Imperial College London

Research Governance and Integrity Team

Imperial College Healthcare NHS Trust

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End of Study Procedure

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Author: Becky Ward, Research Governance Manager	
Approved by: Ruth Nicholson, Head of Research Governance and Integrity	Date: Ruth Nicholson Digitally signed by Ruth Nicholson Date: 2021.11.02 13:33:37 Z

Version	Date	Reason for Change
Version 1.0	30 May 2007	Annual review
Version 2.0	20 Jun 2008	Annual review
Version 3.0	08 Feb 2010	Formation of Joint Research Office
Version 4.0	14 Jul 2011	Annual review
Version 5.0	03 Dec 2012	Annual Review
Version 6.0	18 Feb 2015	Scheduled Review
Version 7.0	25 Oct 2017	Annual Review
Version 8.0	29 May 2018	Update of procedure for clinical trials and the end of study.
Version 9.0	19 Oct 2020	Scheduled Review Templates removed and administrative changes to SOP. JRCO name change to RGIT.
Version 10.0	07 Jan 2021	Updated regarding updates to

		EoS submission for CTIMP studies after Brexit Amendments due to leaving the European Union from 1st January 2021
Version 11.0	25 Mar 2021	Update in line with HRA guidance
Version 12.0	24 Sep 2021	Updated in line with HRA final reporting changes
Version 13.0	02 Nov 2021	Updated for studies using CWOW IRAS

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1. PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to describe the procedure for notifying the relevant bodies about the end of a study for clinical trials of a medicine for human use (CTIMPs) and all other, non-CTIMP clinical research. The procedure for submitting final research reports is also described.

2. INTRODUCTION

The Medicines for Human Use (Clinical Trial) Regulations (2004) and the Heath Research Authority (HRA) state that for all clinical trials of Investigational Medicinal Products (CTIMPs), and for all other clinical research (non-CTIMPs), written notification of the end of study should be submitted within 90 days of the end of project.

The definition of the conclusion of the research should be provided in the protocol. In most cases, it will be the date of the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the protocol. Any change to this definition should be notified as an amendment (see RGIT_SOP_006 on the SOP, Associated Documents & Templates page). It does not mean the completion of data analysis or publication of results.

If the Chief Investigator (CI) requires a study extension, for example because fewer than expected patients were recruited, this extension request should be notified as an amendment to the study.

Before the end of study the CI should review the plans that have been approved by the REC for use of tissue and data collected in the course of the study, providing information to participants, and dissemination of results. If there is a requirement to make any changes to these approved arrangements it should be considered whether a substantial amendment is required before submitting the end of study notification.

HRA guidance now states for studies involving human tissue, the analysis of samples should be undertaken as part of the data collection before the end of study is declared.

Final analysis of the data (following 'lock' of the study database) and report writing is normally considered to occur after formal declaration of the end of the project.

2.1. End of study under HRA Approval

Where a project has HRA Approval and has been reviewed by a REC you need only inform the REC when your study has ended. Where a project has HRA Approval and was not reviewed by an NHS REC, you will need to tell HRA when the project has ended. You should send this notification by email to HRA approvals (Cited 23 June 2020) including your IRAS ID and your contact information (phone and email).

2.2. Declaration of end of a clinical investigation of medical device to MHRA

Manufacturers are required to notify the MHRA when a clinical investigation comes to an end.

2.3. Notification of end of study to Confidentiality Advisory Group

If you have an application with the Confidentiality Advisory Group, when your study is completed you should notify the **Confidentiality Advice Team** as soon as possible in writing. Once received the Confidentiality Advice Team will review the information provided, update the approval register and write to confirm receipt of the application closure notice.

The application will remain on the approval register on the HRA website for at least 12 months following notification of application closure.

