University Hospitals Plymouth NHS Trust

STANDARD OPERATING PROCEDURE

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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

Trial Registries (public access databases)

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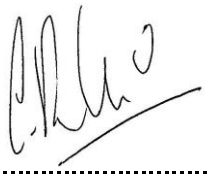
Signature: 

Date: 21st Jan 2019

1 Purpose and Scope

This Standard Operating Procedure (SOP) describes the procedures for registering a study on a clinical trials registry.

The Declaration of Helsinki states: “Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.”

In the UK it is a legal requirement for the registration of Clinical Trials of an Investigational Medicinal Product (CTIMP) on the European Union Drug Regulating Authorities Clinical Trials (EudraCT) database.

In September 2013, the requirement was extended by the Health Research Authority (HRA), as condition to gaining a favourable ethics opinion, to include all NHS interventional research projects, which are now also required to be registered in a publicly accessible trials registry prior to the initiation of a trial.

Furthermore, since 2004, the International Committee of Medical Journal Editors (ICMJE) has set up a policy enforcing the registration of CTIMPs in an accepted public trials registry in order to be considered for journal publication. This policy became mandatory in July 2005 and again stipulates that the registration must take place before the onset of patient enrollment.

The reason for introducing this policy is related to the publication bias phenomenon, i.e., compared to unsuccessful trials, successful trials have a much higher likelihood to be published in a scientific journal. Trial registries allow identification of all trials, including those never published. Free web-based access to information about ongoing clinical trials is regarded as important for other researchers but also for the public. The registries provide information of past research, whether negative or successful.

One of the consequences of this trial registry publication policy is that an investigator may have a manuscript rejected on the grounds that it has not been properly registered before the initiation of the trial. It is the investigator’s responsibility to check and adhere to the publication policy of the journal targeted for publication of their research.

The ICMJE definition of a Clinical Trial is ‘any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes’. The Research Ethics Committees (RECs) follow the definition in the Integrated Research Application System (IRAS). Any study that falls within the first four categories of filter question 2 requires registration on a public database, namely:

I. Clinical trial of an investigational medicinal product
II. Clinical investigation or other study of a medical device

III. Combined trial of an investigational medicinal product and an investigational medical device

IV. Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice

In scope: Interventional research sponsored by University Hospitals Plymouth NHS Trust (UHPNT).

Definitions

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
EudraCT	European Union Drug Regulating Authorities Clinical Trials (The European clinical trials database)
GCP	Good Clinical Practice
HRA	Health Research Authority
ICMJE	International Committee of Medical Journal Editors
IRAS	Integrated Research Application System
ISRCTN	International Standard Randomized Controlled Trial Number
MHRA	Medicines and Healthcare products Regulatory Agency
NIH	National Institutes of Health (US)
NIHR	National Institute of Health Research
NLM	National Library of Medicine (US)
UHPNT	University Hospitals Plymouth NHS Trust
RD&I	Research & Development
REC	Research Ethics Committee
RO	Research Office
SOP	Standard Operating Procedure
WHO	World Health Organisation

2 Who should read this document?

Chief Investigators (CI), Trial Co-ordinators/Managers, RD&I Office staff.

The study Sponsor and Chief Investigator (CI) are responsible for ensuring the study is register on an appropriate public access database prior to the commencement of the study.

3 Procedure to Follow

3.1. Registries

The ICMJE's requirements for an acceptable trial registry are that:

I. It must be electronically searchable
II. Accessible to the public at no charge
III. Any researcher must be able to register their project
IV. The registry must be not for profit
V. It must have in place means of ensuring the validity of the registration data

All study records in the following registries database are freely accessible and searchable and recognised by the ICMJE.

1. European Union Drug Regulating Authorities Clinical Trials (EudraCT) is the European clinical trials database of all CTIMPs with at least one site in the European Union commencing 1st May 2004 or later https://eudract.ema.europa.eu/index.html .
2. The International Standard Randomized Controlled Trial Number (ISRCTN) registry is a primary clinical trial registry recognised by World Health Organisation (WHO) and ICMJE that accepts all clinical research studies. National Institute of Health Research (NIHR) Portfolio-adopted studies are normally registered on the ISRCTN Register at http://isrctn.com .
3. ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world (currently the largest database in the World). The Web site is maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH) in United States of America https://clinicaltrials.gov/ .

3.2. Minimum Data Set

The WHO registration advisory group identified a minimal registration data set of 20 items; see Appendix 1. The ICMJE has supported the minimum data set and adopted it as its requirement.

In order for a trial to be considered for publication, all 20 fields in the WHO minimal data set must be completed. A registration data set will be deemed inadequate if it is missing fields or fields contain uninformative terminology. The online study registries will guide you through the information required, so you do not need to memorise the fields.

