UCL

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

SOP Number: JRO/INV/S07/04	**Effective Date:** 08/08/2017
Version Number & Date of authorisation: V04,02/08/17	**Review Date:** 08/08/2020
SOP eDocument kept: S:_SLMS\RSC_ALL_STAFF\CLINICAL_TRIALS\SOPs\EFFECTIVE_SOPs_ Guides \Investigator SOP\INV_S07 End of Trial notification\INV_S07_SOP for EndOfTrialNotification_V04.docx	

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 Hettiarachchi Gemma Jones
JRO/INV/S07/04	08/08/17	Updated information on EudraCT reporting	Adedayo Akinyemi

ACRONYMS:	
ATMP	Advanced Therapy Medicinal Product
JRO	Joint Research Office http://www.ucl.ac.uk/joint-rd-unit (representative of the Sponsor)
GCP	Good Clinical Practice
SOP	Standard Operating Procedure
ISF	Investigator Site File
PI	Principal Investigator
CI	Chief Investigator
COA	Compliance Oversight Advisor
CRF	Case Report Form
CTIMP	Clinical Trials of an Investigational Medicinal Product
SI	Statutory Instrument
SRA	Sponsor Regulatory Advisor
RM (ATMP)	Regulatory Manager (ATMP)
RM (P)	Regulatory Manager (Pharmaceuticals)
TMF	Trial Master File

Standard Operating Procedure
For Sponsor and Investigators for End of Trial Notification and Trial Close Out procedures

1. PURPOSE

This Standard Operating Procedure (SOP) has been written to describe the procedures for Investigators (both CI and PI if multisite) and Sponsor for the end of trial reporting requirements and trial close out procedures.

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

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 2005/20/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 also describes the process of closing down a Site within a multi-centre trial.

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

Section	Responsible Person	Activity
6.1.1	CI	CI notifies Sponsor of Trial End as defined in the trial protocol or if trial prematurely ended
6.1.2	SRA/ RM (ATMP)	Acknowledge notification of Trial End by issuing End of Trial sponsor acknowledgement letter /email and Request completion of **End of Trial Notification Form.** Remind CI of notification timelines: • 90 days for a planned conclusion of a Trial • 15 days for a Halted or a Premature conclusion of a Trial
6.1.3	CI	Complete the End of trial notification form available on the EudraCT website **https://eudract.emea.europa.eueudract/index.do** and submit to the Sponsor for review.
6.1.4	SRA/ RM (ATMP)	Review and submit completed **End of Trial Notification Form** to MHRA within the following timelines: • 90 days for a planned conclusion of a Trial • 15 days for a Halted or a Premature conclusion of a Trial Send copies of submissions to the CI for filing in the Trial Master File.
6.1.5	CI	Submit **End of Trial Notification** to REC within the same timelines.
6.1.6	CI	Inform all sites and Principal Investigators that Trial declared ended. Send a copy of submission documents to trial sites for their Investigator site files.
6.1.7	SRA/ RM (ATMP)	For trials that do not have a JRO Biostatistical Collaborator request from CI: • **Final Statistical Analysis Plan Declaration Form** • **Final Statistical Analysis Plan**
6.1.8	Trial Monitor/ COA	Monitoring Close Out procedure initiated as per Section 6.4 of this SOP and Trial monitoring plan.

6.2 Acknowledgement of End of Trial Notification

Section	Responsible Person	Activity
6.2.1	SRA	Send to CI: • MHRA acknowledgment of End of Trial Declaration for filing in TMF • Provides **"End of Trial Report Reminder"** letter Documents to be also filed in the JRO Sponsor File
6.2.2	SRA	Request from CI: • REC acknowledgement of end of trial
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 or CI	Depending on contractual agreements, notify relevant

		contracted parties (as per signed agreement) e.g. funder, IMP, supplier and PVG of the end of the Trial.

