The University of Nottingham UNITED KINGDOM · CHINA · MALAYSIA	**Sponsor Standard Operating Procedure**
Title:	**TRIAL INITIATION**
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1.v1.0 5th Nov 2008 2.v2.0 26th Nov 2010 3.v2.5 17th Nov 2014 v3.0 13th Jan 2017	1. Change 'Department of Health Research Governance Framework, 2005' to 'UK Policy Framework for Health and Social Care Research, 2017'.

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1. PURPOSE and SCOPE

PURPOSE:
To provide instruction for the setting up of a new clinical trial at a site, obtaining local approvals, site initiation and training of trial staff, the procedures and documentation required before trial commencement and subsequent record maintenance.

SCOPE:
Applicable to all clinical trials under the jurisdiction of the UK Policy Framework for Health and Social Care Research, 2017; and/or the Medicines for Human Use (Clinical Trials) Regulations, SI 2004, 1031.

2. NOTES

2.1 The processes outlined in this SOP are to occur after national ethics committee and regulatory approvals have been sought. No trial shall commence at any site* before these approvals are given. Training and appointment of staff in anticipation of the trial commencing may occur but no participants may be recruited and no trial interventions may be given at a particular site until the national and individual local approvals are in place, trial agreements have been signed, trial staff are appropriately trained and all resources to carry out the trial at the site are in place.

2.2 The Chief Investigator has overall responsibility for the conduct of the trial, ensuring trial staffs are aware of and their adherence to Sponsor Standard Operating Procedures, GCP and the maintenance of records. For multi-site trials the Principal Investigator at each site is delegated the responsibility for the local trial conduct and management at that site under supervision of the CI. This includes appointment of trial staff, formal delegation of their duties and training in Sponsor SOPs.

2.3 It is the responsibility of the Chief Investigator to provide initial training in aspects of the trial and its management to each participating site. The local PI will then be responsible for ensuring that newly appointed trial staff are given appropriate training to carry out their trial duties.

2.4 It is the responsibility of the Chief Investigator to ensure that local NHS Trust R&D or host organisation approval has been obtained in order to conduct the trial at their site. This will be according to locally defined procedures.

2.5 In conjunction with the CI's team it is the responsibility of the Principal Investigator to obtain local NHS Trust R&D or host organisation approvals in order to conduct the trial at their Site. This will be according to locally defined procedures.

2.6 For international trials the UK Chief Investigator (CI) shall consult with the appropriate international study committee (if any) or collaborators and agree a strategy for the provision of trial training and obtaining local approvals in order to carry out the trial.

* Site is defined as a participating organisation and sub-divisions thereof where recruitment of participants takes place and/or trial interventions are given.

3. CROSS REFERENCES

3.1	Ethics Application	SOP TA006
3.2	Sponsor / Chief Investigator agreement	Issued by RG Team
3.3	Sponsor / Participating Site / Principal Investigator non-commercial trial agreement http://workspace.nottingham.ac.uk/display/ResG/Research+Agreements	Master issued by RG Team

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3.4	(Attendance at) Investigator Training	RF1 TA008
3.5	Site Responsibility (Delegation) Log	RF2 TA008
3.6	SOP Compliance Form	RF3 TA008
3.7	Regulatory Green Light / Site approval Log	RF4 TA008
3.8	Document Control	SOPQA004
3.9	Trial Master File / Trial Site File: Set Up and Maintenance	SOP TA010
3.10	Trial Monitoring	SOP TA012
3.11	Delegated Trial Related Duties	Appendix A

4. PROCEDURE

The Chief Investigator shall:

4.1 In conjunction with the Sponsor's team, obtain HRA and REC approval (as per SOP TA006, Ethics Application) for the trial. These permissions include use of NHS sites, and facilities and these are listed as part of the application.
Where applicable and in conjunction with the Sponsor's team apply for regulatory permission as per SOP TA007, Regulatory Application.

4.1.1 Individual NHS Trust organisations must each give their Confirmation of Capacity and Capability and this is effectively their permission for the study to be conducted at their Site. See SOP TA006, Ethics Application
Where any site is not an NHS Trust permissions must be sought according to the requirement of the host organisation.

4.2 Agree to and sign the Sponsor/Chief Investigator clinical trial agreement between the CI and Sponsor. Two copies are required - one to be retained by the Sponsor and the other for retention in the Trial Master File.

4.3 For CTIMPs only:
Once all approvals and contracts are in place inform the Sponsor who will issue a 'Regulatory Green Light' email confirming that the trial may commence at the Site. Record on RF4 TA008, Regulatory Green Light / Site Approval Log. File this form along with the email in the TMF.

4.4 For the coordinating team:
Ensure that the following trial related duties are covered by delegation as appropriate to suitably qualified and experienced staff. Delegation is to be authorised by the CI and documented on RF2 TA008, Site Responsibility Log:

4.4.1 Document control and dissemination of trial related documents, including but not limited to the protocol, information sheets, consent forms, Case Report Forms, delegation log, subject recruitment log, Serious Adverse Event reporting form and any others as appropriate. Document control shall be according to SOP QA004.

4.4.2 The setting up and maintenance of a Trial Master File as per SOP TA010, Trial Master File / Trial Site File: Set Up and Maintenance.

4.4.3 Appropriate monitoring procedures are in place as per SOP TA012, Trial Monitoring, or according to the trial protocol.

4.4.4 For trials of Investigational Medical Products or Devices that procurement, storage, distribution, accounting and return of the product is managed according to the trial protocol and that appropriate records are retained. These must demonstrate a full audit trail of the product.

