

**Standard Operating Procedure**

**For Investigators and Sponsor for End of Trial Notification procedures**

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| **Revision Chronology:** |
| **Version Number:** | **Effective Date:** | **Reason for Change:** | **Author:** |
| JBRU/INV/S07/01 | 14/01/10 | To implement formatting changes to comply with the SOP on SOPs (JRO/SPON/S01/02).To bring the content up to date with the sponsor’s procedures for the Declaration of the End of Trial Notification Form, close out and trial reporting requirements.  | Anne Marie Downey and Ann Cochrane |
| JRO/INV/S07/02 | 14/10/11 | To further clarify the responsibilities of the Investigators and Sponsor for End of Trial Notification, Trial Close Out Procedures and to add the request of the final statistical plan.  | Anne Marie Downey and Nimrita Verma  |
| JRO/INV/S07/03 | 08/08/14 | Updated end of trial procedure for single site and multi-centre trials and clarified on-site and central close out monitoring procedure | Harshani HettiarachchiGemma Jones |
| JRO/INV/S07/04 | 08/08/17 | Updated information on EudraCT reporting  | AdedayoAkinyemi |
| JRO/SPON/S06/01 | 30/11/20 | Revised all sections of the SOP document.Removed close out procedures (added to a separate SOP document).Added section 6.4 Preparation for Archiving | Samim Patel / Catherine Maidens |

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| **ACRONYMS**: |
| ATMP | Advanced Therapy Medicinal Product |
| CI  | Chief Investigator |
| COA  | Compliance Oversight Advisor |
| CRF  | Case Report Form |
| CTIMP  | Clinical Trials of an Investigational Medicinal Product  |
| EudraCT | European Union Drug Regulating Authorities Clinical Trials Database |
| GCP  | Good Clinical Practice |
| ISF | Investigator Site File |
| ISRCTN | International Standard Registered Clinical/soCial sTudy Number |
| IMP | Investigational Medicinal Product |
| JRO  | Joint Research Office (representative of the Sponsor)<https://www.ucl.ac.uk/joint-research-office/>  |
| PI | Principal Investigator |
| PVG | Pharmacovigilance |
| RM (ATMP) | Regulatory Manager (ATMP) |
| RM (P) | Regulatory Manager (Pharmaceuticals) |
| SAE | Serious Adverse Event |
| SI | Statutory Instrument |
| SOP | Standard Operating Procedure |
| SRA | Sponsor Regulatory Advisor |
| TMF | Trial Master File |

**Standard Operating Procedure for Sponsor and Investigators for End of Trial Notification procedures**

**1. PURPOSE**

This Standard Operating Procedure (SOP) has been written to describe the procedures for Investigators and Sponsor for the end of trial notification procedures and reporting requirements.

**2. JOINT UCLH/UCL RESEARCH OFFICE (JRO) POLICY**

All SOPs produced from the JRO must be used in conjunction with local NHS Trust and UCL policies and procedures.

The JRO acts as the representative of the Sponsor and will be the official name used on all SOPs.

All JRO SOPs will be produced, reviewed and approved in accordance with the JRO SOP on SOPs.

Please refer to the JRO website to ensure that this is the most current version of the SOP.

**3. BACKGROUND**

All SOPs are written in accordance with applicable GCP requirements as outlined in Directives 2001/20/EC and 2005/28/EC (in the UK, these Directives were transposed into UK law by SI 2004/1031, SI 2006/1928) and subsequent amendments and when applicable Regulation 536/2014 and subsequent relevant SIs. Where applicable it incorporates elements of ICH GCP tripartite guidelines (E6).

The Medicines for Human Use (Clinical Trials) Regulations SI 2004/1031 as amended outline the responsibilities of the Sponsor to notify the REC and Competent Authority (MHRA in UK) after the conclusion of a trial (UK Regulation No. 27). End of trial monitoring procedures should be in place to ensure data quality and accurate reporting of trial data for End of Trial Report and final trial analysis, and to ensure that essential documents in the Trial Master Files/Investigator Site Files are complete and ready for archiving as per Sponsor SOP 21.

**4. SCOPE OF THIS SOP**

This SOP will describe the process for Investigators and the Sponsor to follow at the conclusion of a trial and their responsibilities to inform the Competent Authority, REC and those host organisations involved.

This SOP refers to CTIMPs sponsored by UCL. This SOP will not apply to trials that are managed by a third party, where they have contractually been delegated end of trial notification and close out procedures in line with their SOPs.

