Title: Ethical approvals for NHS-based research: an overview

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Introduction

Research is a core function of health and social care. It should be innovate and novel, improve the evidence base, reduce uncertainties and lead to improvements in care. Research projects should be scientifically sound and guided by ethical principles in all their aspects[1].

The purpose of ethical guidelines is both to protect patient volunteers, safeguard participants from exploitation and to preserve the integrity of the science. In response to studies, such as the Tuskegee Syphilis Study where patients were exploited for research purposes at the detriment of their safety, a series of ethical codes of conduct, e.g. Declaration of Helsinki (2000) were developed to help guide key ethical clinical research principles and guidelines. Emanuel *et al*, describes seven guiding ethical principles[2] **(see Table 1)**:

- Social and clinical value
- Scientific validity
- Fair subject selection
- Favourable risk-benefit ratio
- Independent review
- Informed consent
- Respect for potential and enrolled participants

Ensuring these principles are considered is the responsibility of the chief investigator, funder, research sponsor, research site, employers and health and social care regulators involved in each research study[1]. The law may be authoritative regarding boundaries of acceptable practice but it is not exhaustive. Boundaries cannot always be regulated in advance and therefore ethical guidance and approval is needed.

Health Research Authority (HRA) and Health and Care Research Wales (HCRW) process

Applications to key research approval bodies are now made through a single UK-wide Integrated Research Application System (IRAS) provided by the HRA/HCRW. This decision was made in an attempt to streamline the ethical, legal and governance approvals for all project-based research in the NHS in England or Wales. This approval combines an assessment of governance and legal compliance, undertaken by dedicated HRA and HCRW staff, with an independent ethical opinion provided through the UK Research Ethics Service (RES). This process replaces the need for local participating organisations to each carry out

their checks. Adopting this approach allows each of these organisations to better utilise resources on assessing, arranging and confirming their capacity and capability to deliver the study.

For new studies led from Scotland or Northern Ireland but have English and/or Welsh NHS sites, the national R&D coordinating function of the lead nation will share information with the HRA and HCRW Assessment teams, who can issue HRA and HCRW Approval for English and Welsh sites. As mentioned, HRA and HCRW Approval applies only to the NHS in England and Wales. Studies led from England or Wales but have Northern Irish or Scottish sites, will be supported through existing UK-wide compatibility systems, by which each country accepts the centralised assurances, as far as they apply, from national coordinating functions without unnecessary duplication.

To start the approval process, the researcher must make an account and log on to https://www.myresearchproject.org.uk . A new project should be created. A series of project filter questions will be asked. Two key filter questions need to be selected to ensure the project can be put forward to receive ethical opinion:

- Question 4: “IRAS Form” option should be selected (including all other applications that are needed for your research project)
- Question 5: Confirm NHS involvement in your project by selecting ‘yes’

After completing the filter questions, the researcher should go to the Navigation Page, where their application will appear in the Project Forms list labelled as “IRAS Form”. Selecting the label “IRAS Form” will allow the researcher to access this form, and start inputting study-related information. Using the Navigate tab, the researcher can select the section of the IRAS form they wish to complete. Once the relevant information for that section is input, they must click on the “Mark as complete” button to complete that section. It is essential that all sections relevant to the research study should be marked as complete prior to electronic submission as if not, they will not form part of the final IRAS form. Any supporting documentation should be uploaded using the Checklist tab for the IRAS Form.

Electronic authorisations must by requested and received, from both the chief investigator and sponsor of the study, before electronic submission. Once these authorisations have been validated, the application can be submitted using the e-submission tab where a designated IRAS study number will be provided. However, this is slightly misleading as this is actually a pre-submission phase. For the application form to be submitted it must be assigned to a Research Ethics Committee using the central telephone booking system.

Once booked in, the researcher will be able to submit the application electronically using the e-submission tab on the IRAS form.

For further information and support, the following link will provide a step-by-step guide on how to complete an IRAS form (https://www.myresearchproject.org.uk/help/contents/StepByStep_v2-0_20180628.pdf).

The Research Ethics Committee meeting

The Research Ethics Committee (REC) are responsible for reviewing the application submitted via the IRAS system and ensuring that any ethical concerns raised by your project have been addressed. There are numerous committees across the UK, yet you can choose your preferred REC at the time you book in your application. Each REC is comprised of experts from a wide range of healthcare specialties, alongside lay committee members. Between seven and fifteen members of the REC will meet at least 10 times per year, usually in the same location.

