

***Office for Research Ethics Committees  
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***HPSS Research  
Ethics Committees  
Guidance for Applicants***



Important Note: From 22 April 2004 Ethical Review applications must be completed on the standard electronic application form. – Contact this office for details.

## *HPSS Research Ethics Committees in Northern Ireland*

An HPSS Research Ethics Committee (HPSS REC) is an independent committee of the Department of Health, Social Services and Public Safety (DHSSPS), whose task is to consider the ethics of proposed research projects which will involve human subjects, their tissue or data and which will take place, generally, within the HPSS. The key duty of an HPSS REC is to protect the interests of all research participants.

### *Background*

New ethical review arrangements for research involving human subjects, tissue or data are being introduced in Northern Ireland to comply with the requirements of the European Union Directive on Clinical Trials as transposed by the UK Medicines for Human Use (Clinical Trials) Regulations 2004. Full compliance is required from 1st May 2004.

Three ethics committees have been established by the DHSSPS. These HPSS Research Ethics Committees are generalist (that is, capable of considering the ethics of all proposed research projects which involve human subjects, their tissue or data in relation to health and social care research). Each will have a remit covering the whole of Northern Ireland, and will meet monthly. This will create a system where there will be a committee meeting most weeks of the year, capable of reviewing any research proposal.

### *EU Directive 2001/20/EC*

The EU Directive comes into force on 1 May 2004 and will be transposed into UK law by the same date. The requirements of the Directive for ethical review are:

- To deliver a decision on a valid application within 60 days
- One decision for the whole UK
- Restriction of one written request for clarification or further information from applicants (clock stops whilst waiting a response)

### *Recognition of Research Ethics Committees*

The Regulations require RECs to be recognised for the purpose of reviewing clinical trials of medicinal products. In the UK, the UK Ethics Committees Authority (UKECA) will recognise RECs. HPSS RECs will be recognised for this purpose and will also be able to review all other health and social care research. For the purposes of operational management, Northern Ireland is treated as a single domain (See Glossary).

### *Office For Research Ethics Committees Northern Ireland (ORECNI)*

All applications to HPSS RECs will be co-ordinated by the Office for Research Ethics Committees Northern Ireland (ORECNI), and applications to these committees must be submitted to ORECNI. This office will provide administrative support to service all

three HPSS RECs. ORECNI is part of a UK-wide network managed operationally by the Central Office for Research Ethics Committees (COREC) in London. ORECs will process applications and manage RECs according to new national Standard Operating Procedures (SOP's).

### *What do Northern Ireland applicants need to do?*

1. As of 22 April 2004, complete all applications on the standard electronic application form. This can be accessed via the ORECNI website [www.orecni.org.uk](http://www.orecni.org.uk) or downloaded directly from [www.corec.org.uk](http://www.corec.org.uk). Alternatively it can be completed online.
2. Book an agenda slot for a REC meeting via ORECNI or the Central Allocation System (See Figure 2)
3. Submit a completed electronic application form, quoting the unique REC Reference Number, within 4 days to ORECNI or to the assigned GB REC (where the applicant has elected to use a REC outside Northern Ireland).

### *New Definitions*

The Directive requires us to use a new definition for research site. The research site is the single organisation responsible for hosting the research at a particular locality e.g. a HSS Trust.

A Chief Investigator is the person with overall responsibility for a study, for multi-site studies there will also be Principal Investigators at each research site who have responsibility for the study at that site.

Main REC is an operational term used to describe the ethics committee undertaking the ethical review of a multi-site study, where site-specific assessments will be made by other RECs or HSS contacts.

### *Ethical Review Process*

- All RECs will meet on a monthly basis to ensure that decisions can be made within 60 days. Applicants should be invited to attend the REC meeting, and strongly encouraged to do so- or be available by phone if the REC meeting room has speakerphone facilities. Attendance is not compulsory.
- The ethics committee may decide to seek clarification on specific issues before it makes its decision. The committee can only do this on one occasion and it will be in the form of a written request for clarification or further information. The 60 day clock stops whilst the committee is awaiting a response from the applicant. The clock starts again on the date a complete response is received.
- If the response received is not satisfactory then the committee may reject it or may decide if the majority of concerns were answered satisfactorily to let the applicants have a second chance at responding to same questions. No new issues can be raised at this stage. The clock is stopped because a complete response has not yet been received.