**5. RESPONSIBLE PERSONNEL**

Responsibilities of Personnel are outlined in the tables found in section 6.

**6. PROCEDURE**

**6.1 Notification of End of Trial**

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| Section | Responsible Person | Activity |
| 6.1.1 | CI | The CI notifies Sponsor of the Trial End Date as defined in the trial protocol or if the trial has prematurely ended (early termination). |
| 6.1.2 | SRA/RM (ATMP) | Acknowledge notification of Trial End by issuing **End of Trial Sponsor Acknowledgement** email and request completion of the **Declaration of the** **End of Trial Form.** Remind CI of notification timelines:* Within 90 days for a planned conclusion of a Trial
* Within 15 days for a Premature conclusion of a Trial (early termination).
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| 6.1.3 | CI | Complete the **Declaration of the End of Trial Form** available on the EudraCT website: <https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/declaration_end_trial_form.pdf> and submit to the Sponsor for review. |
| 6.1.4 | SRA/RM (ATMP) | Review and submit completed **Declaration of the End of Trial Form** to MHRA within the following timelines: * Within 90 days for a planned conclusion of a Trial
* Within 15 days for a premature conclusion of a Trial (early termination).

Send copies of the submission to the CI for filing in the Trial Master File. |
| 6.1.5 | CI | Submit **Declaration of the End of Trial Form** to REC within the same timelines.  |
| 6.1.6 | CI | Inform all sites and Principal Investigators that the Trial has been declared ended. Send a copy of submission documents to the trial sites for their Investigator site files. |
| 6.1.7 | SRA/RM (ATMP) | Request from the CI:* **Final Statistical Analysis Plan Declaration Form**
* Final Statistical Analysis Plan
 |
| 6.1.8 | SRA/RM (ATMP) | Inform the COA/Trial Monitor and PVG Manager of the End of Trial.  |
| 6.1.9 | COA /Trial Monitor | Monitoring Close Out procedure initiated as per Section 6.2 of the SOP (JRO/SPON/SOP10) and the Trial Monitoring Plan. |
| 6.1.10 | PVG Manager | Request trial team to provide listing of SAEs from trial database. Perform reconciliation of SAEs recorded in trial database with SAE reports received at JRO. |

**6.2 MHRA / REC Acknowledgement of End of Trial Notification**

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| Section | Responsible Person | Activity |
| 6.2.1 | SRA / RM (ATMP) | Send to the CI:* MHRA acknowledgment of the End of Trial Declaration for filing in the TMF (along with the **End of Trial Report Reminder** email).

Documents to be also filed in the JRO Sponsor File. |
| 6.2.2 | SRA/ RM (ATMP) | Request from the CI:* REC acknowledgement of the end of trial notification.

File received documents in the JRO Sponsor File. |
| 6.2.3 | CI  | Notify the participating sites including local R&D offices and pharmacies of receipt of acknowledgement. File all documentation and correspondence in the TMF. |
| 6.2.4 | SRA / RM (ATMP) or CI | Depending on contractual agreements, notify relevant contracted parties (as per signed agreement) e.g. funder, central laboratories, IMP supplier and PVG of the end of the Trial. |

**6.3 End of Trial Report Submission**

Since 2014 it became mandatory for sponsors to post clinical trial results in the European Clinical Trials Database (EudraCT). The final report needs to be uploaded to EudraCT following a pre-determined dataset that has been compiled by the EMA.

A subset of the data included in EudraCT will become available to the public.

In case of a delay, the MHRA and REC must be notified as soon as possible in a cover letter explaining the reason for the delay and future submission date.

