RD&I	NHS University Hospitals Plymouth NHS Trust **STANDARD OPERATING PROCEDURE**

DO NOT USE THIS SOP IN PRINTED FORM WITHOUT FIRST CHECKING IT IS THE LATEST VERSION

The definitive versions of all UHPNT RD&I Dept SOPs appear online, not in printed form, to ensure that up to date versions are used. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the Trust's website: https://www.plymouthhospitals.nhs.uk/researchers

Gaining and maintaining the authorisations for conducting research

SOP No: P3

Version No: 7.1

Effective Date: Jan 2019

Supersedes: Version 7.0, Sep 2017

Last Review Date: Jan 2019 Next review date: Jan 2022

AUTHORISED BY

Name: Chris Rollinson

Job Title: Research Governance Manager

Signature: 

Date: 21st Jan 2019

1 Purpose and Scope

The purpose of this document is to describe what processes researchers should follow in order to gain and maintain the authorisations for conducting research sponsored and/or hosted by University Hospitals Plymouth NHS Trust (UHPNT).

In scope: research hosted by, and/or sponsored by UHPNT.

Out of scope: audit and service evaluation/development which must be reviewed by the Clinical Audit Department.

Definitions

ARSAC	Administration of Radioactive Substances Advisory Committee
CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCP	Good Clinical Practice
HEI	Higher Education Institute
HRA	Health Research Authority
MHRA	Medicines and Healthcare products Regulatory Agency
REC	Research Ethics Committee
RD&I	Research, Development & Innovation
RO	Research Office
SOP	Standard Operating Procedure
UHPNT	University Hospitals Plymouth NHS Trust

2 Who should read this document?

All staff involved in setting up and conducting research e.g. Chief Investigators (CI), Principal Investigators, Research Nurses & Midwives, RD&I Managers and Clinical Trial Administrative staff

3 Procedure to Follow

3.1. Before the research begins

Research is usually defined as being designed and conducted to generate new generalizable knowledge. Researchers should ensure that the work they wish to carry out is research; the following link will support that decision making process: http://www.hra.nhs.uk/research-community/before-you-apply/determine-whether-your-

study-is-research/ . If the work is not research, and can be defined as audit or service evaluation/development, this SOP does not apply and you should contact the Trusts Clinical Audit Team (clinical.audit1@nhs.net [all audits and service evaluations must be registered with them]).

Under the Research Governance Framework all clinical research requires a sponsoring organisation and NHS permission. All NHS research will require approval from the Health Research Authority and will also normally require ethical approval. There may also be other authorisations required, depending on the type of research being conducted. There are national systems for gaining permissions/authorisations and websites describing those systems should be used as reference for those processes. The Research Office will provide advice and guidance in navigating these, where required.

3.1.1 Sponsorship

All clinical research requires a sponsor. For further information on UHPNT acting in this capacity please contact a member of the Research Office (RO). The regulations regarding clinical trials of investigational medicinal products differ slightly to other research, but the principles remain broadly similar. A sponsor is responsible for overseeing the conduct, management, monitoring and finances of research. For this reason it is essential that the sponsor agrees the final version of the protocol and associated documents before they are approved by the Health Research Authority (HRA), and any other applicable regulatory bodies i.e. The Medicines and Healthcare products Regulatory Agency (MHRA) for drug studies.

Researchers should usually approach their substantive employer to sponsor research. For student researchers, the university responsible for the academic course should be approached to sponsor the research in the first instance. For complex research, early discussions with the RO will help support the application for sponsorship. Researchers should contact the RO when considering application for sponsorship through the following routes: email: plh.tr.research&innovation@nhs.net or Int. tel. 39991

Researchers wishing to ask UHPNT to sponsor their research should complete the form 'Request for UHPNT to be Research Sponsor' which can be found on the RD&I intranet pages
http://staffnet.plymouth.nhs.uk/Departments/ResearchandDevelopment/Documents.aspx

3.1.2. Costing a study

Any applications for funding associated with the research must be discussed with the RD&I department to ensure costs are appropriately covered. It is important that the proposed research project is accurately costed, factoring in sponsorship and monitoring costs. These costs have to be agreed with the proposed sponsor and relevant NHS RD&I office. To ensure that the costings for the proposed research are an accurate

reflection of the true costs, please contact the RD&I Clinical Trials Finance Co-ordinator, for further assistance.