The REC will usually invite a member of the study team to attend the meeting to discuss the application. Whilst attendance is not essential, it is highly recommended. Being present at the meeting enables you to explain your study further, and clarify any issues that the REC may have identified. If you have not attended a REC meeting before, it may be beneficial to ask a more senior researcher from your study team to attend with you to provide further support.

Studies that raise no material ethical issues may only require a ‘proportionate review’, in which case attendance at the meeting is not normally necessary. Further guidance on whether your study will require ‘full’ or ‘proportionate’ review can be found on the HRA website.

The REC meetings are formal, and the panel will discuss a number of applications during each meeting. You will be invited to enter the room once the panel have discussed your application and highlighted any concerns that require further clarification. Following introductions, the Chairperson may ask you to briefly summarise your research project to ensure the panel fully understand the study in question. Next, the Chairperson will discuss the concerns raised by the panel, giving you the opportunity to justify your study plan. The

rest of the panel will then be invited to ask you any further questions, and may make comments or suggestions on how potential ethical issues could be avoided.

The panel will not provide you with an opinion at the time of the meeting, yet this will be provided via email shortly after. If the REC continue to hold concerns about the project, the email will contain a 'no opinion' letter, detailing any changes or clarification that would be required before the project can commence. Once these changes have been made, a favourable opinion letter may be issued at the discretion of the Chairperson, often without necessitating another REC meeting.

Top tips for a positive REC meeting:

1. **Be organised**
   Read through your application in advance of the meeting and take note of any potential ethical issues that you may have not addressed. Consider the ways in which you could minimise any negative impacts on your study participants and be prepared to explain these to the REC. Remember that the application form is a large document – the panel won't expect you to have memorised every minute detail about the project, especially if it is a large study. It is useful to bring a copy of your application with you to the meeting, so that you can refer to it if necessary.

2. **Stay calm**
   Despite the formality, the REC meeting is not meant to be a nerve-wracking experience. The panel aim to be supportive and encouraging of the research, and allows researchers the opportunity to ask their own questions or for further clarification.

3. **Don't take criticism to heart**
   Researchers often put a lot of time and effort into planning a research project, which can make it hard for them to hear their hard work being criticised. It is important to remember that the REC have a responsibility to ensure that your project meets the ethical standards, and that ultimately, their comments and feedback will make your study stronger. Try not to be disheartened; it is better to address any issues early, rather than risk complications arising later.

Conclusion

The ethical basis of a study is a primary concern for researchers and participants alike. Seeking appropriate ethical approval is a key part of any study, and so it is beneficial for those involved in research at any level to familiarise themselves with the requirements. Whilst applying for ethical approval for NHS-based research may at first seem to be a daunting process, it is important to remember that there is a wealth of information and support available through the HRA.

1. *UK policy framework for health and social care research*, D.o. Health, Editor. 2017: London.
2. Emanuel, E.J., D. Wendler, and C. Grady, *What makes clinical research ethical?* JAMA, 2000. 283(20): p. 2701-2711.

Table 1

Ethical Principle	Description
Social and clinical value	The answer to the specific research question should be important enough to justify asking people to accept some risk or inconvenience for others.
Scientific validity	The study design should be scientifically robust, valid and feasible to answer the research question. It should follow accepted research principles; have clear methods, and reliable practices.
Fair subject selection	Participants should recruited for the scientific goals of the study and not based on vulnerability, privilege, or other unrelated factors. Participants who accept the risks of research should be in a position to enjoy its benefits.
Favourable risk-benefit ratio	Everything should be done to minimize the risks and inconvenience to research participants to maximize the potential benefits, and to determine that the potential benefits are proportionate to, or outweigh, the risks.
Independent review	An independent review panel should review the proposal, prior to commencing, to make sure the study is ethically acceptable. An independent panel should be use to minimise potential conflicts of interest.
Informed consent	Potential participants should make their own decision about whether they want to participate or continue participating in research. This is done through a process of informed consent.
Respect for potential and enrolled participants	Individuals should be treated with respect from the time they are approached for possible participation — even if they refuse enrollment in a study — throughout their participation and after their participation ends.

Table 1: A description of the seven guiding ethical principles