South Eastern Health and Social Care Trust

Standard Operating Procedure (SOP) Research and Development Office

Title of SOP:	Applying to the MHRA – Clinical Trial Authorisations
SOP Number:	16
Version Number:	2.0
Supercedes:	1.0
Effective date:	August 2013
Review date:	August 2015

Author:	Alison Murphy, Research Manager Endorsed by Paul Carlin
Approved by:	Dr David Hill
Signed:	
Date:	01 August 2013

Version History:

Version No.	Date	Author	Reason for Change
1.0	Oct 2007	Katrina Hughes	N/A
2.0	Aug 2011	Alison Murphy	Updated to new SOP template. Updated and incorporated IRAS guidance. Removed appendices.

Table of Contents

1. INTRODUCTION

The MHRA is the government agency responsible for ensuring that medicines and medical devices are safe.

A Clinical Trial Authorisation (CTA) is required only in trials of medicinal products. These are substances, or combinations of substances, which either prevent or treat disease in human beings or are administered to human beings with a view to making a medical diagnosis, or to restore correct or modify physiological functions in humans.

Any research that fulfils the definition of a clinical trial, as described by the EU Directive 2001/20/EC Article 2 (a), will require a CTA from the Competent Authority in the Member State in which research is being carried out. A CTA will only be issued by the Competent Authority if it has no objections to the research proposal. The Competent Authority for the United Kingdom is the MHRA.

The EU Directive 2001/20/EC definition of a clinical trial is:

"… any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects to one or more investigational medical product)s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy".

Clinical studies involving only medical devices, food supplements or other non-medicinal therapies (such as surgical interventions) are **not** covered by the EU Directive, but may require other regulatory approvals. Please see other SOPs for further details.

It is the responsibility of the Chief Investigator (CI) to establish whether regulatory approval is required for their study and that it is obtained prior to initiating the trial.

2. OBJECTIVE

This Standard Operating Procedure (SOP) describes the procedure for applying for a Clinical Trial Authorisation (CTA) from the Medicines and Healthcare Products Regulatory Agency (MHRA).

3. SCOPE

This SOP applies to all Clinical Trials of Investigational Medicinal Products

4. PROCEDURE

4.1 Procedure for obtaining a EudraCT number

You will need to obtain a EudraCT number for a CTA application. You will need to request a Security Code and then obtain a EudraCT number. Once you have obtained this, there is no need to complete any further information on the EudraCT website as the remainder of your application can be made in IRAS.

To obtain a security code, use the following sequence:

1. Go to the EudraCT website at https://eudract.emea.europa.eu/eudract/index.do
2. From the EudraCT Welcome Screen take the link: 'Apply for Security Code'.
3. Complete the fields, both of which are mandatory. The e-mail address should be accurate so that the e-mail containing the security code is sent to the correct recipient.
4. When the fields have been correctly completed press the "Get Security Code" link and a confirmation screen will appear. The e-mail will arrive shortly afterwards (depending on network traffic etc.).
5. Check the e-mail address printed on this confirmation screen to be sure that it does not contain any typing errors. If the e-mail address is incorrect then the e-mail cannot be delivered.
6. At this point press 'Continue' to return to the EudraCT Welcome Screen. The e-mail that contains the security code is sent to the e-mail address used in the request form.
7. Open the e-mail account used on the request from to find the e-mail. This will be from user: EudraCT@eudra.org and with the subject: Application for Security Code
8. Open the message to obtain the security code.
9. Keep the e-mail containing the security code for use in your request for a EudraCT number. The security code may be copied and pasted from the e-mail into the EudraCT number request form.