- In the case of multi-site studies, each site-specific assessor will notify the Main REC undertaking the ethical review whether or not there is any objection to the research on site-specific grounds. The site-specific assessor will not issue local approval to the Principal Investigator. Approval for each site will be given by the Main REC as part of the single ethical opinion for the study. A letter of ethical approval will not usually be issued until the Main REC has received at least one notification of no objection from an assessor. Each time a site is approved the Main REC re-issues the approval letter with the additional site.
- New sites may be added at a later stage by the same process.
- In the case of multi-domain studies the same site-specific arrangements apply. Northern Ireland is regarded as a single domain. Therefore, from a Northern Ireland perspective, a multi-domain study is one that also involves a research site outside Northern Ireland

### Amendments

- The EU Directive defines an amendment as something that happens after a trial has started. COREC is defining a revision as something that happens before the trial has started. Revisions and amendments will be managed in the same way.
- All substantial revisions and substantial amendments must be reported to the Ethics Committee from which ethical approval was given. A standard notice of amendment form must be submitted. In the case of multi-site studies only the Main REC needs to be notified.
- Administrative amendments are purely administrative details that do not need review and can be acknowledged by the administrator if the REC is advised. Substantial amendments are all amendments that are not administrative and these must be approved by the committee or sub-committee within 35 days. If the amendment is rejected the applicant may submit a modified amendment, which will be reviewed within a further 14 days.

### Multi-Site Studies with No Local Investigators

In the case of multi-site studies with local collaborators who are not carrying out clinical interventions or other significant research procedures, Part A of the application form may state that the study has 'no local investigators' (NLI). The Main REC will consider this at the meeting, taking into account new guidelines on the type of procedures involved. If it is agreed that the study is NLI there will be no need to apply for Site Specific Assessment (SSA). Local Collaborators and agents must however seek R&D management approval from their host organisation.

If the Main REC decides that the procedures involved locally are significant, it may instruct the Chief Investigator to appoint a Principal Investigator at each site, who would then need to apply for SSA.

### Research Governance in Northern Ireland

The new arrangements for ethics review are being introduced as part of a broader research governance agenda described in the Research Governance Framework for Health & Social Care Research (RGF). ORECNI, and the HPSS RECs together form part of a UK wide system of ethical review. This sits alongside other research governance systems, developed to discharge the specific responsibilities of other research governance stakeholders including: research sponsors; care organisations; and employing organisations. While each of these systems complement each other each has a different emphasis reflecting the varying responsibilities of the different stakeholders. (Available at R&D Office website [www.centalservicesagency.com](http://www.centalservicesagency.com) )

Northern Ireland based Chief Investigators submitting applications to HPSS RECs are expected to meet the wider requirements of research governance as set out in the RGF. In particular Chief Investigators should comply with the new research management systems being developed by HPSS care organisations. Therefore before submitting an ethics application that involves the HPSS in the role of a care and/or an employing organisation Chief Investigators should:

