Standard Operating Procedure (SOP) for Submitting a Clinical Trial for Ethical Approval

Scope

This SOP describes the process of submitting a research project for ethical approval and the requirements post approval.

This SOP does not cover specific requirements of ethics committees (EC), which can be country/institution specific. The relevant EC should be contacted in order to ascertain their procedures and requirements.

Abbreviations

CA  Competent authority
CTA  Clinical trial Authorisation
EC  Ethics committee
EU  European union
IEC  Independent ethics committees
IRB  Independent review board
PI  Principle Investigator
PIS  Patient information sheet

Introduction

The declaration of Helsinki, ICH GCP and the EU clinical trials directive (2001/20/EC) state that clinical trials must be reviewed and approved by an Institutional review board (IRB)/independent ethics committee (IEC) (referred to in this SOP as ethics committee (EC)). The ethical review process is required to ‘safeguard the rights and well being of all trial subjects’.

The EC will examine and consider the following points:

- The relevance of the clinical trial and the trial design.
- Whether the evaluation of the anticipated benefits and risk is satisfactory and whether the conclusions are justified.
- The suitability of the Investigator and supporting staff.
- The quality of the facilities.
- The data available on the drug, procedure or device under study.
- The suitability of the protocol.
- The suitability of the patient information, consent forms and procedure.
- The arrangement for the recruitment of subjects.
Clinical Trials Offices
(London and Leiden)

- The provision for compensation and/or treatment in the case of injury or death of a subject if attributable to a clinical trial,
- Any insurance or indemnity to cover the liability of the Investigator and Sponsor,
- The extent to which Investigators and subjects may be rewarded and/or compensated for participation.

In the European Union (EU) multi-centre clinical trials must receive a single opinion from an EC in each member state concerned; this is referred to as the National Ethics Committee Approval. However the requirements and procedure of ethics committees are country specific, consequently, the relevant ethics committees in each country should be consulted to ensure that all the ethical, legal and regulatory requirements of that country are adhered to.

In addition to the national ethics approval, most institutions will require that the study is submitted to their local committee to ensure that the institution has the resources to conduct the study.

Submission in non-EU countries differs and the requirements should be checked in each participating country prior to submission.

Responsible Personnel

It is the responsibility of the assigned lead investigator/coordinator in each country in collaboration with the trial coordinator/data manager to submit the trial to the ethics committee in their respective country and gain approval before the start of the trial. Local ethics submission is the responsibility of each Institution’s PI.

Procedure

Eudract Database - Registration of the trial

The trial must be registered onto the Eudract database before an application is made (SOP3) Register the trial at: http://eudract.emea.eu.int/
Once registered the trial will be given a Eudract number, which should then be quoted on all further correspondence regarding the trial.

When to apply

If the research is a clinical trial of an investigational medicinal product, you may apply for a clinical trial authorisation (CTA) from the CA either at the same time as you make your EC application or in sequence.

Application supporting documentation

The applicable application form should be completed in full and submitted to the relevant EC. The following documentation is the minimum mandatory documentation that is usually required to be sent:
Clinical Trials Offices
(London and Leiden)

- Application Form
- Research protocol (X number of copies)
- C.V. for Chief Investigator  (Or summary)
- Research participant information leaflet (PIL)
- Research participant consent form
- Evidence of insurance or indemnity

The following should be sent in with the application if required/applicable:

- Covering letter on headed paper
- Request form for authorisation from the Competent Authority
- Investigator's brochure or summary of medicinal product characteristics
- GP/consultant information sheets or letters
- Letter from sponsor
- Letter from statistician
- Letter from funding body
- Referees’ or other scientific critique report
- Summary, synopsis or diagram (flowchart) of protocol in non-technical language
- Details of Data Monitoring Committee
- Sample diary card/patient card
- Validated questionnaire
- Non-validated questionnaire
- Copies of advertisement material for research participants, e.g. posters, newspaper adverts, website.

This list is not exhaustive; each EC will have individual requirements and could request further documentation.

After submission of EC application

The ECs have a period of 60 days from receipt of a valid application to give their reasoned opinion to the applicant. The application is valid if the application form is complete and all of the required supporting documentation is enclosed. The EC will usually notify the applicant if the application is valid or not.

The EC can send a single request for further information to be supplied. At this point the clock on the 60 day time period is stopped until the supplementary information is supplied.

No extension of the 60 day-period is permissible, except in the case of a trial involving medicinal products for gene therapy or somatic cell therapy or medicinal products containing genetically modified organisms.
Clinical Trials Offices
(London and Leiden)

If the research is not given a favourable ethical opinion
If the application is not given a favourable ethical opinion and it is felt that the reasons given for this by the main REC can be addressed, the research proposal should be revised accordingly and resubmitted to the EC, if convenient, as a new application.
Alternatively if it is felt that the EC that reviewed the application gave an unfavourable opinion based on a misunderstanding of the research proposal, you can appeal against the decision.

If your project is given a favourable ethical opinion
The research project must have a favourable opinion from the EC, in addition to CA approval (In EU member states)/ applicable regulatory approvals (as required) in the country concerned before it is commenced.
The post approval function of the ethic committee is country specific, however the following are probable requirements from the applicant after approval of the project:

1. Applications to the EC for approval of any substantial amendments
A ‘substantial amendment’ is defined as an amendment to the terms of the EC application, or to the protocol or any other supporting documentation, that is likely to affect to a significant degree:
   a. The safety or physical or mental integrity of the subjects of the trial;
   b. The scientific value of the trial;
   c. The conduct or management of the trial; or
   d. The quality or safety of any investigational medicinal product used in the trial.

2. Provide appropriate safety reports
   - Suspected Unexpected Serious Adverse Reaction (SUSAR) reports
   - Quarterly and/or annual safety reports

3. Notify the EC for any subsequently enrolled research sites
4. Supply progress reports to the EC
5. Inform the EC when the project finishes

References
ICH GCP Guidelines (1996)
Declaration of Helsinki (2000)