Research & Development Guidance Sheet for
Clinical Trials Involving the Investigation of Medicinal Products

MHRA Clinical Trial Authorisation application process

Guidance Notes for University Hospitals of Leicester Investigators

These notes are intended for clinicians planning to conduct an in-house investigator-led trial involving the investigation of a medicinal product

To undertake research of this type you will need authorisation from all the following before starting the trial:

- ✓ The Competent Authority (the MHRA in the UK)
- ✓ Ethics in the form of a favourable opinion
- ✓ Trust Research and Development permission

The Research and Development Office can assist with queries concerning authorisation. The process is intended to protect participants in trials and ensure that research produces quality data that can be applied to healthcare practically on the basis of a strong, auditable evidence base. It is therefore necessary to liaise with the Research and Development Office immediately you plan a trial.

1. The website http://www.ct-toolkit.ac.uk gives a good overview of the process of planning a clinical trial through illustrated route maps with interactive stations.

2. The MHRA authorisation (CTA) process is started via the EudraCT website (https://eudract.emea.europa.eu/) where you obtain a EudraCT number. A security code is first applied for (takes about 5-10 minutes to come through via e-mail), then using that code, a EudraCT number is applied for (again takes about 5-10 minutes to arrive). Keep copies of these e-mails with your trial documentation

3. Once you have a EudraCT number, you use the Integrated Research Applications System at https://www.myresearchproject.org.uk/ to answer one set of questions with which to populate all required forms for approvals and ethics.

4. To obtain a log in select the 'create account' option and follow the online instructions.

5. Once you are logged in your IRAS homepage will show a list of all your research projects, and an option to create a new project.

6. When you create a new project the system will ask you a set of questions called the IRAS Project Filter. These questions determine what forms the system will generate for you. For additional guidance on any question click on the green button by the question.

7. After completing the filter remember to save using the 'save now' button

8. Click on the 'navigate' button to bring up the navigate page for your project. This shows you an integrated data set on the right hand side and a list of forms on the left. Completing the integrated data set completes all the forms for you, so complete the integrated dataset. If you do this over several sessions remember to save it.

9. If you select a form from the left hand side e.g. NHS / HSC R&D Form the system shows you just the data associated with that form, which you can print or save in the appropriate format for submission under the 'submission' tab.

10. You can make your submissions to R&D, Ethics and the MHRA concurrently as per http://www.ct-toolkit.ac.uk.

11. Research and Development Approval

You can complete the documentation for Research and Development approval through local processes of through the National Institute of Health Research (NIHR) process if eligible. In all cases you should be speaking to the R&D office in the earliest stages of planning the trial.

11a Research and Development Approval through NIHR

In the Project Filter you need to have answered yes to the question about completing R&D approval through the NIHR process.

To complete your Research and Development approval through IRAS you need to be adopted onto the National Institute of Health Research Portfolio, so begin by completing the Portfolio Adoption Form allowing you to select a Comprehensive Local Research Network. Submit this form as per the instructions on IRAS. You will be notified of adoption within 2 working days by email.

Next you submit your R&D form as per the instructions on IRAS (including the required supporting documentation – see the checklists in the policies section on the R&D office webpage http://www.uhl-tr.nhs.uk/our-services/rd).

The R&D Form is checked to ensure all information is given, then a Governance Review is undertaken.

At this point complete, with the help of the Principal Investigators, Site Specific Information forms through IRAS for each site involved in the project (if you are working across more than one site – Leicester Royal, Glenfield General and Leicester General are all one site). Submit as per the instructions on IRAS to R&D (not to ethics).

Once global and local governance checks are completed you will receive a confirmation email in respect of your first study site, and the associated Organisation i.e. UHL will receive a governance report. Within 3 weeks you will be issued with authorisation from the Research and Development Office for your first site. Additional sites must await individual approval.

11b Research and Development Approval for Non-Portfolio Trials

This process is detailed in UHL SOP CLIN/123. Checklists available on the Research and Development Office website detail the documentation required for Trust Research and Development approval.

The process is undertaken by submitting the IRAS R&D form and SSI to the R&D office, by saving it in both pdf and xml formats and then sending it electronically. In the project filter you will not have selected to complete R&D approval through the NIHR process. Once appropriately completed documentation has been received you will be allocated a unique trial number (please use this on all correspondence) and a Facilitator will be allocated to process your request.

The Facilitator will undertake a number of checks based on the information supplied in the form concerning financial risk, access to facilities and services, and data protection. If they are satisfied in all respects, and once they have evidence of ethics favourable opinion and the competent authorities authorisation R&D will confirm that research can commence.

12. Ethics Approval

The IRAS dataset will populate the ethics form for you. Submission requires that you book a slot with the Main REC through the Central Allocation System (CSP organise this for portfolio trials, or the Research and Development Office can advise where they are the Sponsor). Documentation will be required with 4 days of booking as specified in the relevant checklist on www.nres.npsa.nhs.uk.

Within 60 days you will receive either a favourable or unfavourable opinion. You need a favourable opinion to start the research. The Ethics Committee can provide a favourable opinion subject to certain conditions, in which case you must meet the identified conditions and inform the ethics committee, sending any updated documentation, for information. No further review will take place. The Ethics Committee can also make one request for additional information in this time, and the 60 day clock will halt until this information is received.

13. CTA (MHRA) Approval

On IRAS select the MHRA Medicines Form. Details of how to make a submission are contained on the submissions tab. For further details visit the MHRA webpages at www.MHRA.gov.uk.

Assemble to documentation in the appropriate formats and send them to the MHRA. A request for a Clinical Trial Authorisation consists of:

- Covering letter
- The completed Clinical Trial Application Form
- Protocol

- IMPD or SmPC where relevant
- The specified particulars and documents (supporting data)
- The XML file of application form (complete data set)
- Applicable fee

Check against the MHRA document checklist that you are submitting all documentation in the correct format, preferably electronically.

The applicant should submit and sign a covering letter to the MHRA with the application. Its heading should contain the EudraCT number and the protocol number with the title of the trial. The text of the letter should draw attention to any special issues relating to the application, e.g. unusual trial design (perhaps that licensed product tablets are being packed into capsules to match placebo capsules being prepared), and indicate where the relevant information is in the application

14. Sponsorship Details

The Sponsor for an in-house, investigator-led study is usually the University Hospitals of Leicester NHS Trust
Gwendolen House
Leicester General Hospital
Gwendolen Road
Leicester
LE5 4PW

You must identify a person in Research and Development to be the contact. Please contact the Research and Development Office for the appropriate contact.

15. Starting Your Research

The R&D office will contact you to confirm that you have permission to commence research. Permission will be site specific – each study site requires approval. They will be confirming that you have approval / favourable opinion from ethics, the competent authority and your local R&D office.