3.1.3. Amendments

Any changes to the protocol and associated documents must be agreed by the sponsor in advance of those changes being made. In conjunction with the study team, the sponsor will determine and document whether protocol amendments are substantial or minor, prior to authorisations being sought.

3.2 Approvals

Prior to study commencement it is the responsibility of the CI to ensure sponsorship, and relevant regulatory approvals are obtained, as well as Trust confirmation of capacity and capability (C&C). Regulatory approvals include Research Ethics Committee (REC), Medicines and Healthcare Products Regulatory Agency (MHRA) and Health Research Authority (HRA).

For multi-centre studies it is the responsibility of the CI and/or PI at each site to ensure that local NHS C&C is in place, and that the appropriate agreements (for multi-centre studies) are in place before recruitment begins.

3.2.1 HRA Approval

HRA approval is the process for applying for approvals for all project-based research in the NHS led from England. This means that:

- Research described by any of the IRAS filter question 2 categories, except those for “Research Tissue Bank” and “Research Database”, must apply for HRA Approval if the lead NHS RD&I Office is in England.
- HRA Approval will be used wherever the project involves NHS organisations in England.
- Where a project also involves NHS/HSC organisation(s) elsewhere in the UK (i.e. other than in England) the study will be supported through existing UK-wide compatibility systems, by which each country accepts the centralised assurances, as far as they apply, from national coordinating functions without unnecessary duplication.
- Projects that have previously sought or gained NHS Permission for participating NHS organisations in England, or applied for REC review, now come under HRA Approval.

Details of the approval procedures can be found at http://www.hra.nhs.uk/research-community/hra-approval-the-new-process-for-the-nhs-in-england/

3.2.2 NHS research ethics committee (REC) Opinion

The majority of research will require a positive REC opinion. However, some research carried out in the context of the NHS is exempt from the requirement for a NHS research

ethics committee opinion. See http://www.hra-decisiontools.org.uk/ethics/ to determine whether you need to apply for a NHS REC opinion. Different types of NHS RECs review different types of research proposals, and there are full details on the HRA website (given below).

Your research may require a different type of ethical review. These are provided by the Gene Therapy Advisory Committee, the Social Care Research Ethics Committee, the Ministry of Defence Research Ethics Committee and the Higher Education Institution (HEI) Research Ethics Committees.

For detailed information for researchers about REC approval and the types of NHS RECs, please see the HRA website, here: http://www.hra.nhs.uk/research-community/ .

3.2.3 Authorisation from the MHRA for CTIMPs (Clinical Trials of Investigational Medicinal Products)

CTIMPs (drug studies) require authorisation from the MHRA before they can proceed. Details about the procedure for application are available on the MHRA website (https://www.gov.uk/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk). For support and advice in preparing the application, which is done using IRAS, please liaise with the sponsor in the first instance (if the sponsor is the Trust then liaise with the RO).

If the protocol which has been approved by the MHRA is to be amended, it must be approved by the sponsor before submitting to the MHRA. Adequate notice must be given prior to submission of amendments in order for proper review to take place by the sponsor; this should be not less than one week.

All applications to the MHRA have to made *via* the Common European Submission Portal (CESP). The RO can either give researchers access to the portal or upload documents on their behalf.

3.2.4 Other authorisations

There may be other authorisations required prior to the start of the trial, depending on the type of research being carried out.

For research requiring CAG (Confidentiality Advisory Group) approval see: http://www.hra.nhs.uk/resources/confidentiality-advisory-group/

For research involving the administration of radiopharmaceuticals or sealed radioactive sources, the ARSAC notes for guidance should be used, found at: https://www.gov.uk/government/publications/arsac-notes-for-guidance .

If it is unclear which other authorisations are required consult with the sponsor in the first instance, and/or the Research Office for advice.

3.2.4. Trust Capacity and Capability Statement

A statement confirming that the Trust and /or NHS organisation will participate in a study once all the arrangements have been put in place. The statement confirms that the participating NHS site is able to provide the capacity and capability to deliver a study and HRA Approval is in place. This will be done in the Trust by the RD&I Office sending out an e-mail confirming capacity and capability. Once in receipt of this statement you may be begin your study, however, the actual date at which the sponsor/CI wishes to start research activities at the site should have already been agreed and may be dependent on a site initiation visit or similar.

