers
  (d) Analysis of DNA in material from the living, where consent for research is not in place from the person whose body manufactured the DNA

* The Governance Arrangements for Research Ethics Committees (GAfREC) was updated in September 2018 and now **requires NHS REC review for research involving human DNA extracted from acellular material.**

- **Research involving the premises or facilities of care organisations.** REC review is not required for research involving use of or access to a care organisation's premises or facilities, provided that review is not required under any other applicable legal or policy requirement. For example, a Phase 1 clinical trial undertaken by a Contract Research Organisation on premises rented from a NHS Trust would legally require REC review under the Clinical Trials Regulations. But research undertaken by a university department on NHS premises, involving healthy volunteers not recruited as NHS patients and not subject to any legal requirements, would not require review by a REC within the UK Health Departments' Research Ethics Service and could be reviewed by the university's research ethics committee.

- **Research involving staff as participants**. REC review is not normally required for research involving NHS or social care staff recruited as research participants by virtue of their professional role.

How do I apply for NHS REC review

If the tool indicates that you will need to apply for NHS REC review then you will need to generate an application in IRAS (Integrated Research Application System); the online system can be accessed at www.myresearchproject.org.uk.

The process for getting regulatory approvals in England and Wales has been streamlined with the introduction of the HRA and HCRW approval process; HRA and HCRW approval pulls together NHS REC review with NHS approval (see appendix 5). For studies led from Scotland or Northern Ireland, an application will need to be submitted directly to the NHS REC.

Whether you are applying directly for REC approval (Northern Ireland or Scotland) or HRA and HCRW approval (England and Wales), the same 'IRAS form' is created for all projects. The HRA have produced clear, stepped guidance for each stage of preparing and submitting your application which can be accessed here: https://www.hra.nhs.uk/approvals-amendments/.

Tips for completing the IRAS form:

1. Make sure you ready the questions carefully, especially the filter questions as these will dictate questions appear later in the form.
2. There is question specific guidance available for virtually all questions on the form – look out for the green help buttons. Not only will this guidance help you answer the questions but it is regularly updated.
3. Check for typos. It can be difficult to spot typos on the online system and so you might find it easier to print off and review a PDF copy of the form.
4. Contact your Trust as sponsor of the study to see if they have any standard answers to help completing the form.
5. Peer review: you will be asked to submit evidence of peer review. You speak to your University supervisor to get confirmation that the study is of sufficient quality.

Once you have generated the IRAS form you need to send it along with a copy of the protocol to:

- the Trust R&D office as they will need to authorise the application on behalf of the research governance sponsor. The review process may vary between the Trusts and so you will need to discuss with your R&D office to make sure you send everything they need for review.

- your academic supervisor(s) at the University. Your supervisor(s) need to authorise the application to confirm they are satisfied with the scientific content of the research and that it is satisfactory for an educational qualification at this level.

When the application has been fully authorised you can book it in for review via the Central booking service http://www.hra.nhs.uk/resources/applying-to-recs/nhs-rec-central-booking-service-cbs/. This is the same process for booking in applications for REC review and HRA approval.

Depending on the type of study, your project may be eligible for Proportionate Review (PR). This is a streamlined ethics review process for studies with the minimal ethical issues. The benefit of going through this process is that you don't need to attend the REC meeting and it takes on average only 10days from the submission of the application to getting an ethical opinion. You will be able to discuss whether your study is eligible for proportionate review when you book your application via the Central Booking Service.

If your study is not eligible for proportionate review, it will go to a full meeting and you will be sent details of the REC and the meeting dates and times. You and your supervisor are advised to attend the meeting.

Once you have a copy of the final REC approval letter, you should send a copy to the Programme Director.

If my study is exempt from NHS REC review, does this mean I need to apply for University REC (UREC) approval?

NO. If you do not need NHS REC approval, you WILL NOT require University REC (UREC) approval. If your study is exempt from NHS REC review and this has been agreed with the Trust, you should send confirmation to your Programme Director. A copy of the report generated by the online tool should be sent with details of the sponsor contact for your Trust (in case further information is required).

Appendix 5 Site approvals: HRA and HCRW approval and R&D approval

Getting appropriate ethics approval for your study is essential but so too is making sure that you have approval from the Trust for the research going ahead on their premises. The benefit of the Trust acting as sponsor for any research taking place on their premises is that they are able to consider both aspects (sponsorship and hosting the research) at the same time.

HRA and HCRW approval (England and Wales)

In the case of the studies taking place in England and Wales, an application for HRA and HCRW approval will be made. HRA and HCRW approval brings together the NHS REC approval process and the study wide governance checks carried out on behalf of the NHS. An application for HRA and HCRW approval needs to be submitted for all research studies being undertaken in the NHS. The single application which is submitted via IRAS is reviewed in parallel by an NHS REC (unless the study is exempt from NHS REC review) and an HRA assessor.

Even though you have to submit a single application, you will receive confirmation of the NHS REC approval and HRA and HCRW approval separately; HRA and HCRW approval will only be issued once REC approval is in place. Once the HRA and HCRW approval has been received and the Trust (as sponsor and host organisation) has confirmed that everything is in place, you may start the study.

Statement of Activities (SoA) and Schedule of Events (SoE)

The SoA and SoE are key documents that need to be completed for the HRA and HCRW approval process. They are used to communicate details of the study from the research governance sponsor to the sites involved in the study. However, these documents are not required where the host site is also the research governance sponsor.

R&D approval (Scotland and Northern Ireland)

In the UK nations, other than England and Wales, the NHS REC review process and NHS approval processes (R&D approval) are coordinated but separate processes. You only need to generate one form in IRAS but, the form needs to be submitted separately to the NHS REC via IRAS e-submission **and** to the relevant national coordinating function:
Scotland: NHS Research Scotland Coordinating Centre (nhsg.NRSPCC@nhs.net)
NI: HSC R&D Division (research.gateway@hscni.net)

Site Specific Information (SSI) forms

SSI forms are generated in the IRAS system used to communicate study specific details to the sites i.e. what would happen at the site if they took part in the study. An SSI form needs to be completed for any NHS site in Scotland and Northern Ireland only, they are not required for sites in England and Wales. In the case where the host organization is also the sponsor, the SSI forms may not be necessary. Before completing the SSI form, you should speak to the Trust R&D office and find out exactly what is required by the Trust.

There are ongoing discussions about the use of SSI forms in Scotland and NI and specifically about whether they can be replaced by the local information packs currently used in England and Wales. Please check with the HRA website and/or your R&D office.