6.3 Closing of a Site

The closing of a Site within a multi-centre trial may be due to various reasons including:

- Completion of target recruitment at Site/ trial
- Failure or prolonged lack of recruitment at Site
- Change of protocol inclusion/exclusion criteria or trial endpoints that deems a Site unsuitable for recruitment of trial subjects or data collection
- Change or absence of key personnel at Site such as Principal Investigator (PI) or key Research Nurse
- Any other reason whereby Site is unable to commit to the trial

Depending on the progress of the entire trial, it may be necessary to close down a trial site/s whilst there is on-going recruitment/patient activity at other sites. The process for closing a Trial Site/s in this instance is as follows:

Section	Responsible Person	Activity
6.3.1	CI	Decision to close down Site and JRO informed
6.3.2	CI/Sponsor	Inform PI and site personnel of Site closed for further recruitment and confirm plan for on-going participants if required. Inform local site pharmacy and R&D of intention to close site.
6.3.3	CI / RM (Pharm) /SRA/ RM (ATMP)	Confirm plan for unused IMP supplies
6.3.4	Trial Monitor/COA	Following last patient, last visit at the site- complete Close out monitoring procedure for site as detailed in Section 6.4

6.4 Monitoring Close out Procedure

As per SPON SOP 19 on Oversight and Monitoring, the monitoring strategy for a trial is documented in the Trial Monitoring plan prior to the start of the Trial.

6.4.1 On–site close out monitoring procedure

Section	Responsible Person	Activity
6.4.1.1	COA /Trial monitor	Schedule close out monitoring visit with site team to include pharmacy. Issue **Intent to close out Letter.** Carry out on site close out visit on scheduled date and review items as per trial Monitoring plan
		Issue **Close Out monitoring Visit Report** to trial site team including Sponsor authorisation to destroy IMP (as applicable)
6.4.1.2	COA /Trial monitor	Arrange follow up visit or email/teleconference to close any further remaining queries and send confirmation email/letter
6.4.1.3	COA /Trial monitor	Inform SRA when all queries from close out visit are closed
6.4.1.4	SRA/RM (ATMP)	Issue **Confirmation of Site Close Down Letter** to site for filing in ISF. Inform PI and site staff to archive ISF as per local procedures.

6.4.2 Central monitoring close out procedure

6.4.2.1	COA	Compliance Oversight Advisor will request the following documents from site for close out preparation in **Intent to Close Out letter**: • Completed Final UK Regulation Compliance Form Part 2 • Final Delegation Log • Final Subject Enrolment, Completion & Withdrawal Log • Final SAE Log • Completed IMP accountability logs • IMP storage records (e.g. temperature records) • Final Log of Protocol Deviations, Serious breaches • Any other documents specific to the trial for Sponsor oversight
6.4.2.2	CI/PI team & Trial Staff	The CI/PI if multi-site trial, completes and returns a final copy of the above and any other requested documents as listed above to the Sponsor COA
6.4.2.3	COA	Perform review of documents requested from site and raise any discrepancies with trial team
6.4.2.4	RM (Pharm) /SRA/ RM (ATMP)	Authorise destruction return of unused IMP and IMP returns Request certificates of destruction (if applicable).
6.4.2.5	COA	Issue Site with summary of remaining queries to be addressed in **Compliance form part 2**
6.4.2.6	COA	Arrange follow up email/teleconference to resolve and confirm all queries are closed
6.4.2.7	CI/PI	Complete **Declaration of Site Close Down Form**
6.4.2.8	COA	Inform SRA when all queries are closed
6.4.2.9	SRA/RM (ATMP)	Issue **Confirmation of Site Close Down Letter** to site for filing in ISF. Inform PI and site staff to archive ISF as per local procedures.

6.5 End of Trial Report Submission

		Since 2014, It became mandatory for sponsors to post clinical trial results in the European Clinical Trials Database (EudraCT). These summary results will become available to the public. The final report needs to be uploaded to EudraCT following a pre-determined dataset that has been complied by the EMA. In case of a delay, the MHRA, Ethics and HRA must be notified as soon as possible in a cover letter explaining the reason for the delay and future submission date.
6.5.1	CI	The End of Trial Report needs to be submitted within 12 months of the date of declaration of end of trial.
6.5.2	SRA/ RM (ATMP)	SRA/RM Refers to "Submission of Clinical Trial Results in EudraCT-Sponsor guidance". SRA/RM Sends CI "Submission of results investigators".