3.3. After Trial commencement

There are a number of other events which require notification/discussion with the MHRA (and REC) after trial commencement, listed below.

3.3.1. Suspending your research and then restarting it.

If a CTIMP has to be suspended, the Sponsor, MHRA and REC must be notified. The CI or delegated representative within the research team must contact the sponsor immediately to discuss this, and ensure the appropriate steps are taken to inform the REC/MHRA of the halt within the defined timeframes (at the latest within 15 days). Details of the process to halt/suspend and restart a trial are found here: https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#suspend-or-terminate-a-trial . Documents found on the MHRA website should be used as a guide to inform the discussion between sponsor and research team about suspending the trial. All discussions must be documented.

For non CTIMP research, the Sponsor and REC must be notified. The CI or delegated representative within the research team must contact the sponsor immediately to discuss this, and ensure the appropriate steps are taken to inform the REC of the termination within the defined timeframes. For further details, http://www.hra.nhs.uk/resources/during-and-after-your-study/ . All discussions must be documented.

3.3.2. Terminating your research.

If a CTIMP has to be terminated, the Sponsor, MHRA and REC must be notified. The CI or delegated representative within the research team must contact the sponsor immediately to discuss this, and ensure the appropriate steps are taken to inform the REC/MHRA of the termination within the defined timeframes (at the latest within 15 days). For further details, see https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial . Documents found on the MHRA website should be used as a guide to inform the discussion between sponsor and research team about terminating the trial. All discussions must be documented.

For non CTIMP research, the Sponsor and REC must be notified. The CI or delegated representative within the research team must contact the sponsor immediately to discuss this, and ensure the appropriate steps are taken to inform the REC of the termination within the defined timeframes. For further details, http://www.hra.nhs.uk/resources/during-and-after-your-study/ . All discussions must be documented.

3.3.3. Urgent Safety Measures for a CTIMP

The CI or delegated representative within the research team must contact the Sponsor immediately to discuss this. For urgent safety issues which put a patient at risk during a Clinical Trial of an Investigational Medicinal Product (CTIMP, a drug study) the MHRA must be contact immediately, ideally within 24 hours (ideally the sponsor will do this). Appropriate RD&I contacts are the Research Governance Manager or the RO senior management team. If an appropriate sponsor representative cannot be contacted then the MHRA should be telephoned directly. All discussions must be documented.

The phone call must be followed up in writing within 3 days of the incident and with a substantial amendment. For further details, see https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#report-an-urgent-safety-issue.

If the study is multi-centre, all participating sites must be notified immediately of the urgent safety measure and the CI must inform each site of the subsequent action to be taken.

It is important to remember that a study can be suspended or terminated by the study sponsor in discussion with the CI or PI, without reference to the regulatory bodies, if there are serious concerns for the research participant's safety. The sponsor will notify the REC and the MHRA if a CTIMP (see UHPNT SOP T7 Urgent Safety measures).

3.3.4. Unexpected serious safety events in non-drug studies.

As above, a study can be suspended or terminated by the study sponsor in discussion with CI or PI, without reference to the regulatory bodies, if there are serious concerns for participant's safety. Again, the Sponsor will inform the Research Ethics Committee that gave the ethics opinion for the study (see UHPNT SOP T7 Urgent Safety measures).

3.2.5. Development Safety Update Reporting

Annual reports must be submitted to the MHRA in relation to the investigational medicinal product(s) in use. Please see UHPNT SOP T9_Periodic Reports to REC & MHRA for details of how this must be managed for our sponsored studies. Reports are due on the anniversaries of the date the MHRA authorisation was issued. Technical details for the submission can be found on the MHRA website: https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#submit-development-safety-update-reports-dsurs

3.3.6. Annual Safety and Progress reports

Annual safety and progress reports are required to be submitted to the ethics committee as a condition of the favourable opinion (see UHPNT SOP T9_Periodic Reports to REC & MHRA). Failure to do so can invalidate the favourable opinion. Both the progress and safety reports are due on the anniversaries of the date the REC favourable opinion was given. Further information on annual reporting requirements to RECs can be found: http://www.hra.nhs.uk/resources/during-and-after-your-study/progress-and-safety-reporting/