3. PROCEDURE FOR NOTIFICATION OF END OF STUDY FOR CLINICAL TRIALS OF INVESTIGATIONAL MEDICINAL PRODUCTS (CTIMPs)

3.1. Lines and method of communication

It is the responsibility of the Chief Investigator (CI), or someone delegated by the CI, to notify the end of the trial by completing the EudraCT 'Declaration of the end of a Clinical Trial' form – Appendix 1-RGIT_TEMP_041

The end of trial declaration must be sent to the following:

i) Emailed to the Research Ethics Committee (REC) which gave a favourable opinion of the research;

ii) Emailed to the Sponsor - for Imperial College Academic Health Science Centre (AHSC) studies, this is the RGIT CTIMP team.

iii) Uploaded to the Medicines and Healthcare Products Regulatory Agency (MHRA) via the MHRA submissions portal. Please contact the RGIT monitor for MHRA submissions account registration and submission guidelines. On the Human Medicines Tile please select 'Clinical Trial' as the Regulatory Activity and 'CT-EOT'- from the Regulatory sub activity dropdown list.

N.B For multi-national trials, the CI (or someone delegated by the CI) must notify the competent authorities of all member states concerned, as well as the Ethics Committee that the clinical trial has ended.

The end of trial form should only be submitted when the trial has ended in all countries. However, the MHRA may be informed by letter/e-mail when the trial finishes in the UK which will signal the suspension of the annual service fee for maintaining the Clinical Trial Authorisation.

3.2. Timing of notification

LOCATION OF TRIAL	WHEN TO NOTIFY END OF STUDY
Trial is running **only** in the UK	When the trial ends
Trial is running **only** in countries outside the UK	When the trial ends
Trial is running in the UK **and** in other countries, trial ends in all countries *at the same time*	When the trial ends
Trial is running in the UK **and** in other countries, trial ends in UK *at a different time*	When trial ends in the UK **and** When trial ends in all other countries

The Chief Investigator, acting on behalf of the Sponsor, must notify the required organisations of the end of the trial ***within 90 days*** of the trial ending (as defined in the protocol).

3.2.1 Trial suspended or early termination

If a trial is terminated early, the CI must notify the REC, Sponsor and the MHRA within 15 days of the halt and clearly explain the reasons for suspension or termination, using the Notification of the End of a Clinical Trial form (Appendix 7.1) and submit to REC and sponsor by email, and MHRA via CESP.

N.B. Where it is necessary to seek ethical review of related actions, such as informing subjects and arranging continuing care and follow-up outside the trial, a notice of substantial amendment would need to be submitted alongside a declaration of early termination.

3.2.2 Trial does not commence

If the CI decides not to commence a trial, they should notify the REC, the Sponsor and the MHRA as soon as possible and clearly explain the reasons for not starting the trial.

4. PROCEDURE FOR NOTIFICATION OF END OF STUDY FOR ALL OTHER CLINICAL RESEARCH (non-CTIMPs)

4.1. Lines and method of communication

It is the responsibility of the Chief Investigator (CI), or someone delegated by the CI, to notify the end of the study to the following:

i) the Research Ethics Committee (REC) which gave a favourable opinion of the research;
ii) the Health Regulatory Authority (Cited 23 June 2020) **only for studies exempt from REC approval**
iii) the Sponsor - for Imperial College Academic Health Science Centre (AHSC) studies, this is the RGIT.
iv) the Confidentiality Advisory Group (CAG) **(if applicable)**

The NRES declaration of the end of a study form (Appendix: 2-RGIT_TEMP_042) must be completed and sent by email.

If the study uses the Combined Ways of Working (CWOW) IRAS system then the End of Trial can be submitted via the system by clicking on the Reporting button

4.2. Timing of notification

LOCATION OF TRIAL	WHEN TO NOTIFY END OF STUDY
Trial is running **only** in the UK	When the trial ends
Trial is running **only** in countries outside the UK	When the trial ends
Trial is running in the UK **and** in other countries, trial ends in all countries *at the same time*	When the trial ends
Trial is running in the UK **and** in other countries, trial ends in UK *at a different time*	When trial ends in the UK **and** When trial ends in all other countries

The Chief Investigator, acting on behalf of the Sponsor, must notify the required organisations of the end of the study ***within 90 days*** of the study ending (as defined in the protocol).

4.2.1 Study suspended or early termination

If a study is terminated early, the CI must notify the REC and the Sponsor within 15 days, and clearly explain the reasons for suspension or termination. For this purpose, use the Declaration of End of a Study form (Appendix 7.2).