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| Section | Responsible Person | Activity |
| 6.3.1 | CI | The End of Trial Report needs to be submitted within 12 months of the end of trial date. For paediatric trials the report needs to be submitted within 6 months of the end of trial date. |
| 6.3.2 | SRA/ RM (ATMP) | Refer to the **Submission of Clinical Trial Results in EudraCT- Sponsor Guide** document.Send CI the **End of Trial Report Reminder** email attaching the **Submission of Clinical Trial Results in EudraCT – Investigator Guide** document.  |
| 6.3.3 | CI | CI must follow the **Submission of Clinical Trial Results in EudraCT - Investigator Guide** to ensure study information is captured in the pre-determined dataset, validated and uploaded in EudraCT. |
| 6.3.4 | SRA/ RM (ATMP) | Once the data has been uploaded review the information and complete the **EudraCT Report Checklist**.Send **End of Trial Report Approval** (EudraCT) email to the trial statistician to request confirmation that the statistical findings uploaded to EudraCT are accurate.Send **End of Trial Report Approval** (EudraCT)email to the CI to request confirmation that the content of the report uploaded to EudraCT is accurate.File the completed EudraCT checklist and the CI and Statistician approval emails in the Sponsor File.The SRA/RM will post results in EudraCT, no later than one year (or 6 months for paediatric trials) after the end of trial has been declared. |
| 6.3.5 | CI | CI must submit the PDF summary result to the ethics committee, along with copies of any end of study information sheets that have been provided to the participants and send the SRA/RM (ATMP) the relevant correspondence for filing in the Sponsor File. |
| 6.3.6 | SRA/ RM (ATMP) | SRA/RM (ATMP) must notify the MHRA by email that the report has been uploaded (posted) to EudraCT.File the sent email in the Sponsor File and send to CI for filing in the TMF. |
| 6.3.7 | SRA/ RM (ATMP) | SRA/RM (ATMP) sends the CI the proof of upload and PDF report for filing in the TMF. |
| 6.3.8 | CI | Complete results section on all trial registries such as ClinicalTrials.gov or ISRCTN.Notify SRA/ RM (ATMP) when completed.  |
| 6.3.9 | SRA/ RM (ATMP) | Send **End of Trial Report Approval** (Trial Registry) email to the trial statistician to request confirmation that the results uploaded or completed on the trial registries are accurate and consistent with the final study report.Send **End of Trial Report Approval** (Trial Registry) email to the CI to request confirmation that the trial information including the results reported on the registries is accurate and consistent with the final study report.File the CI and Statistician approval emails in the Sponsor File. |

**6.4 Preparation for Archiving**

Preparation for archiving of the trial documents can begin after the End of Trial Results have been reported. Prior to archiving a full review of the TMF and Sponsor File should be carried out to ensure all documents are filed and any missing documents are file noted.

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| Section | Responsible Person | Activity |
| 6.4.1 | CI | Perform a full review of the TMF. Any missing documents should be filed or file noted.When the Sponsor has issued the Archiving Confirmation email, proceed to archiving the TMF as per the Sponsor’s SOP on Archiving (SOP 21). |
| 6.4.2 | SRA/ RM (ATMP) | Perform a full review of the Sponsor File. Any missing documents should be filed or file noted.Archive the Sponsor File as per the Archiving SOP (SOP 21). |

**7. REFERENCES**

1. The Medicines for Human Use (Clinical Trials) Regulations 2004 (Statutory Instrument 2004/1031, implemented 1st May 2004, and as amended thereafter.
2. Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 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.
3. European Comission: Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1), March 2010
4. Commission Guideline — Guidance on posting and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006
5. Sponsor’s SOP on Archiving

# 8. APPENDICES

# No Appendices are associated with this SOP.

**9. TEMPLATES/LOGS ASSOCIATED TO THIS SOP**

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| 1. | End of Trial Sponsor Acknowledgement Email Template |
| 2. | Final Statistical Analysis Plan Declaration Form |
| 3. | End of Trial Report Reminder Email Template |
| 4. | Submission of Clinical Trial Results in EudraCT - Sponsor Guide |
| 5. | Submission of Clinical Trial Results in EudraCT - Investigator Guide |
| 6. | EudraCT Report Checklist |
| 7. | End of Trial Report ApprovalEmail Template |

**10. SOP DISSEMINATION & TRAINING**

This SOP will be available to the CIs on <https://www.ucl.ac.uk/joint-research-office/>

Trial team staff concerned by this SOP will sign the SOP training log (12. SOP TRAINING LOG) part of this SOP.

This SOP will be distributed to the concerned JRO staff. Staff concerned by the SOP will sign the SOP training log (12. SOP TRAINING LOG) which is part of each SOP.

The training will constitute of the person reading the SOP and being provided with the opportunity to ask specific questions to the author of the SOP.

**11. SIGNATURE PAGE**

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| **Author and Job Title:** | Samim Patel, Sponsor Regulatory Advisor  |
| **Signature:** |  |
| **Date:** | 22/10/2020 |
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| **Authorised by:****Name and Job Title** | Helen Cadiou, Head of Quality Assurance  |
| **Signature:** |  |
| **Date:** | 22/10/2020 |

 **12. SOP TRAINING LOG:**

|  | **Name of Staff (**Capital letters**):** | **Job Title:****Department:** | **Training Date** | **I confirm that I understand & agree to work to this SOP** **SIGNATURE** | **Name of Trainer (if applicable)** | **Signature** | **Date** |
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