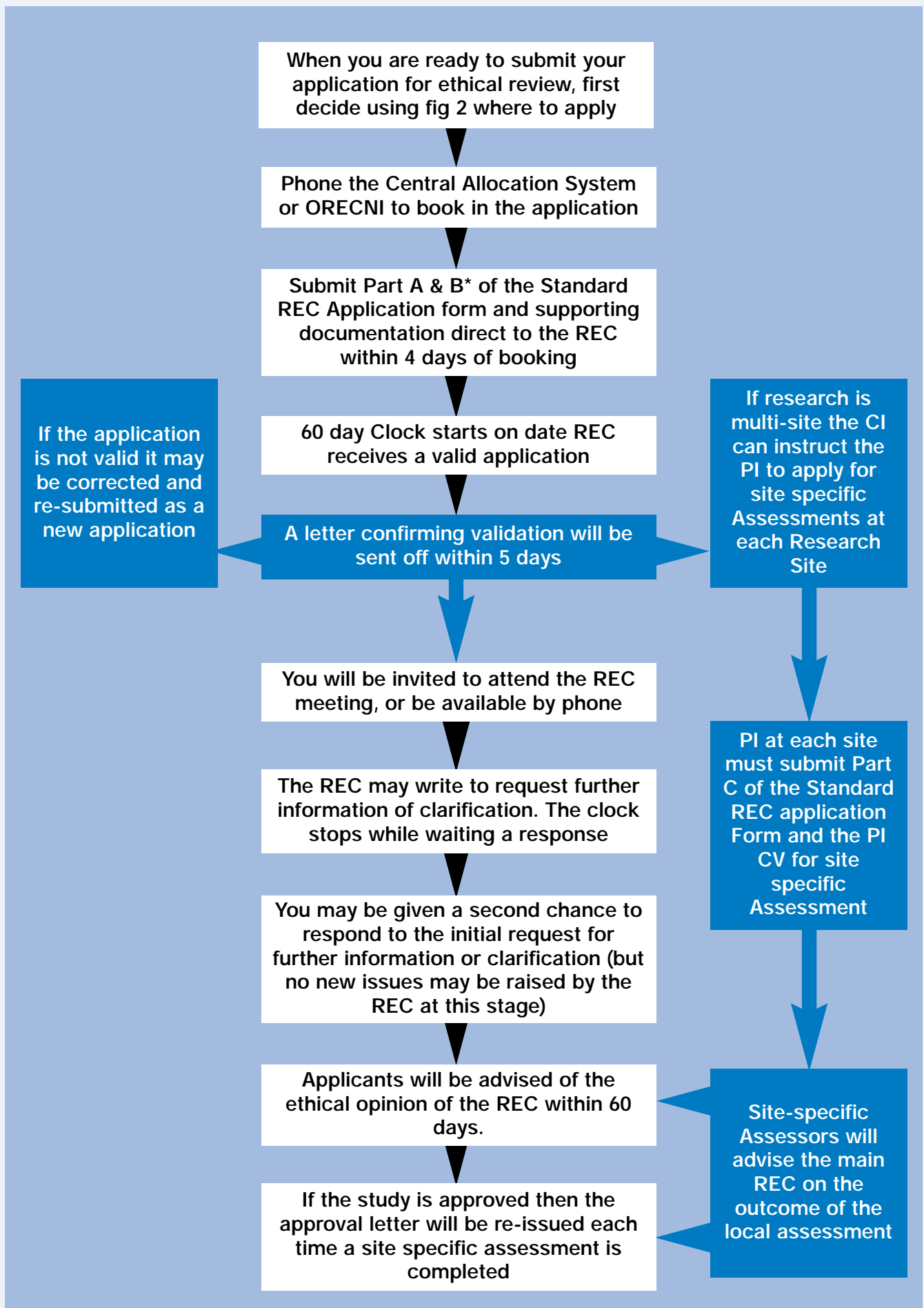
- secure explicit preliminary approval of the relevant HPSS organisations to host the research
- secure adequate funding arrangements
- secure agreement from an appropriate organisation to act as sponsor for the proposed research
- secure appropriate peer review

Under the RGF the HPSS is required to ensure that appropriate funding and sponsorship arrangements are in place before an ethical opinion is sought from an HPSS REC. A key role of a sponsoring organisation is to conduct appropriate peer review as a means of assuring the scientific quality of any research it sponsors. Peer review should have been completed before an ethical opinion is sought from an HPSS REC.

The new SOPs followed by HPSS RECs meet the specific obligations of the United Kingdom under EU Directive 2001/20/EC. These SOPs do not always provide the opportunity to exclude applications where RGF obligations are not met e.g. securing adequate funding arrangements. However, any HPSS care organisations, identified in the application, will be sent a copy of the validation letter, by ORECNI. It is then open for those care organisations to ask the Chief Investigator to withdraw the application where they do not wish to support the proposed research or where the Chief Investigator has failed to comply with an HSS Trust's research management system.

As a research study with a favourable ethical opinion cannot commence until final management approval has been confirmed by the HPSS organisation(s), hosting the research, Chief Investigators are advised to adhere to the relevant research management system(s) from the outset.

Figure 1



\* Multi-site studies involving medicinal product complete only sections A and B of the standard REC application form at this stage.

## How to Apply

- From the 22 April 2004 all applications must be made on the standard electronic application form. Copies of this can be accessed via the ORECNI website at [www.orecni.org.uk](http://www.orecni.org.uk) or downloaded directly from the COREC Website ([www.corec.org.uk](http://www.corec.org.uk)). An online version of the electronic application is also available. Guidance notes for downloading, using and submitting the form are on the COREC website. Please take the time to read this guidance.
- Once an application is complete and ready to send, applicants must phone to book in the application either to the Central Allocation System or direct to ORECNI according to Figure 2. When the application is booked in, the applicant will be given a REC reference number that must be entered on the application form.
- Once the application has been booked, sections A, B and C\* of the completed application form should be sent electronically to ORECNI or the relevant GB REC office within 4 days or by a closing date agreed with the Administrator. Failure to do so may result in the agenda slot being lost. One paper copy of the application form, with all relevant signatures in ink, should also be sent. The applicant should also send, either electronically or on paper, the completed application checklist and all supporting documents as indicated on the checklist. One copy only of each document is required to be submitted, except for the protocol (6 copies) and if applicable the Investigator Brochure. (3 copies)
- On receipt of the application the administrator will check the application is valid. This is a simple administrative check that the application is complete, including support documentation.
- A standard letter confirming validation, or not, will be sent within 5 days.
- For multi-site studies once the Chief Investigator receives the letter confirming the application to be valid they can instruct Principal Investigators to apply for Site Specific Assessments (SSA) at each site so these can be carried out within the 60 days allowed for ethical review. To facilitate this, the Chief Investigator sends to each Principal Investigator the whole form (Parts A, B and C), with Parts A and B completed. This should be done electronically. The Principal Investigator then completes Part C, and submits to ORECNI to organise SSA.
- The application for Site Specific Assessment (SSA) will consist of Part C of the new form and Principal Investigator CV only. Where the ethical review results in changes that are of relevance to the SSA the Chief Investigator will be instructed to ask each Principal Investigator to re-apply for SSA.

