How to….

Start and navigate your way through the ethics application process

Introduction

Fantastic, you've worked up you research proposal and the study protocol is defined to the smallest of detail. One hurdle remains... the ethics application! This application, though not the most exciting part of your research journey is a vitally important exercise and, is essential. With more of us contemplating research it is important to be more aware of the processes involved. The aim of this guide is to give an overview of the research application process for those who may be embarking on or thinking of going into research. For those of you who have already started, a short paragraph is dedicated to the process of getting an amendment to your study protocol.

First, why we need research ethics

During the mid-1990s there were unusually high mortality rates in babies and infants that had undergone heart surgery in Bristol leading to an investigation that ultimately led to the suspension of two heart surgeons. In 1999, it emerged that the hospital was retaining the hearts and other organs of babies and that this was standard practice. It transpired that other hospitals around the country e.g. within Birmingham and Alder Hey, Liverpool did the same. In an official enquiry, it was concluded that fetal tissue and body parts had been illegally and unethically removed which highlighted wider issues over consent and tissue retention that needed addressing. As a consequence of the Bristol inquiry, the NHS Reforms and Healthcare Professions bill was laid before parliament. It formed the legislative basis for several post-Bristol inquiry reforms, such as the strengthening of the NHS inspectorate and the commission for health improvement. In 2001, the government published 'Learning from Bristol', its formal response to the inquiry, which set out how it plans to make the NHS safer, more open and accountable.

As a consequence of half a decade worth of inquiry, the research governance framework (RGF) was introduced by the DH with the aim of improving research quality, safe guarding the public as well as treating patients with mental health illness, establish high standards for all aspects of research activity, change policy regarding retention of human tissue and introduce mechanisms for delivery of those standards. The RGF also clarifies who is actually responsible for conducting research.

In order to fulfill stringent criteria as set out by the RGF, an application to conduct research had to be made that was reviewed by an ethics committee. There were initially concerns that this process was lengthy, inconsistent and had a negative impact on would be researchers. Actually, having been though it I found it to be streamlined and efficient but I do understand it can be daunting for those applying for the first time.

Who's who, roles and responsibilities

Chief investigator (CI- overall lead/your boss) and Principal Investigator (PI - who conducts research. Most often it is you)

- Responsible for proposing the study and ensuring the study is conducted exactly to protocol e.g. 5mls of blood means 5mls, no more.

The sponsors - usually the NHS trust and the associated R&D department unless commercial i.e. pharma sponsored.

- Responsible for scientific quality through peer review and ensure researchers have necessary expertise and resources. The care organisation ensures research on staff, patients or participants meets standards set out in RGF. It is usual but not always the case (i.e. in the case of commercial studies) that the care organisation and sponsors are the same trust.

Ethics committees

- Located nationwide as Research Ethics Committees (REC). They comprise individuals drawn from the public as well as health professions and can include patients, clinicians, nurses, pharmacists and allied health care professionals. Their main responsibility is to provide independent review of research involving patients or volunteers, their organs, tissue or data. Their remit is to consider the dignity, rights, safety and well being of participants for example, by ensuring written informed consent and data protection are obtained.

CLRN (Comprehensive Local Research Network)

- Originated from the DOH publication 'Best Research for Best Health', a 5-year research strategy for the NHS in England. The CLRNs, are based locally within R&D departments. Their remit is to ensure all patients, health professionals and participants benefit from clinical research through a central portfolio of research studies that facilitate collaboration across the country. They streamline processes involved in the R&D approval process and support NHS costs use incurred by the study e.g. nursing staff, clinical consumable costs. They do not pay lab fees. The study has to be included in the CLRN portfolio. To benefit from the CLRN, recruitment data must be uploaded every month - this is the way the DH funds the CLRNs. Geriatrics had an Age and Ageing CLRN led by Marion McMurdo (Dundee) and Helen Roberts (Southampton). For an in depth explanation of the CLRN see guide by James Fisher.