To obtain a EudraCT number:

1. From the EudraCT Welcome Screen take the link: 'Apply for EudraCT number'
2. The requestor now completes all the mandatory fields which are marked with (*).
   - "**Requestor's organisation name**". Include the name of the organisation that the requestor works for in this field.
   - If the requestor is not making the request on behalf of an organisation, but on their own behalf, then the "Requestor's organisation name" should be left blank. However, you should use the fields "Requestor's organisation town/city" and "Requestor's organisation country" to enter your ***own*** Town or City and Country respectively.
   - "**Requestor's organisation town/city(*)**". This is a mandatory field.
   - "**Requestors organisation country (*)**". This is a mandatory field. Select the appropriate country from the drop-down list of all the countries of the world.
   - "**Sponsor's Protocol Code Number (*)**". This is the Protocol Code Number for the clinical trial that will be linked to the EudraCT number obtained from this request and is not generated by the system. If you are unsure what this value is, you should contact the Sponsor. It should be entered in the normal format used by the requestor's organisation. This is a mandatory field.

Note: The sponsor's Protocol Code Number field cannot contain blank spaces.

- **"Requestor name(*)".** Enter your name. This is a mandatory field.
- **"E-mail to which the EudraCT Number will be sent(*)".** Enter the e-mail address to which the EudraCT number should be sent. Any valid e-mail address is acceptable and need not be the requestor's e-mail. This is a mandatory field.
- **"Enter the security code sent earlier (*)".** Enter the EudraCT security code obtained by using the 'Get Security Code' link. It may be found in the "Application for Security Code" e-mail you should have received. This security code must not have been used on another application and it should be used within 24 hours, or a new security code must be requested. This is a mandatory field.
- **"Is it anticipated that this EudraCT Number will be used for a Clinical Trial contained in a Paediatric Investigation Plan (PIP)? (*)"** This is a mandatory field.
- "Is it anticipated that this EudraCT number will be used for a Clinical Trial conducted in a third country (outside of the EU/EEA). (*)" This is a mandatory field.

  Note: A third country is any country outside the European Economic Area (EEA). The EEA contains member states of the EU, plus Iceland, Liechtenstein and Norway.
- "Please select the Member States where it is anticipated that the trial will be run". This is not mandatory information (unless it relates to the above question), but completion will provide some advanced indication of likely Clinical Trial applications in each Member State. The Member States selected should be the best available information at the time the EudraCT number is requested. This might change, but if it does there is no requirement to notify any Member States of the changes.

3. When the fields have been correctly completed you should press the "Get EudraCT Number" link and a confirmation screen appears. The e-mail will arrive shortly afterwards (depending on the speed of your local e-mail servers).
4. Check the e-mail address printed on this confirmation screen to be sure that it does not contain any typing errors. If the e-mail address is incorrect then the e-mail cannot be delivered.
5. At this point press "Continue" to return to the EudraCT Welcome Screen. The e-mail that contains the EudraCT number will be sent to the e-mail address used in the request form.
6. Open this e-mail account to find the e-mail. This will be from user: EudraCT@eudra.org with the subject: Application for EudraCT Number
7. Open the message to obtain the EudraCT Number.
8. This e-mail also includes the Sponsor Protocol Code Number, you supplied previously for this request.
9. Save this e-mail. It is the 'Receipt of confirmation of EudraCT Number' document and is one of the supporting documents that must be included in the request for the Clinical Trial.

4.2 Completing the CTA application form

The standard application for a CTA is the European Commission application form available from the EudraCT website at http://eudract.emea.europa.eu.

The whole of the EudraCT dataset is available in the Integrated Research Application System (IRAS). Applicants can choose to complete the EudraCT dataset completely in IRAS. Alternatively, applicants may choose to use the EudraCT website to make their application to the MHRA. If the latter option is chosen, the information on the IMP(s) must be imported into IRAS to form part of the REC and R&D applications, or entered separately in IRAS.

You will need to obtain a EudraCT number for this application. Once a EudraCT number has been obtained it is possible to use IRAS to complete the whole EudraCT dataset and to save the application in the format required for submission to MHRA.

See the IRAS website for guidance on applications www.myresearchproject.org.uk

4.3 Applying to the MHRA

For detailed submission guidance, please see the MHRA website.

4.3.1 Who can apply?

The application must be made by the sponsor or by someone authorised to submit the request on their behalf. If the sponsor is not established in the European Community then he/she must have a legal representative who is.
If the South Eastern Trust is acting as sponsor you will be provided with a letter confirming sponsorship and authorisation to apply.