4.2.2 Study does not commence

If the CI decides not to commence a study, he or she should notify the REC and the Sponsor as soon as possible and clearly explain the reasons for not starting the study.

If the research does not commence within 12 months of the favourable opinion being issued, the Chief Investigator should send a written explanation for the delay. A further written explanation should be sent after 24 months if the research has still not commenced.

5. FINAL REPORT ON THE RESEARCH

A final research report must be sent to the REC and Sponsor, as well as the MHRA if the study is a CTIMP. For the REC and HRA the final report should be submitted via the HRA website using the standard form As a minimum, the REC and Sponsor should receive information on whether the project achieved its objectives, the main findings, and arrangements for publication or dissemination of the research, including any feedback to participants. MHRA (devices) may request a copy of the final report from a clinical investigation of a device.

For studies using the CWOW IRAS system the Final Report can be submitted to both REC and the MHRA using the reporting button.

Where this is a multi-national study, this is the end of study in all participating countries and not just in the UK.

It should also be ensured that participants are informed of the results of the study, depending on the information given in A51 of the IRAS form and the participant information sheet.

5.1. Lines and method of communication

The Chief Investigator, acting on behalf of the Sponsor, must submit a final research report to the REC, sponsor and MHRA (CTIMPS only). The report must be submitted as follows:

5.1.1 Sponsor: email a copy of the final report to the sponsor; for Imperial College Academic Health Science Centre (AHSC) studies, this is the RGIT (non-CTIMPs) or RGIT CTIMP team CTIMPS);

5.1.2 REC and HRA: Submit via the standardised form on the HRA website

5.1.3 MHRA: Posting of clinical trial results in European Clinical Trials Database (EudraCT) is mandatory (since 21 July 2014).

The end of trial results must be uploaded to EudraCT (Cited 23 June 2020) by the CI (or delegated study member). The RGIT monitor will provide a letter from the sponsor authorising the trial to be assigned to the CI (or delegated user) EudraCT account. For further guidance on completing the full dataset upload, please contact the RGIT CTIMP team.

Once final results have been uploaded and completed, the user must email the MHRA:

- send a short confirmatory email to CT Submission with 'End of trial study report: EudraCT XXXX-XXXXXX-XX' as the subject line.

- N.B You will not get an acknowledgment email or letter from the MHRA.
- For studies set up post Jan 2021 where EudraCT registration is no longer a requirement then reporting should be done on the relevant public database

5.2. Timing of notification

Final results must be submitted to the relevant authorities within 6 months of the 'end of trial' for paediatric clinical trials, or within one year of the 'end of trial' for non-paediatric clinical trials.

5.3. Public database reporting requirements for non-CTIMPs

If a study has been registered on a public database, the records must be maintained and the results need to be reported within the required time frame regardless of the outcome of the trial and regardless of potential planned or pending publications. See RGIT_SOP_022 on the SOP, Associated Documents & Templates page.

6. REFERENCES

Clinical Trials Toolkit (Cited 23 June 2020)

NHS Health Research Authority progress reports (Cited 23 June 2020)

NHS Health Research Authority ending your project (Cited 23 June 2020)

Contacting HRA (Cited 23 June 2020)

Research in human subjects other than clinical trials of investigational medicinal products (Cited on 23 June 2020)

Medicines for Human Use (Clinical Trials) Regulations 2004 (SI: 1031),Schedule 3, Part 4 (Cited 23 June 2020)

MHRA. Managing your clinical trial authorisation: End of trial (Cited 23 June 2020)

EC Europa reporting final results (Cited 23 June 2020)

Common European Submission Portal (Cited 23 June 2020)

RGIT website (Cited 08 October 2020)

RGIT Staff list (Cited 08 October 2020)

RGIT_SOP_006 Amendments to Healthcare Research

RGIT_SOP_022 Adding Study Details to Public Databases

7. APPENDICES

The following Appendices list the following Templates associated to this SOP which can be found on the SOP, Associated Documents & Templates page.

Appendix 1: Notification End of Clinical Trial Medicine – RGIT_TEMP_041
Appendix 2: Declaration of the End of a Study – RGIT_TEMP_042