SUBMITTING AN ETHICS APPLICATION

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Introduction

Over the last decade the Ethical Committee approval process for human research studies has been substantially revised. The process is now "online" and integrates with other related regulatory bodies (e.g. MHRA and ARSAC) in order to try and streamline the whole process and avoid multiple applications to the various agencies. The Integrated Research Application System (IRAS) can be accessed via: www.myresearchproject.org.uk/.

Registration is free and there is extensive guidance for new users, question specific help, and FAQs available on the site.

The system allows you to "build" your application in stages and then transfer control (online) of the application between yourself and your colleagues in order to add further details and the other information required to complete the forms. Once complete, the application is then "locked" for submission. In future you will be able to upload all the relevant associated documents.

Locking usually requires the prior approval of your local hospital R&D office, which checks that you have appropriate peer review, insurance and indemnity arrangements and clarification of project funding streams. They will then confirm that they will sponsor your study – unless you already have an external sponsor. Once ready for submission currently you telephone the local or national Ethics service (*Local or Central Allocation System – details on NRES website)* to choose an Ethics Committee and confirm a review date. This does not have to be with your local committee but this usually makes it easier if you want to attend in person. At this stage you have four working days to send them actual signed "wet ink" copies of the relevant document pages.

There are several important components of an IRAS application that occur in typical human imaging studies and these are highlighted in the following sections. The IRAS system is deliberately flexible and uses "active filters" to adapt the form and the questions you must answer to the type of project you are undertaking. An exhaustive and comprehensive overview of every IRAS question would be impractical in this short guide but the online help pages and staff in your local R&D or Trials office (if you have them) can often provide additional advice and guidance on specific questions at the time of building your application.

Project Prefiltering

After registering on the IRAS system you start a "**new project**" and answer a series of key initial questions about the project so the system knows which parts of the application you need to complete.

You will be asked at this stage if you want your study to be included on the NIHR portfolio. There are advantages to this and also required criteria. For details see:
http://www.crncc.nihr.ac.uk/

Although there is a **navigation page** for the IRAS forms only a few questions are visible on each online screen. However even at this initial stage it is possible to save or print a PDF of all the subsequent questions – and this can often be helpful at the start – so you can get an idea of the information you will need to complete the application. Typically there are three main components – Ethics, R&D and SSI.

Retrospective studies which utilise anonymised data, and avoid "interventions" may be able to avoid a formal Ethics Committee application but will still usually require completion of an R&D form and local R&D department approval.

If your study is similar to one undertaken recently in your department you can **import** a previous IRAS or Eudract XML form and use this as the basis for your application which can help save you time.

If your study involves **ionizing radiation** then you will need a formal Medical Physics assessment of all radiation exposure within study, plus Clinical Radiation Expert assessment of this exposure to evaluate if this is reasonably justified.

Required Documents

Each IRAS application generates a **checklist** of required documents that would typically include at least a **Research Protocol**, **Patient Information Sheet**, **Consent Form** and **SSI (Site Specific Information) form.**

1. **Research Protocol**
   Unless you have already had your research project peer-reviewed (for example by an external funding body) then your research protocol will require independent peer review – often organised by your local R&D office – to decide if your project is worthwhile and appropriate. This is frequently required for small imaging research studies and is important as it determines whether or not your hospital will take on the insurance risk if any non-negligent participant harm occurs during your research. The protocol needs to be clear, explain the rationale for the study, outline a hypothesis and indicate how your project will address/answer the hypothesis. It is usually written in a similar way to a formal paper

2. **Research Team**
   You will need to identify in the application who your research collaborators are and if they are trained in obtaining consent, have undertaken any research training such as "Good Clinical Practice" or "consent" courses. It is better to be over-inclusive at this stage if in any doubt. Each member of the team will need to submit a short CV with the application containing details of their employment, relevant research experience and skills.

3. **Patient Information Sheet**
   Ethics committees require information sheets to be clear and avoid the use of technical language. Failure to observe these requirements is one of the commonest reasons for Ethics Committees' to reject or delay submissions. They also require numerous important pieces of information, e.g. relating to risk, insurance, and discomfort, to be clearly stated. This can lead to a long document but you should also make every effort to keep it as clear and concise as possible. This document forms a key part of the consent process and detailed information on consent is available on the IRAS website. A particular topic of current imaging interest is the need to clarify how any "incidental" imaging findings would be managed if found during the research (for a discussion, see the RCR's document *Management of Incidental Findings Detected During Research Imaging* available to download from the following web link:
   http://www.rcr.ac.uk/publications.aspx?PageID=310&PublicationID=357)

4. Consent

The required format and information that must be on research participant consent forms is described on the IRAS site and you must submit your version of this form for approval. Increasingly the consent process is under scrutiny and for example it is now good practice to record both date and time that consent was obtained.

5. SSI

Many imaging projects will only be undertaken on one site and you will be asked to provide information and details about that site in the SSI section of the application. This is so the local R&D department can confirm that the research environment is appropriate for the planned research. There are different arrangements for multi-centre trials which are more complicated but fully described on the website.

6. Checklist

The IRAS system generates a project specific "checklist" to help you ensure you have all the necessary documentation uploaded before you "lock" and submit the application.

The Ethical Committee review

Attendance at the Ethical Committee review meeting is not mandatory but desirable, particularly if there are any complex issues. You should remember that the committee is unlikely to have a Radiologist on the panel and also includes lay members that have to understand your application and what it entails for the research participant.

Approval& Reporting

Frequently approval is granted subject to minor modifications such as some changes on the patient information sheet. These changes have to be resubmitted and then if all goes well you will receive written approval and a start date and duration of the approval.

Before you can start your projects you will also need to have the written approval of your local R&D department along with any required governance checks.

The Ethics Committee will require regular reports on the progress of your project, patient recruitment numbers and information on any protocol variations or unforeseen problems that materially affect the study or the participants. At the conclusion of the project an "end of study" report is also required.

Amendments

If you make any material alterations to the project protocol or for example change the research team membership then a formal amendment may be need to be approved by the Ethics Committee. There are minor or major amendments and these are made via the IRAS website and require sponsor signatures.

Details of what constitutes an amendment are outlined on the website. It is also important to consider this requirement carefully when writing the protocol and identifying your research team to try and avoid the need for later amendments.

Conclusion

The IRAS process can be time-consuming (months) and at times frustrating but once familiar with the process you will become much faster and skilled at using it. The questions are appropriate and indirectly they will help you to design appropriate and robust research projects. The IRAS application process continues to evolve and there is broad agreement that it has helped support a safer, more consistent approvals process designed to protect research participants and enhance research transparency.