4.3.2 What to send

In order for an application to be considered as valid, a submission should contain a file for each of the following documents:

- Covering letter
- Clinical Trial Application + valid xml
- Protocol
- IB or document replacing the IB
- IMPD/simplified IMPD
- NIMP Dossier (if required)
- Scientific advice - A summary of scientific advice from any Member State or the EMA with regard to the clinical trial (if available).
- EMA Decision - A copy the EMA's Decision on the decision of the Paediatric Investigation Plan and the opinion of the Paediatric Committee (if applicable).
- The content of the labelling of the IMP (or justification for its absence)
- Proof of payment
- Manufacturer's authorisation or Importer's authorisation plus QP declaration on GMP for each manufacturing site.

In cases where a document is not required in support of an application, for example the type of submission does not require details of the content of the labelling, the file should still be provided however it should contain an explanation for why the document has not been supplied.
The MHRA Information Processing Unit will use the above list to validate the application; any application which does not contain a file for each of the documents listed above will be rejected.

4.3.3 Submitting the application

Applicants are required to submit electronic documents on disk with one PDF file for each document. In exceptional cases where the use of PDF files is not feasible, (for example, in the case of small, non-commercial clinical trials) electronic documents using Word are acceptable and will be processed to the same target timescales. Disks should be submitted with no subdirectory structure.

Each disk should be labelled in the following manner:

- EudraCT number
- Description of contents eg
    - Initial Application
    - Response to Remarks from an Initial Application
- Company name
- Date sent

The disk may be printed or labelled with an adhesive paper label or a permanent marker pen.

All disks should be sent to the address below:

Information Processing Unit
Area 6
MHRA
151 Buckingham Palace Road
Victoria
SW1W 9SZ

4.3.4 What are the fees?

Fees charged for the application should be considered during the early stages of planning when costs are been collated for funding applications.

The MHRA charge a fee for each CTA application submitted. Current information on the fees and how to pay them can be found on the MHRA website.

4.3.5 What Happens Next?

When the MHRA receives an application for a clinical trial authorisation (CTA), it will be validated. If the application is not valid (eg incomplete information is supplied) then the person making the application will be contacted and told that there are deficiencies. If the deficiencies are minor, you may be asked to provide the missing

information. Nothing will happen to the application until the missing components are provided, although once the application is complete it will be processed as normal. If the deficiencies are major, you may be required to resubmit a complete application. Once the application is valid (ie complete) the assessment period will begin and an acknowledgement letter will be sent to the person submitting the application. This is the person named in Section C1 of the clinical trial application form. The assessment period starts from the date of receipt of a valid application. If you have not been told that your application is invalid or received an acknowledgement letter within 10 days of sending the application, please contact RIS.CT@mhra.gsi.gov.uk

4.3.6 What is the timeframe?

The initial assessment will be performed within 30 days. For the purposes of this calculation, the day of receipt of the valid application by the Clinical Trials Unit is day 0. Applications for phase 1 healthy volunteer studies will be assessed and processed within an average of 14 days or less.

4.3.7 What are the possible outcomes?

When the application has been assessed (within 30 days) the applicant will be sent a letter informing them of one of the following:

1. acceptance of the request for a clinical trial authorisation
2. acceptance of the request for a clinical trial authorisation subject to conditions
3. grounds for non-acceptance of the request for a clinical trial authorisation.

If you have not received a letter within 35 days of sending the application, please contact RIS.CT@mhra.gsi.gov.uk.

4.3.8 Do I have to apply anywhere else?

All clinical trials also require a favourable opinion from an Ethics Committee. Depending on the type of product you may also need to make an application to other bodies.

5. REGULATIONS, GUIDELINES, REFERENCES, SOP LINKS etc.

EU Clinical Trials Directive 2001/20/EC

Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of a substantial amendment and declaration of the end of the trials, April 2004

Medicines for Human Use (Clinical Trials) Regulations 2004

IRAS Guidance

6. APPENDICIES

None