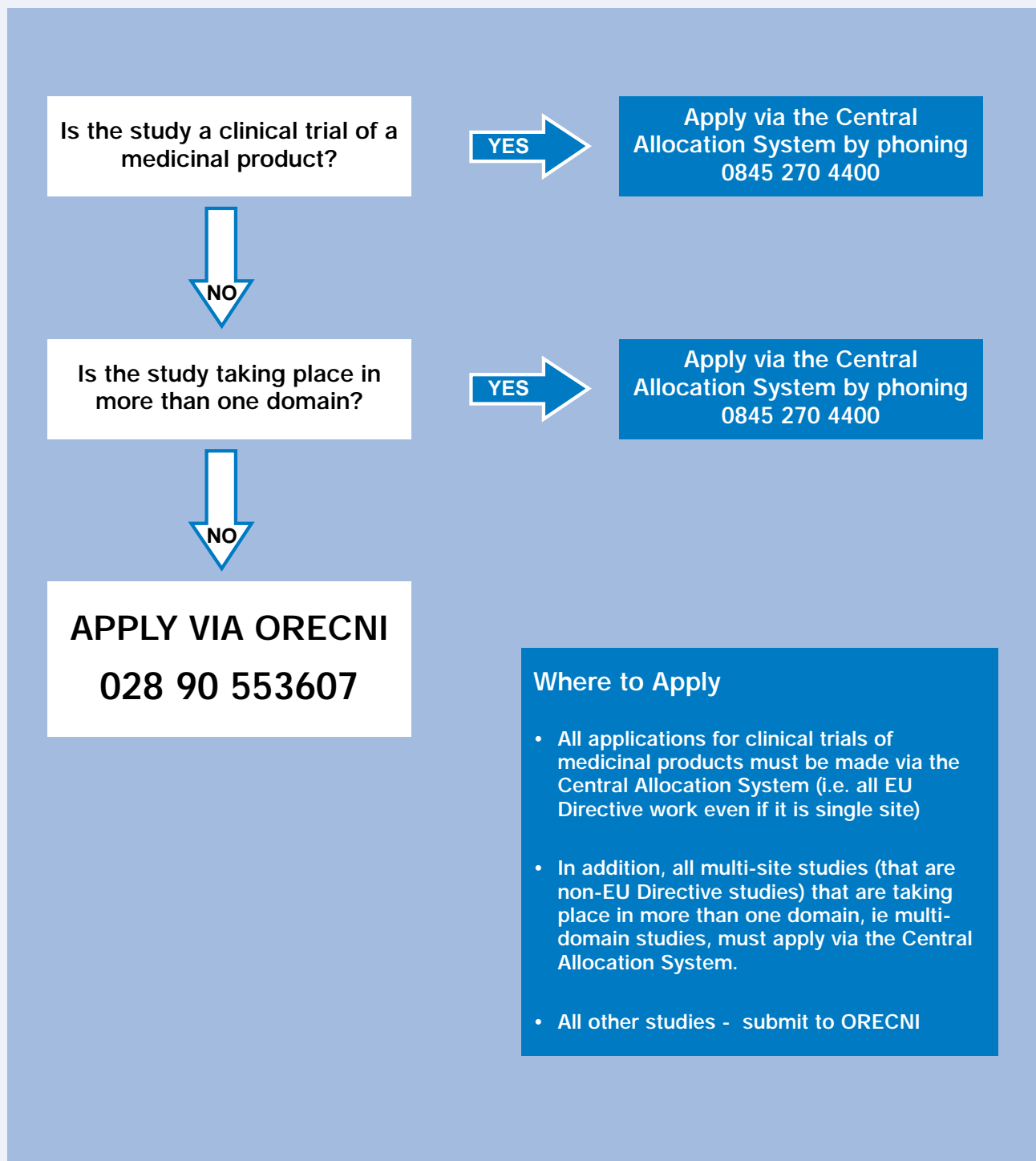
\* Multi-site studies involving medicinal product complete only sections A and B of the standard REC application form at this stage.