3.3.7. Serious Breaches

Serious Breaches must be notified to the MHRA, in accordance with their guidance, which can be found here: https://www.gov.uk/good-clinical-practice-for-clinical-trials . A serious breach is a breach of good clinical practice or a breach of the trial protocol that has the potential to impact on the safety of a participant or the integrity of the trial data. If you think that a serious breach has occurred, please contact the Sponsor as soon as possible. A Sponsor is required to report a serious breach to the MHRA within 7 days of being made aware of it. Where UHPNT is sponsor we will make a decision about whether the notified breach is in fact a serious breach and requires onward reporting. Serious breaches should also be notified to the HRA. Please also cross refer to SOP T6_Non compliance reporting.

3.3.8. End of trial

The MHRA (where applicable) and the REC must be notified that a trial has ended, within 90 days of the end of the trial, using a Declaration of End of Trial Form. Following that, an end of trial study report must be submitted to the MHRA (where applicable) and the REC within a year of the end of the study. See https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial and http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/ for details of both of these processes.

Where UHPNT is sponsor, each of these must be agreed by the RD&I department prior to submission. A minimum of two weeks prior to the submission deadline, the report/form must be submitted to the RO, so that the RO acting on behalf of the Trust (as Sponsor) can agree and authorise submission.

4 Document Ratification Process

The review period for this document is set as ***default of three*** years from the date it was last ratified, or earlier if developments within or external to the Trust indicate the need for a significant revision to the procedures described.

This document will be approved by the ***RD&I Manager or their Deputy***.

Non-significant amendments to this document may be made, under delegated authority from ***a senior RD&I manager***, by the nominated author. These must be ratified by the ***a senior RD&I manager***.

Significant reviews and revisions to this document will include a consultation with ***appropriately knowledgeable staff***. For non-significant amendments, informal consultation will be restricted to ***staff*** who are directly affected by the proposed changes.

Dissemination and implementation

4.1. Dissemination of this SOP

4.1.1. New SOPs and new versions of existing SOPs: The Research Governance Manager will be responsible for ensuring authorised SOPs are uploaded on the RD&I intranet site. Internal Trust Staff are expected to use the RD&I intranet site to access latest versions of SOPs and to check the website regularly for updates.

Notice of new or amended procedural documents that have undergone a major amendment will be given *via* the following routes:

- Inclusion in the Trust weekly e-bulletin Vital Signs
- Direct email to Trust Researchers and or teams

