



Standard Operating Procedure For Initiation of a CTIMP

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Revision Chronology:			
SOP ID Number:	Effective Date:	Reason for Change:	Author:
JBRU/07/INT/S06/00	20/12/07	N/A	Ira Jakupovic
JBRU/SPON/S20/01	15/10/08	To separate the Trial and Site Initiation Procedure. To implement a new numbering system and formatting changes to comply with SOP on SOPs (JBRU/SPON/S01/02)	Ira Jakupovic
JBRU/SPON/S20/02	29/01/10	Slight change of name Standard Operating Procedure for Initiation of a CTIMP instead of "Standard Operating Procedure for site Initiation". Added a SOP training log, and a "List of template & Logs associated with the SOP" table. Added an "Acronyms table". Added on the front page a row "SOP eDocument kept: ", to facilitate the location of the electronic version of the SOPs. Added in the header "file name and path" to facilitate the identification of the electronic document Changed the logo to UCL.	Ann Cochrane and Gurjinder Kahlon
JBRU/SPON/S20/03	12/01/12	SOP needed to be updated to reflect current staff titles, unit name, templates and processes relevant to site initiation.	Anne Marie Downey and Gurjinder Kahlon
JRO/SPON/S20/04	08/08/14	Updated to add Open to recruitment checklist and provision for on-site review of ISF. Clarification of procedure and addition of related documents.	Harshani Hettiarachchi, Gemma Jones, Mitesh Kunwardia
JRO/SPON/S20/05	08/08/17	Updated to incorporate HRA changes and the Initiation Report Follow up template	Gemma Jones

ACRONYMS:	
ATMP	Advanced Therapy Medicinal Product
COA	Compliance Oversight Advisor
CRF	Case Report Form
IMP	Investigational Medicinal Product
ISF	Investigator Site File
JRO	Joint Research Office http://www.ucl.ac.uk/jro/
MnCA	Model Agreement for non commercial research (site agreement)
PI	Principal Investigator
PSF	Pharmacy Site File
RM(ATMP)	Regulatory Manager for ATMPs
PVG Manager	Pharmacovigilance Manager
RM (P)	Regulatory Manager (Pharmaceuticals)
SI	Statutory Instrument
SRA	Sponsor Regulatory Advisor

Standard Operating Procedure for Initiation of a CTIMP

1. PURPOSE

This Standard Operating Procedure (SOP) describes the procedure for Initiation of all UCL Sponsored CTIMPs, where the responsibilities of initiation are conducted by JRO. Please check that you are reading the latest version of this SOP: <http://www.ucl.ac.uk/jro/>.

It is recommended that a trial is not initiated until the JRO are satisfied that all essential documents, agreements and approvals are all in place at the relevant site(s).

2. JOINT RESEARCH OFFICE (JRO) POLICY

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

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. For convenience, this document will use the term 'Regulations' to cover the requirements of the UK SI legislation.

The JRO, which represents the Sponsor for UCL, is responsible for putting in place the necessary procedures to secure the quality of every aspect of a clinical trial including clinical trial activities carried out by institutions and investigators participating in trials sponsored by UCL.

The site initiation process is designed to ensure that;

- ensure all essential documentation is in place prior to starting the study
- each site has all essential documents in place for the site to conduct the study in compliance with the approved protocol and sponsor SOPs
- each site is aware of their responsibilities
- each site is aware of Sponsor's processes and SOPs
- the site team has had relevant training which is current and documented
- the delegation of tasks log is completed before any trial related activities are performed by those members and they are authorised to do so by the CI/PI
- the pharmacy (and/or individual(s) responsible for IMP at site) are informed of procedures for ordering IMP (if applicable) and that procedures for receipt, storage, dispensing, accountability and destruction are documented.
- the contact details are up to date and correct and site/pharmacy know how to contact the sponsor for day to day enquiries.

