UNIVERSITY OF LINCOLN

CLINICAL GOVERNANCE - STANDARD OPERATING PROCEDURE

REGULATORY APPLICATION

CG-QMS SOP CG06

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Approved by: Signature:	UREC See original

Version History	**Reason for change**

NOTE: All SOPs are subject to regular review.

Please ensure that the version of this SOP is the most up-to-date.

OUT OF DATE DOCUMENTS MUST NOT BE USED AND HARD COPIES SHOULD BE DESTROYED

1. PURPOSE

To outline the process for developing a clinical trial regulatory application (Clinical Trial Authorisation CTA) to the Medicine Health Regulatory Authority (MHRA).

2. SCOPE

This SOP applies to all UoL sponsored clinical research or where LinCTU (Lincoln Clinical Trials Unit) are providing support in obtaining necessary regulatory permissions.

3. BACKGROUND

3.1 The Chief Investigator (CI) has overall responsibility for the submission of the regulatory application / Clinical Trial Authorisation (CTA) application for a Clinical Trial of an Investigational Medicinal Produce (CTIMP) or Medical Device. However, preparation may be delegated to a person with the relevant knowledge, skills and experience.

A regulatory application / CTA is required where:

3.2 A clinical trial falls within the scope of the EU Clinical Trials Directive and the Medicines for Human Use (Clinical Trials) Regulations 2004 or the Medical Devices Regulations 2002 (SI 2002 No 618, as amended) (UK MDR 2002).

3.3 This process runs parallel to that of the ethics committee submission as per SOP CG05 Ethics Application, using the same protocol, information sheets and consent forms as for that application. An investigator brochure or Summary of Product Characteristics may also be required.

EudraCT

3.4 EudraCT (European Union Drug Regulating Authorities Clinical Trials Database) is the European database for all interventional clinical trials on medicinal products authorised in the European Union (EEA) and outside the EU/EEA if they are part of a Paediatric Investigation Plan (PIP).

3.5 A EudraCT number is required for all CTA applications

Registration of clinical trials

3.6 Registration of clinical trials is a formal condition of Research Ethics Committee (REC) favourable opinion. Registration should occur before the first participant is recruited and no later than six weeks after recruitment of the first participant.

3.7 'Clinical trials' are defined as:

- Clinical trial of an investigational medicinal product
- Clinical investigation or other study of a medical device
- Combined trial of an investigational medicinal product and an Investigational medical device
- Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice.

3.8 A clinical trial may not commence until all approvals are in place and the sponsor has confirmed (via email – Sponsor Green Light) that the study may commence.

Lincoln Clinical Trials Unit (LinCTU)

3.9 Lincoln Clinical Trials Unit (LinCTU) may support the Chief Investigator in applying for regulatory approval in accordance with the terms and conditions of a signed service level agreement (SLA)

4. CROSS REFERENCES

4.1 Electronic Health Records MHRA Position Statement

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/470228/Electronic_Health_Records_MHRA_Position_Statement.pdf

4.2 CG-QMS SOP CG02 Sponsorship

4.3 CG-QMS SOP CG04 Protocol Development

4.4 CG-QMS SOP CG05 Ethics Application

4.5 CG-QMS SOP CG07 Trial Master/Site File(s)

4.6 CG-QMS SOP CGD4 Database Design

4.7 CG-QMS SOP CGIB1 Investigator Brochure

4.8 Service level agreement (LinCTU involvement only)

5. PROCEDURE

Where the Chief Investigator is employed by the University of Lincoln

The Chief Investigator or delegated nominee shall:

5.1 Use the online algorithm is it a clinical trial of a medicinal product to determine whether the study/trial is a CTIMP and requires MHRA authorisation

5.2 The algorithm is a set of questions that determine:

- whether the substance you're testing counts as a medicinal product
- whether your trial counts as a clinical trial within the scope of the relevant EU directive

Note: Where the CI is still unsure whether to obtain an opinion on whether a study involving a medicinal product falls within the scope of the clinical trial regulations and it requires a clinical trial authorisation (CTA), a request for an opinion on whether a study is a clinical trial of an investigational medicinal product under The Medicines for Human Use (Clinical Trials) Regulations 2004 form should be completed and emailed with a copy of the protocol to clintrialhelpline@mhra.gov.uk, with 'Scope - protocol review' followed by the study title (shortened)' as the subject line. Where the University of Lincoln is sponsor, Sponsor@lincoln.ac.uk should be copied into any correspondence.

Medical Devices: If the query relates to a clinical investigation of a medical device an email should be sent to devices.regulatory@mhra.gov.uk. Where the University of Lincoln is sponsor, Sponsor@lincoln.ac.uk should be copied into any correspondence.