		SRA/RM Will post results in EudraCT, no later than one year after the end of trial has been declared following the "Submission of Clinical Trial Results in EudraCT- Sponsor guidance".
6.5.3	CI	CI must follow the "Submission of results investigator's" guidance to ensure study information is captured in the pre-determined dataset, validated and uploaded in Eudract CI must submit the PDF summary result to the ethics committee, CI must send SRA/ ATMP the relevant correspondence
6.5.4	SRA/ RM (ATMP)	SRA/RM must notify the MHRA by email that the report has been uploaded to EudraCT.
6.5.5	CI	SRA/RM sends the CI the proof of upload and PDF report for filing in the TMF

6.6 Release of Final Trial Close & Archiving Letter to CI

6.6.1	SRA/ RM (ATMP)	Issue **"Confirmation of Trial Close & Archiving"** letter and notifies the CI to archive the TMF and all study related material as per Sponsor's SOP 21 or Local Trust SOP on Archiving. For multi-site studies, the "Confirmation of Trial Close & Archiving is sent to the CI site and "Confirmation of site Close Down is sent to site/s.

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. EC Detailed guidance for the request for authorization of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial October 2005

4. Sponsor's SOP on Archiving

5. **APPENDICES:** No Appendices are associated with this SOP.

6. TEMPLATES/LOGS ASSOCIATED TO THIS SOP

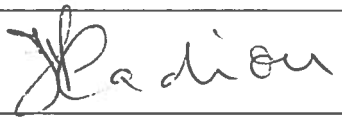
1	End of Trial Sponsor Acknowledgement email/letter
2	Final Statistical Analysis Plan Declaration Form
3	Declaration of Site Close down Form
4	End of Trial Report Reminder letter
5	Intent to Close out Letter
6	Close out visit monitoring report
7	Confirmation of Site Close Down letter
8	Confirmation of Trial Close and Archiving letter

10. SOP DISSEMINATION & TRAINING

This SOP will be available to the CIs on http://www.ucl.ac.uk/joint-rd-unit. Trial team staff concerned by this SOP will sign the SOP training log (12. SOP TRAINING LOG) part of this SOP. In addition each PI trial team member should have an "Individual staff SOP and courses log" which will need to be updated once trained on this SOP. These documents should be filed in the ISF.

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

Authors:	Adedayo Akinyemi, Sponsor Regulatory Advisor (CTIMPs)
Signature:	
Signature:	
Date:	02/08/2017
Authorised by:	Helen Cadiou, Head of Quality Assurance
Signature:	
Date:	02/08/17

S:_SLMS\RSC_ALL_STAFF\CLINICAL_TRIALS\SOPs\EFFECTIVE_SOPs_Guides\Investigator SOP\INV_S07 End of Trial notification\INV_S07_SOP for EndOfTrialNotification_V04.docx

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**
1							
2							
3							
4							
5							
6							
7							

S:_SLMS\RSC_ALL_STAFF\CLINICAL_TRIALS\SOPs\EFFECTIVE_SOPs_Guides\Investigator SOP\INV_S07 End of Trial notification\INV_S07_SOP for EndOfTrialNotification_V04.docx

	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**
8							
9							
10							
11							
12							
13							
14							
15							

S:_SLMS\RSC_ALL_STAFF\CLINICAL_TRIALS\SOPs\EFFECTIVE_SOPs_Guides\Investigator SOP\INV_S07 End of Trial notification\INV_S07_SOP for EndOfTrialNotification_V04.docx

	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**
16							
17							
18							
19							
20							
21							
22							
23							

S:_SLMS\RSC_ALL_STAFF\CLINICAL_TRIALS\SOPs\EFFECTIVE_SOPs_Guides\Investigator SOP\INV_S07 End of Trial notification\INV_S07_SOP for EndOfTrialNotification_V04.docx

	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**
24							
25							
26							
27							
28							
29							
30							