The following definitions will be used throughout this SOP:

Co-ordinating centre- The central site or location where trial-related activities are coordinated from in a multi centre trial. The coordinating centre may also conduct patient recruitment and treatment activity as a Trial Site. The coordinating centre will generally be the location of the CI and hold the TMF.

Trial Site – The location(s) where trial-related activities are actually conducted as per the REC and MHRA submissions.

Site Feasibility Form – The form sent to each site to collect the site contact details and facilities to allow assessment of the site versus requirements for a given trial

Site Pharmacy Questionnaire –Completed by each (new) site pharmacy prior to obtaining local approvals. It is recommended this is completed every two years.

UK Regulations Compliance Form (Part 1)- Trial specific form to be completed by the CI/PI or delegate to demonstrate the content of the TMF/ISF (including presence of Essential Documents)

Investigator Site File (ISF) - the file(s) held at each site taking part in the trial which hold the essential trial document set necessary for local approval and trial conduct at site. In a single centre trial the ISF may be contained within the TMF (See JRO/INV/SOP 02).

Trial Master File (TMF) – the file held at the lead chief investigator site which contains all the essential trial documentation for the trial (See JRO/INV/SOP 02).

Pharmacy Site File (PSF) - the file(s) held at each site pharmacy taking part in the trial which hold the essential trial pharmacy documents deemed necessary for pharmacy trial conduct at site.

Trial Initiation Slides – This is the presentation that will be presented to the CI/PI and their research team at the site and will cover the following topics as a minimum:

- Responsibilities of Site
- Delegation of Responsibilities
- Sponsor's forms and Logs for trial conduct
- Sponsor's SOPs
- Informed consent and Recruitment
- Trial IMP
- Monitoring
- Data management
- Biological Sample handling (if applicable)
- Pharmacovigilance & Urgent Safety Measures
- Amendments
- End of Trial and Archiving
- Training
- UK Regulations and CTIMP legislations
- Sponsor Contact Details

4. SCOPE OF THIS SOP

This SOP covers the procedure that the JRO must follow to ensure that a site is initiated prior to the screening and recruitment of any trial participant and covers the procedures pre initiation, during initiation and post initiation.

This SOP does not apply to UCL Sponsored CTIMPs where site initiation has been delegated to a contracted Third Party and details of this arrangement are documented in a written agreement between JRO and the Third Party.

5. RESPONSIBLE PERSONNEL

The roles and responsibilities of JRO staff are detailed in the table found in section 6 of this SOP.

The Sponsor will perform the initiation visit prior to first subject being recruited at the site.

Where a trial specific monitor is appointed, the duties of the compliance oversight advisor may be delegated to the individual(s).

6. PROCEDURES FOR JRO

6.1 Pre-initiation Procedure

	Role/Task	Responsible Person
6.1.1	Review the Sponsor File to ensure all essential documentation and contracts are complete and in place prior to initiation. Document the review in the Sponsor File Review Template	SRA/RM (ATMP)
6.1.2	Review trial progress and outstanding items by initiating completion of Open to Recruitment checklist	SRA/RM (ATMP))
6.1.3	Ensure IMP Sourcing and Release form is completed as per JRO/SPON/SOP24 and Request Pharmacovigilance (PVG) manager to initiate the PVG checklist.	SRA/RM/RM(P)/PVG Manager
6.1.4	Send to site research team the following documents: 1. Site Initiation Pack 2. List of SOPs for Investigators 3. UK Regulations Compliance Form (Part 1) to be completed (if applicable (see Monitoring plan)) 4. Essential IMP Documents for Pharmacy Site File (either paper or electronic copies) 5. TMF/ ISF Index	SRA/RM