3.3. How to register

EudraCT Register

Before any functionality of EudraCT can be used for a given clinical trial, a EudraCT number must be created in order to provide a unique reference for a trial. From the login page, select Create> EudraCT Number and follow the screen instructions (https://eudract.ema.europa.eu/eudract-web/components/eudractnumber/eudractNumber.faces?showHome=false)

ISRCTN Register

You will need to create an account to register your trial https://www.isrctn.com/login . You will then be able to log into the Central Portfolio Management System and select 'Edit' to go into Edit mode. Then click ‘Apply for ISRCTN Number’ on the ‘Identifier & Status’ tab. This will take you to the ‘ISRCTN Registration’ page where you will be required to complete the extended minimum dataset before selecting ‘Apply for ISRCTN’ at the bottom of the page. N.B. The application form consists of four sections. The whole application must be completed in one session - it is not possible to save one section and return to it later.

ClinicalTrials.gov

University Hospitals Plymouth NHS Trust (UHPNT) has a Protocol Registration System (PRS) account with ClinicalTrials.gov. Investigators wishing to register studies on this database should contact the Research Governance Manager who is the local administrator for the site to arrange access.

3.4. Study Results

All registries require the uploading of study results within 12 months of the end of study declaration. For CTIMPs conducted in Europe this is a legal requirement.

You should refer to the registry websites for the format the results are required in. However, the "basic" results information required by Trial Registries includes the following:

- Participant Flow. A tabular summary of the progress of participants through each stage of a study, by study arm or comparison group. It includes the numbers of participants who started, completed, and dropped out of each period of the study based on the sequence in which interventions were assigned.

- Baseline Characteristics. A tabular summary of the data collected at the beginning of a study for all participants, by study arm or comparison group. These data include demographics, such as age and gender, and study-specific measures (for example, systolic blood pressure, prior antidepressant treatment).
- Outcome Measures and Statistical Analyses. A tabular summary of outcome measure values, by study arm or comparison group. It includes tables for each pre-specified Primary Outcome and Secondary Outcome and may also include other pre-specified outcomes, post hoc outcomes, and any appropriate statistical analyses.
- Adverse Events. A tabular summary of all anticipated and unanticipated serious adverse events and a tabular summary of anticipated and unanticipated other adverse events exceeding a specific frequency threshold. For each serious or other adverse event, the summary includes the adverse event term, affected organ system, number of participants at risk, and number of participants affected, by study arm or comparison group.

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 ***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

The European Clinical Trials Database (EudraCT)
https://eudract.ema.europa.eu/

European Commission; Guidance on posting research results
http://ec.europa.eu/health/files/eudralex/vol-10/2012_302-03/2012_302-03_en.pdf

The International Standard Randomized Controlled Trial Number (ISRCTN)
http://isrctn.com

ClinicalTrials.gov
https://clinicaltrials.gov/

Appendix: Minimal Registration Data Set Table — Appendix 1

Unique Trial Number	The unique trial number will be established be the primary registering entity (the registry).
Trial Registration Date	The date of registration will be established by the primary registering entity.
Secondary IDs	May be assigned by sponsors or other interested parties (there may be none).
Funding Source(s)	Name of the organisation(s) that provided funding for the study.
Primary Sponsor	The main entity responsible for performing the research.
Secondary Sponsor(s)	The secondary entities, if any, responsible for performing the research.
Responsible Contact Person	Public contact person for the trial, for patients interested in participating.
Research Contact Person	Person to contact for scientific inquiries about the trial.
Title of Study	Brief title chosen by the research group (can be omitted if the researchers wish).
Official Scientific Title of Study	This title must include the name of the intervention, the condition being studied, and the outcome (e.g., The International Study of Digoxin and Death from Congestive Heart Failure).
Research Ethics Review	Has the study at the time of registration received appropriate ethics committee approval (yes/no)? (It is assumed that all registered trials will be approved by an ethics board before commencing).
Condition	The medical condition being studied (e.g., asthma, myocardial infarction, depression).
Intervention(s)	A description of the study and comparison/control intervention(s) (For a drug or other product registered for public sale anywhere in the world, this is the generic name; for an unregistered drug the generic name or company serial number is acceptable). The duration of the intervention(s) must be specified.
Key Inclusion and Exclusion Criteria	Key patient characteristics that determine eligibility for participation in the study.
Study Type	Database should provide drop-down lists for selection. This would include choices for randomized vs. non-randomized, type of masking (e.g., double-blind, single-blind), type of controls (e.g., placebo, active), and group assignment, (e.g., parallel, crossover, factorial).
Anticipated Trial Start Date	Estimated enrolment date of the first participant.
Target Sample Size	The total numbers of subjects the investigators plan to enrol before closing the trial to new participants.
Recruitment Status	Is this information available (yes/no) (If yes, link to information).
Primary Outcome	The primary outcome that the study was designed to evaluate Description should include the time at which the outcome is measured (e.g., blood pressure at 12 months).
Key Secondary Outcome	The secondary outcomes specified in the protocol. Description should include time of measurement (e.g. creatinine clearance at 6 months).

***** *The data fields were specified at a meeting convened by the WHO in April 2004; the explanatory comments are largely from the ICMJE.*

6 Amendment History

Version Number:	1.1
Date Of Amendment:	Jan 2019
Details Of Amendment:	Update logo and Trust name