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For multi-site trials:

4.5 Confirm suitability of the facilities and appoint through agreement a Principal Investigator at each participating site.

Note: Suitability and availability of facilities is assessed as part of the HRA approval and R&D review at each site. The possibility of participating is usually determined before the ethics and regulatory applications.

4.6 Ensure that a non-commercial trial agreement between the PI, participating site and the Sponsor is disseminated to each site. Three original agreements are signed and two returned - one to the Sponsor and the other for retention in the Trial Master File, the third to be retained by the participating site.

4.7 Lead and instigate appropriate training in trial related procedures and responsibilities for their own and each participating site – see section 4.12.

The Principal Investigator shall:

4.8 Where required, obtain NHS Trust R&D or host organisation approvals for the trial at their site. The latter may be according to local procedures.
Where the site is not an NHS Trust permissions must be sought according to the requirement of that organisation.

4.9 Ensure that there are appropriate medical, paramedical and clerical/data management staff to support the trial. Ensure that there are proper physical location and facilities to undertake the trial. Sign (themselves) and ensure that officials of the host organisation agree to and sign the non-commercial trial agreement. Copies are retained as given in 4.5. A (photo)copy may also be retained for the Trial Site File.

4.10 Ensure that the following trial related duties are covered, by delegation as appropriate to suitably qualified and experienced staff. Delegation is to be authorised by the PI and documented on RF2 TA008, Site Responsibility (Delegation) Log. Use the example codes given in Appendix A to identify the duties on this form.

4.10.1 Local document control and dissemination of trial related documents, including but not limited to the protocol, information sheets, consent forms, Case Report Forms, delegation log, recruitment log, Serious Adverse Event reporting form and any others as appropriate. Document control shall be according to SOP QA004.

4.10.2 The setting up and maintenance of a Trial Site File as per SOP TA010, Trial Master File / Trial Site File: Set Up and Maintenance.

4.10.3 Appropriate local monitoring procedures are in place as per SOP TA012, Trial Monitoring, or according to the trial protocol.

4.10.4 For trials of Investigational Medical Products or Devices that local procurement, storage, distribution, accounting and return of the product is managed according to the trial protocol and that appropriate records are retained. These must demonstrate a full audit trail of the product.

4.11 Participate in any trial training initiated by the Chief Investigator and take subsequent responsibility for the ongoing training of all staffs participating within any of the trial's activities.

Trial Training / Site Initiation Visit

The **Chief Investigator** shall:

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4.12 Arrange for and deliver trial specific training to all staff likely to be involved in the trial. This must occur for the staff at both the Chief Investigator's site and all participating sites. The CI may delegate the responsibility for training at each participating site to the local Principal Investigator, after assuring that each PI is appropriately trained.

4.13 Training sessions should cover key aspects of the protocol and address logistical and resource implications for the trial. A signed record should be maintained of training sessions and attendees. Record local training sessions on RF1 TA008, Investigator Training form, and file in the Trial Master File.

4.13.1 Regular updates should occur to provide training for new members of staff and to give direction in the event of any amendments to the trial regime and / or documentation. All training sessions should be recorded on RF1 TA008, Investigator Training form.

4.13.2 Ensure that all personnel engaged in trial related duties are aware of, have read and understood and agree to abide by the Sponsor SOPs as relevant to their role in the trial. All staff to sign the SOP Compliance Form, RF3 TA008, and this retained in the Trial Master File.

The **Principal Investigator** shall:

4.14 Arrange and deliver trial specific training to all local staff likely to be involved in the trial. Training sessions should cover key aspects of the trial and local logistical arrangements. Particular attention should be given to the reporting of safety incidents.

4.14.1 Regular updates should occur to provide training for new members of staff and to give direction in the event of any amendments to the trial regime and / or documentation. All training sessions should be recorded on RF1 TA008, Investigator Training form.

4.14.2 Ensure that all personnel engaged in trial related duties are aware of, have read and understood and agree to abide by the Sponsor SOPs as relevant to their role in the trial. All staff to sign the SOP Compliance Form, RF3 TA008 and this retained in the Trial Site File.

5. FLOW CHART

Not applicable.

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Appendix A **Delegated Trial Related Duties**

The following trial related duties may be delegated and authorised as such by the Principal Investigator. Overall responsibility remains that of the PI and shall not be delegated but day-to-day practice, documentation and administration of the activity may be delegated to suitably qualified trial staffs.

A. Overall responsibility for study at Site and responsible for local financial management where appropriate B. Medical care and supervision of trial patients C. Obtain local ethics committee and R&D approvals and communication of subsequent amendments D. Ensuring all staff delegated to work on the trial are adequately informed as to the protocol requirements and trained in study procedures E. Delegation and authorisation of study related duties F. Act as document controller for trial related documents G. Set up and maintenance of Site File H. Implementation of subject recruitment strategy and obtaining informed consent I. Screening of potential subjects J. Obtaining consent and signing of consent forms (as appropriate to local policy & practice) K. Randomisation (allocation of trial intervention)	L. Completion and return of CRFs, including electronic entries M. Authorisation of CRFs N. Respond to data queries O. Prescription of and administration of IMP P. Be familiar with IMP safety data and disseminate to staff Q. Ensure IMP accountability R. Documentation of adverse events and timely SAE reporting S. Adhere to CI recommendations in response to SAEs T. Collection of trial related biological samples U. Initiation (training) of new trial personnel V. Prepare and be available for audit and inspections W. Archiving of trial data X. Responsibility for data monitoring. Y. Unblinding Others as locally applicable or trial specific (list): Z.

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