	<p>6. Pharmacy Site File Table of Contents (if applicable)</p> <p>7. Essential Documents as per the TMF/ISF Index (hard/electronic copies)</p> <p>8. Source Document List – Send draft of completed source document list based on CRF design for trial and request site staff to complete site specific sections</p>	
6.1.5	<p>Request from site the following documents (if absent from the JRO Sponsor File as per 6.1.1):</p> <ol style="list-style-type: none"> 1. CI/PI signed and dated CV 2. Copy of CI/PI GCP Certificate 3. Completed Staff signature and Delegation Log 4. Completed Central Trial Responsibilities Log (only for CI site for delegation of specific central tasks by CI core trial team) 5. Completed Site Feasibility Questionnaire 6. Completed Pharmacy Questionnaire (as applicable) 7. Completed UK Regulations Compliance Form (Part 1) (if applicable) 8. Source document List – Final list to be reviewed at site initiation visit/ call 	SRA/ RM
6.1.6	<p>In a multicentre trial the coordinating centre will be initiated first.</p> <p>The CI and staff responsible for the coordination of a multicentre trial along with relevant documentation will need to be reviewed prior to the first site initiation. If the coordinating centre is co-located with a Trial Site then the initiation visits may be combined to a single initiation visit.</p> <p>Review Completed UK Regulations Compliance Report Part 1 against the completed current Sponsor File Review Template to verify that site has all the required essential documents on file. (if applicable, see Monitoring Plan)</p> <p>Highlight any missing documents from either file and arrange for them to be sent prior to opening the site for recruitment.</p>	COA
6.1.7	<p>Once local R&D have confirmed Capacity and Capability and Clinical Trial Site agreement has been signed, arrange Initiation visit/ call as per the monitoring plan for the trial</p> <p>Send Initiation invitation to Site and Lead Pharmacist (and/or individual(s) responsible for IMP) and ensure that the CI / PI and Lead Pharmacist/individual(s) responsible for IMP are present for the initiation.</p>	SRA/ RM (ATMP)/

	<p>All staff involved in the study on a daily basis will be encouraged to attend.</p> <p>A separate visit/call to the site pharmacy (and/or individual(s)/department responsible for the IMP at site) may also be necessary in order to discuss the IMP Management plan and other IMP related documents. This should be done as close to the site visit date as possible.</p>	
6.1.8	Confirm intended initiation visit/teleconference date(s) and initiation arrangements (i.e. Location or Dial in details)	SRA/ RM
6.1.9	Prepare trial initiation slides (as per template) and send to the investigator team ahead of initiation.	SRA/RM/ PVG Manager

6.2 Site Initiation Procedure

	Role/Task	Responsible Person
6.2.1	<p>Present the initiation slides and document who is present at initiation using the Site Initiation Visit sign in sheet.</p> <p>If a separate visit is planned to the pharmacy, IMP management procedures must also be presented to the trial team.</p>	SRA/RM (ATMP)/ COA
6.2.2	<p>Ensure queries from review of UK Regulations Compliance Form (Part 1) are resolved</p> <p>Or</p> <p>Complete a review of the TMF/ISF on appropriate TMF/ISF Review Template as per the monitoring plan</p>	SRA/ COA
6.2.3	Ensure lead pharmacist (and/or individual responsible for IMP) is familiar with the IMP documentation and that they are satisfied with the Summary of Drug Arrangements and other IMP related documents. Request details of the IMP storage arrangements and where necessary, review IMP storage facility at site.	SRA/ RM (ATMP), , COA
6.2.4	If applicable and feasible, visit local laboratory where samples may be analysed or stored to ensure facilities are	SRA/COA/RM (ATMP)

	adequate for the trial.	
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6.3 Post Initiation procedure