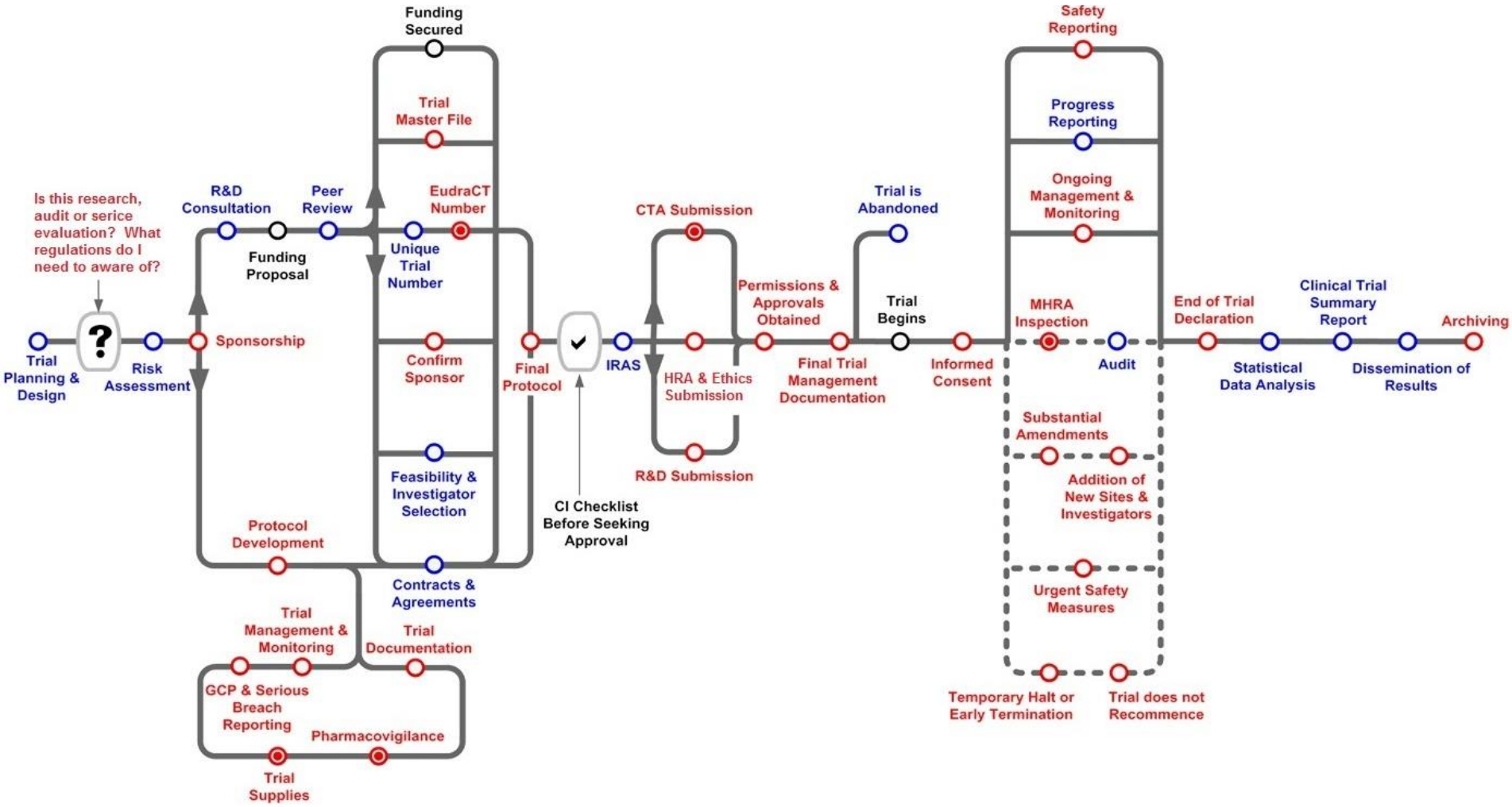
4.2. Training in this SOP

4.2.1. All staff whose activities are subject to this SOP should ensure that they read and understand the content of the SOP.

5 Reference material

- Clinical Trial & Medical Device Regulations.
- Research Governance Framework (2005).
- ICH GCP (E6) guideline and ICH E6(R2) Integrated Addendum.
- HRA & MHRA websites.

Appendix: Adapted Clinical Trial Tool kit Route map — Appendix 1



7 Amendment History

Version Number:	7.1
Date Of Amendment:	Jan 2019
Details Of Amendment:	Update Trust Logo and name.

Version Number:	7.0
Date Of Amendment:	Aug 2017
Details Of Amendment:	Update SOP to include details of HRA approval. SOP renamed. Update CT Toolkit route map of study procedure.

Version Number:	6.0
Date Of Amendment:	Jan 2015
Details Of Amendment:	Deletion of appendices to leave only two flow diagrams to illustrat the processes. Update Risk Assessment

Version Number:	5.0
Date Of Amendment:	Jan 2013
Details Of Amendment:	Re wording of the following: 6.2.2 Medium Risk Studies A review form and checklist will be provided (See Appendix 8.2). This reviewer will not be associated with the research proposed. Researchers will be given the opportunity to address any issues that arise from the review prior to the protocol being submitted to the RD&I Manager for final approval. The RD&I Manager will then

either consult with the peer reviewer for studies of lesser risk or meet with the RD&I Director to ensure any issues have been addressed. This will all be discussed with the researcher and encouragement and support with his/her research given.

Table 1 Medium risk studies approval given by……..RD&I Manager in consultation with peer reviewer and/or RD&I Director

---

Version Number:	4.1 (minor amendment)
Date Of Amendment:	Mar 2012
Details Of Amendment:	Cover page - Change of SOP location address.

Version Number:	4.0
Date Of Amendment:	September 2011
Details Of Amendment:	Changes in review processes.