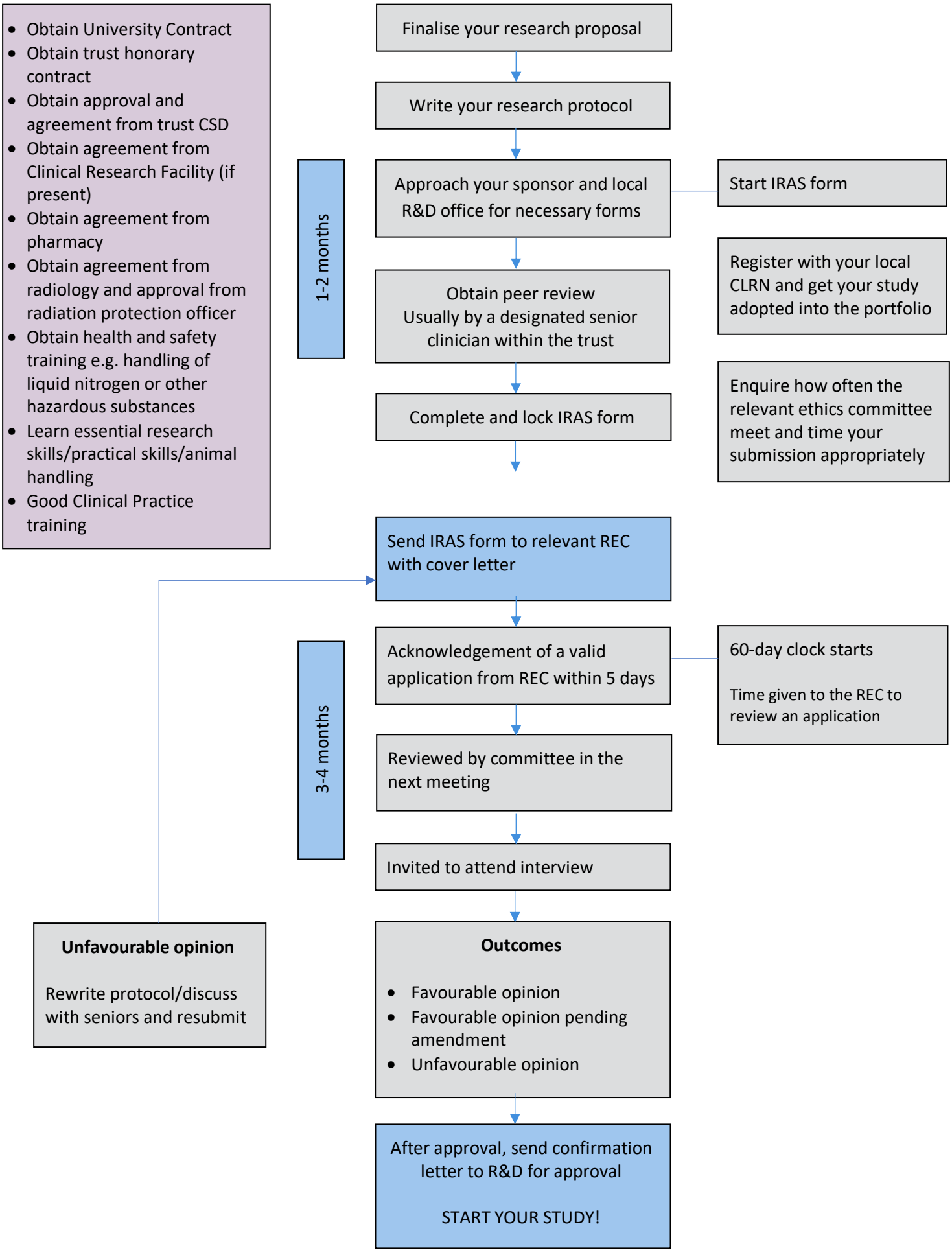
Application Process

The online ethics application has gone through different iterations and labels. The latest is the Integrated Research Application Service form (IRAS - register at www.myresearchproject.org.uk). The form allows you to enter a minimum amount of data that, through filters that you set in the beginning of the form, automatically populates other sections of the form for necessary permissions from review bodies e.g. NHS R&D, MHRA (Medicines and Healthcare products Regulatory Agency) or GTAC (Gene Therapy Advisory Committee) depending on the nature of your study that may fall into a CTIMP (Clinical Trial of an Investigational Medicinal Product) or non-CTIMP type of study.