	Role/Task	Responsible Person
6.3.1	<p>Complete the trial Open to Recruitment checklist and assess whether trial site is ready to be opened.</p> <p>If all items on the checklist are completed, request review and sign off of Open to Recruitment checklist by an Authorised Signatory, file in JRO Sponsor File. Continue to next steps.</p> <p>If there are outstanding items that require completing before trial site can be opened, advance to 6.3.4 prior to completing 6.3.2 and 6.3.3.</p>	SRA/RM
6.3.2	<p>On authorisation of the Open to Recruitment Checklist issue the Open to Recruitment Letter to the trial site.</p> <p>Send a copy of the Open to Recruitment Letter to the PI and trial site team including the Pharmacy/ IMP representative. File a copy in the TMF/ISF and JRO Sponsor File.</p>	SRA/RM
6.3.3	<p>On authorisation of the Open to Recruitment checklist (regulatory Green Light), IMP may be shipped to trial site. Follow trial specific Summary of Drug Arrangements/ IMP Management Plan for further details.</p> <p>Where the trial IMP is being supplied for a trial (rather than hospital stock) the supplier must be informed that the site is active; this will allow the shipment of IMP to the site.</p> <p>If IMP is shipped to site prior to completion of the OTR checklist (i.e for logistical reasons) then the site must be instructed to Quarantine the IMP until receipt of the Open to Recruitment letter.</p>	SRA/RM/
6.3.4	Complete Site initiation report along with outstanding actions.	SRA/RM

	<p>Request review and sign off by an Authorised Signatory.</p> <p>Send the site initiation report to site representatives and include pharmacy (and/or individual responsible for IMP). The timeline of sending the report to the site will be specified in the trial's monitoring plan. The site initiation report is to be filed in the TMF, ISF and JRO Sponsor File.</p> <p>Ensure the site staff and pharmacy/ IMP representative are aware of the outstanding items listed.</p>	
6.3.5	<p>Follow up with the site to ensure that action items for open to recruitment are completed.</p> <p>Once outstanding actions completed, document using the Initiation Visit report follow up template and proceed to 6.3.2 and 6.3.3, before continuing,</p>	SRA/RM
6.3.6	<p>Action items that are not required for Open to Recruitment should be followed up to completion within appropriate time frames and documented on the Initiation Visit report follow up template and carried over to the first monitoring visit report if not completed by this date.</p>	SRA/RM (Pharm)/ COA
6.3.7	<p>File all site initiation documents and relevant correspondence in the sponsor file and TMF including a copy of the current site delegation log.</p>	SRA/RM/ TC

7. REFERENCES

1. (SI 2004/1031) as amended

8. APPENDICES None

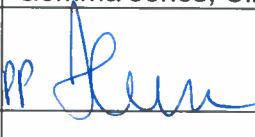
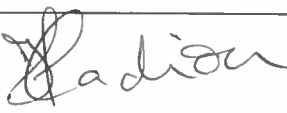
9. TEMPLATES/LOGS ASSOCIATED TO THIS SOP:

1	JRO Site Initiation Pack, 1. Staff Signature and Delegation of Tasks Log 2. Subject Screening Log 3. Subject Enrolment, Withdrawal and Study Completion Log 4. Subject Master Identification Code List 5. Log of Substantial and Non-Substantial Amendments (see SOP13) 6. Log of protocol Deviations, Violations, potential serious breaches/serious breaches and urgent safety measures(see SOP15) 7. Trial Monitoring Visit Log (see SOP19) 8. Individual Staff SOP and courses training log (see SOP01) a. Trial/Protocol Training Log
2	UK Regulations Compliance Form (Part 1)
3	Central Trial Responsibilities Log
4	Source Document List
5	Open to Recruitment Letter
6	Open to Recruitment Checklist
7	Site Initiation Visit Sign in sheet
8	Site Initiation template slides
9	Site Initiation Visit Report
10	Initiation Report Follow up template

10. SOP DISSEMINATION & TRAINING

SOPs relevant to the JRO only, will be distributed to the concerned JRO staff. Staff involved by the SOP will sign the SOP training log (Section 12. SOP TRAINING LOG) which is part of each SOP.

11. SIGNATURE PAGE

Author and Job Title:	Gemma Jones, Clinical Trials Operations Manager
Signature:	 (Clinical Trials Operations Manager)
Date: 04/08/17	
Authorised by: Name and Job Title	Helen Cadiou, Head of QA
Signature:	
Date: 04/08/17	

9. 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							
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	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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	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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	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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