# Central Allocation System

A central system has been developed by COREC to allocate research studies to recognised RECs throughout the UK in an efficient and balanced manner. This system will be able to determine for the applicant, slot availability at any recognised REC throughout the UK. This gives the applicant the choice to submit an application to the next available recognised REC whether or not it is an HPSS REC. Naturally, the applicant can choose to wait until a slot comes available at an HPSS REC. The applicant will be given a reference number to include in their application form, which is then submitted by the applicant to ORECNI or the appropriate GB REC.

Applications submitted to ORECNI must be on the standard electronic application form

## Figure 2



## **Administrative Amendment-**

Amendments that can be acknowledged by the REC administrator (e.g. change of contact details) and do not require review

**Amendment-** Defined by the EU Directive as a change to the study after the trial has started. See 'Revisions' for changes prior to the start of the trial.

**Appeal-** A rejected application submitted in essentially its original form to a second committee.

**Booking in Application-** Applicants book in applications by telephone via the Central Allocation System or direct to ORECNI

**Central Allocation System-** Booking system for EU Recognised RECs. All EU Directive work must be made via the Central Allocation System. Other Multi-site studies in more than one domain must also go via Central Allocation System.

**Chief Investigator (CI)-** The Chief Investigator is the person with overall responsibility for the research and all applications must be submitted by the Chief Investigator.

**Clock-** The 60 day clock for delivering a decision on a valid application.

**30 day clock-** 30 day clock for Site Specific Assessments (no stopping)

**35 day clock-** 35 day clock for amendments (no stopping)

**Clock Starts-** On the day a valid application is received. If clock has been stopped it starts again on the date a complete response to a request for written clarification is received.

**Clock stops-** On the date of letter seeking written clarification or further information from the applicant.

**CTA-** Clinical Trial Authorisation, the regulatory approval for a clinical trial of a medicinal product issued under the Directive. It replaces the previous CTX and DDX schemes.

**Domain-** The area covered by a SHA (England), a Health Board (Scotland), a regional office of the NHS Wales Department or the whole of Northern Ireland.

**EU Directive-** EU Directive 2001/20/EC of the European Parliament and of the Council on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

**Main REC-** An operational term to describe the ethics committee that is undertaking the ethical review for a multi-site study. (A Main REC may or may not be recognised)

**Medicinal Product-** Definition to be announced by MHRA- see [www.mhra.gov.uk](http://www.mhra.gov.uk)

**MHRA-** Medicines and Health-Care Products Regulatory Agency- the competent authority for the regulation of all EU Directive trials in the UK. Application to the MHRA for Clinical Trial Authorisation (CTA) may be made in parallel with the ethical review.

**Non-** EU Directive Studies- All studies that are not clinical trials of medicinal products (including other clinical trials)

**Principal Investigator (PI)-** The Principal Investigator is the person who is responsible for the research at a site. One Principal Investigator per site.

**Provisional Opinion-** Decision reached subject to seeking further information or clarification from applicant on specific issues. The clock stops while waiting for a response.

**REC-** Research Ethics Committee

**REC Reference Number-** Reference number assigned by the REC accepting the application for review. This includes a REC local identifier, specific project number and year.

**Recognition-** The regulations will provide that in order to undertake reviews of Clinical Trials of Medicinal Products RECs must be recognised for this purpose. UKECA will recognise Ethics Committees within the UK.

**Recognised RECs-** Committees recognised by UKECA to undertake EU Directive work, i.e. review clinical trials of medicinal products.

**Regulations-** The Medicines for Human Use (Clinical Trials) Regulations 2004 will legally implement the EU Directive in the UK. The Regulations are currently in draft and will be laid before Parliament shortly. The draft is published at [www.mhra.gov.uk](http://www.mhra.gov.uk)

**Research Site-** The research site is the single organisation responsible for hosting the research at a particular locality e.g. HSS Trust

**Revisions-** Changes made prior to the start of the study (and processed in the same way as Amendments)

**SHA-** Strategic Health Authority (England)

**Site Specific Assessment (SSA)-** Assessment made by local site assessors to advise Main REC on the suitability of the local investigators and support staff and appropriateness of the local research environment and facilities.

**Site Specific Assessors-** Relevant R&D personnel in HSS Trusts.

**Substantial Amendments-** Changes affecting patient safety or the conduct of the trial, any amendment that is not purely administrative.

**UKECA-** The UK Ethics Committee Authority.

**Validation-** An administrative check to confirm application is complete (including supporting documentation)

## How to find us

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OREC Offices



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