Brief overview of data required in the IRAS form

- Study background and rationale
- Who are the Chief and Principal investigators?
- Who is sponsoring the study?
- Who is funding the study?
- Where is the study being co-ordinated and how long the study is going to last
- How many sites are being used for research – to include site-specific information
- Who are the participants/patients?
- How are you going to approach them, obtain consent and protect their personal data
- What is involved i.e. tests, investigations and their invasiveness?
- What are the costs?
- What are the risks posed to the participants by taking part in the study e.g. radiation, drug side effects
- How much time do participants/patients have to give up?
- What are the proposed outcomes?

It is essential to be specific and succinct when populating the IRAS form. Your local trust R&D department will have their own forms as well as the important peer review form that will need similar if not the same information. It is therefore necessary and best if the R&D and IRAS forms are completed simultaneously. Don't forget that you will need additional documentation/approvals from your local research facility, radiation protection officer if for example DXA or CT/XR is going to be used on your study participants. The following schema outlines the application process and the estimated time needed. It also highlights what additional activities you need to achieve during the application process.


Finalise your research proposal
Write your research protocol
Approach your sponsor and local R&D office for necessary forms
Start IRAS form
1-2 months
Obtain peer review
Usually by a designated senior clinician within the trust
Register with your local CLRN and get your study adopted into the portfolio
Complete and lock IRAS form
Enquire how often the relevant ethics committee meet and time your submission appropriately
Obtain University Contract
Obtain trust honorary contract
Obtain approval and agreement from trust CSD
Obtain agreement from Clinical Research Facility (if present)
Obtain agreement from pharmacy
Obtain agreement from radiology and approval from radiation protection officer
Obtain health and safety training e.g. handling of liquid nitrogen or other hazardous substances
Learn essential research skills/practical skills/animal handling
Good Clinical Practice training
Send IRAS form to relevant REC with cover letter
Acknowledgement of a valid application from REC within 5 days
60-day clock starts
Time given to the REC to review an application
3-4 months
Reviewed by committee in the next meeting
Invited to attend interview
Unfavourable opinion
Rewrite protocol/discuss with seniors and resubmit
Outcomes
Favourable opinion
Favourable opinion pending amendment
Unfavourable opinion
After approval, send confirmation letter to R&D for approval
START YOUR STUDY!

Additional information

The interview

- Attended by a committee panel of up to 10 members
- Specifically interested in the safety of the participants
- Less focus on the scientific background – that is the remit of the designated peer reviewer in your trust
- Answer all questions truthfully and accurately
- If you don't know – send details in an email/post afterwards

Your study protocol

- Follow local R&D template that will include a pre-formatted patient/participant information sheet and consent form
- Must have a succinct background and rationale
- Detail the CI and the research team
- Detail your study group and power
- Detail all proposed investigations even though you know you may not perform some – better to have approval for them than not

Obtaining an amendment to your protocol once the study has begun

- As often happens, you think of new ideas/investigations once your study has started. NRES has a system to allow these ideas to be incorporated into your protocol. Amendments can either be non-substantial or substantial. In my experience any change or addition to the protocol has been classed as substantial. Amendments to the protocol must be highlighted in bold as well as underlined and sent as an updated version e.g. *protocol ver. [2] 030312.* In addition, the REC requires you to send new versions of the information sheet and consent if they reflect the changes in the protocol. All the documents should then be sent to the REC with a 'Notice of Substantial Amendment' form found at https://www.hra.nhs.uk/approvals-amendments/amending-approval/ For a non-CTIMP study, an acknowledgement comes from the REC within 5 days. The committee have 35 days to either give a favourable or an unfavourable opinion on the amended protocol. Note: RECs are wising up to investigators sending in a protocol for a new study as an amendment to avoid the lengthy approval process therefore, any new versions of the protocol should always mirror the original closely.

Grant applications and costings

- Your local Research Design Service (RDS) and Trust R&D Offices are invaluable sources of help and information and will help with writing a grant application as well as necessary power calculations.

Good Clinical Practice (ICH-GCP) training

- Essential for all researchers
- Online or day courses are available through your institution and are free

Aims

- Understand the main difference between research and audit
- Be familiar with the regulatory aspects of conducting clinical research
- Be familiar with the approvals systems for R&D, Ethics and the MHRA
- Be able to identify adverse events and the reporting procedures
- Understand the importance of maintaining a good site file
- Be able to identify 'essential documents' and know what to do with them
- Be familiar with processes for monitoring, audits and inspections

Harnish Patel, March 2012