Once the requirement for a CTA is confirmed the following steps should be undertaken:

5.3 Prepare the ethics application and Study/Trial protocol and supporting documents in accordance with SOP CG05 Ethics Application and SOP CG04Protocol Development

5.4 Obtain a EudraCT number (contact sponsor@lincoln.ac.uk for Sponsor's protocol code number) and add to the protocol, IRAS form and any other supporting documents.

5.5 Prepare an Investigator Brochure, investigational medical product dossier (IMPD) or a simplified IMPD (SOP CGIB1 Investigator Brochure) or provide a copy of the Summary of Product Characteristics (SmPC).

5.6 Complete all applicable sections of the IRAS form, prior to requesting electronic authorisations, confirm sponsorship in accordance with SOP CG02 Sponsorship.

5.7 Once sponsorship is confirmed the IRAS form and supporting documents shall be finalised and authorisations requested.

Note: Any changes made to the IRAS form after electronic signatures have been assigned shall invalidate all signatures on the form. If changes must be made, they shall be notified and approved by Sponsor prior to implementation; the form must be re-signed by all parties prior to submission.

Payment to the MHRA

5.8 There are different fees based on the type of clinical trial application.

5.9 See MHRA fees for current application fee and MHRA payment for payment instructions.

5.10 Obtain Purchase Order from the finance officer in accordance with your school's finance procedures. Upon receipt of the invoice, payment should be made, a copy of the payment should be saved as a PDF for upload to the submission package.

Submission package:

5.11 Prepare the submission package for submission to the MHRA. The submission package must include:

- a covering letter (when applicable, the subject line should state that the submission is for a Phase I trial and is eligible for a shortened assessment time, or if it is submitted as part of the notification scheme). The covering letter should clearly highlight the Purchase Order (PO) number; this will help to ensure invoicing and allocation of payments is processed promptly and efficiently.
- a clinical trial application form in PDF and XML versions
- a protocol
- an investigator's brochure (IB) or document replacing the IB
- an investigational medical product dossier (IMPD) or a simplified IMPD (note an ASMF is not acceptable)
- a non-investigational medicinal product dossier (if required)
- a summary of scientific advice obtained from the MHRA or any other regulatory authority, if available
- manufacturer's authorisation, including the importer's authorisation and Qualified Person declaration on good manufacturing practice for each manufacturing site if the product is manufactured outside the EU. Further guidance covering this area.
- a copy of the UK or EMA's decision on the paediatric investigation plan and the opinion of the paediatric committee, if applicable
- the content of the labelling of the investigational medicinal product (IMP) (or justification for its absence)

Note: All documents must have copy and paste functionality. We do not currently accept password-protected documents.

5.12 Once the submission package is complete, and electronic authorisations are received, the IRAS form should be submitted following the instructions in the eSubmission tab in IRAS.

Note: You must create XML and PDF versions of the MHRA application form, save and sign them electronically, and submit them via MHRA submissions with the rest of the required documents.

Where LinCTU are providing support in preparing an ethics application.

A member of LinCTU shall:

5.13 Provide support to the Chief Investigator in the preparation of a CTA application in accordance with the steps 5.1-5.12 above.

Registration of clinical trials

The Chief Investigator or delegated nominee / LinCTU staff shall:

5.14 Register the study on ClinicalTrials.gov.

5.15 Add the ClinicalTrials.gov reference to the protocol

5.16 Maintain the ClinicalTrials.gov entry throughout the life of the study.

Note: Where the CI does not have a clinicaltrials.gov account they should contact the University's PRS administrator samlewis@lincoln.ac.uk or where the University is not the sponsor, contact the PRS administrator of the sponsoring organisation.

MHRA response

5.17 The initial assessment will be completed within 30 days of being submitted. The MHRA will notify you of the outcome of your submission, which could be:

- acceptance of the request for a clinical trial authorisation
- acceptance of the request for a clinical trial authorisation subject to conditions
- grounds for non-acceptance of the request for a clinical trial authorisation

The Chief Investigator or delegated nominee / LinCTU staff shall:

5.18 Respond to any requests from the MHRA regarding the application or queries with the protocol.

5.19 Copies of all correspondence should be stored in the Trial Master File. A copy of all correspondence should be provided to the sponsor.

5.20 Once approval is obtained store the letter in the Trial Master File. Copy to any relevant participating sites/organisations and to the Sponsor.

5.21 Notify the sponsor that the final approval letter has been obtained. The sponsor will (once all permissions are in place) give the study the green light to start.

Note: Green light confirmation is required for a participating site before the first participant is recruited.