STANDARD OPERATING PROCEDURE 28

Transparency in Clinical Research Studies (Registering studies, dissemination of results and data sharing)

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Author:	Claire Daffern, Quality Assurance (QA) Manager, Warwick Clinical Trials Unit (WCTU)		
WCTU Reviewers:	Amy Smith, Clinical Trial Coordinator, WCTU Emily Long, Clinical Trial Monitor, WCTU		
Sponsor Reviewers:	Mathew Gane, Research Governance & QA Manager, Research & Impact Services (R&IS)		
WCTU approval:	Natalie Strickland, Head of Operations, WCTU		
Sponsor approval:	Carole Harris, Assistant Director, R&IS (Systems & Strategic Projects) & Head of Research Governance		
Review Lead:	WCTU QA Team		

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Revision Chronology:	Effective date:	Reason for change:
Version 4.0	08 November 2023	Biennial review: Updates to trial registration requirements.
Version 3.0	24 August 2021	Biennial review: Change to new format. Web links updated, minor amends to text.
Version 2.0	25 July 2019	Change of title, addition of information on ensuring research transparency throughout research study
Version 1.5	8 January 2019	Biennial review: Change to new format. Minor amends to text. Web links updated. Addition of requirement to keep registration data up to date.
Version 1.4	4 December 2015	Web links updated. Changes to instructions for using the ISRCTN website.
Version 1.3	25 November 2013	Addition of HRA requirement to register all trials as a condition of favourable ethical opinion.
Version 1.2	23 April 2012	Website links updated. Trial detail requirements for registration updated.
Version 1.1	21 April 2010	Addition of information on free ISRCTN registration for eligible NIHR CRN Portfolio trials.
Version 1.1	31 January 2008	Biennial review: Format change.
Version 1.0	March 2006	

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Transparency in Clinical Research Studies
(Registering studies, dissemination of results and data sharing)

1. Purpose and Scope

This Standard Operating Procedure (SOP) describes the requirement for ensuring transparency in clinical research and is applicable to all University of Warwick staff working on clinical research studies.

2. Definitions

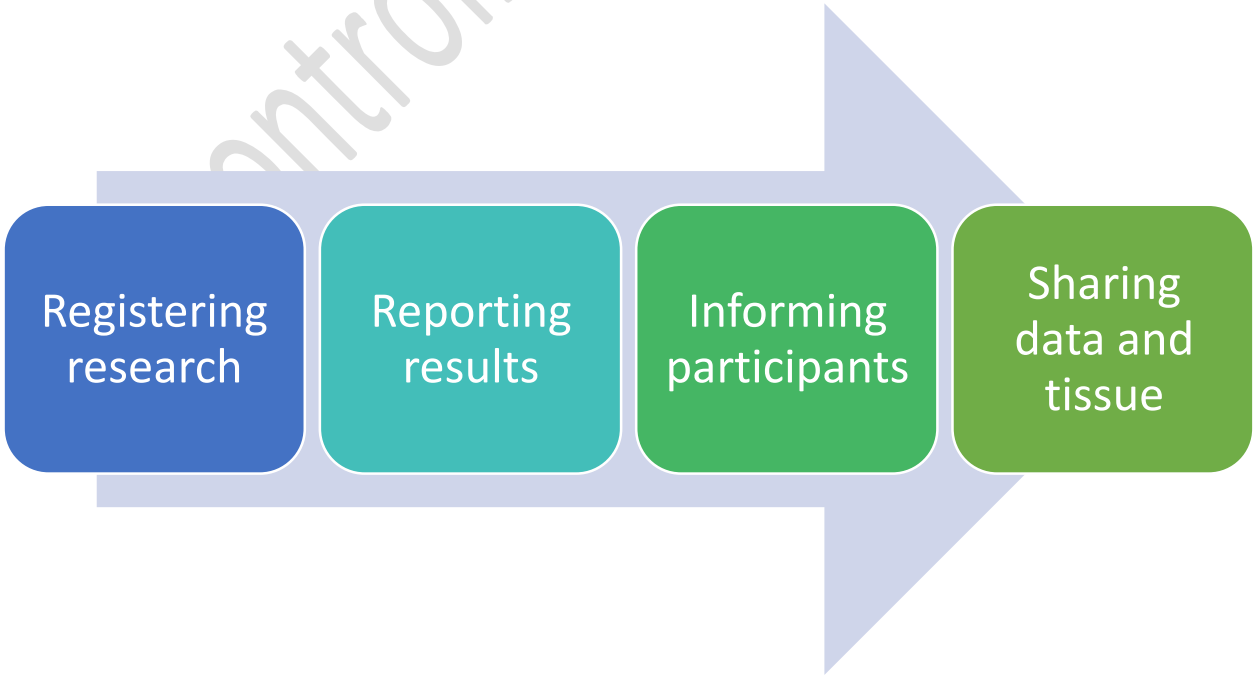
Research Transparency	Clinical research transparency means ensuring clinical trials are registered in a publicly accessible registry, participant data are made accessible for subsequent analyses, summary results are published within a set time upon trial completion (usually 12 months) and results are reported in full, irrespective of the study outcome.

3. Background

Research transparency is central to ethical research practice. Research studies should be registered, and the results made public, so that participants are protected from unnecessary research, and patients benefit from improved outcomes and care informed by high quality studies.

The Declaration of Helsinki of the World Medical Association states: "Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject". It is also government policy in the UK to promote registration of clinical trials.

Research transparency has four key elements:



When applying for approval for a study, it is expected that researchers have a plan for meeting ethical standards in research transparency. Research Ethics Committees (RECs) will only give a favourable opinion on the condition that the study is registered on a public database.

When research is carried out openly and transparently, everyone benefits:

- patients and the public can see what research is taking place and access clear information about the results
- patients, service users and carers know about research that is relevant to them, giving them the opportunity to join studies
- health professionals, commissioners, researchers, policy makers and funders can use research findings to make informed decisions.

The International Standard Registered Clinical/soCial sTudy Number (ISRCTN) register is the main database used by UK researchers.

All studies designed to assess the efficacy of healthcare interventions (both observational and interventional) are eligible to be registered with the ISRCTN scheme.

Registration of studies not involving IMPs on a publicly accessible database is not a legal requirement, but the study must be registered for written articles to be included in journals and publications belonging to the International Committee of Medical Journal Editors (ICMJE) group.

The ICMJE does not advocate one particular registry, but its member journals will require authors to record their trial/study in a registry that meets several criteria. For further details on publication requirements, refer to SOP 22 'Publication and Dissemination'.

The registry must be accessible to the public at no charge. It must be open to all prospective registrants and managed by a not-for-profit organisation. There must be a mechanism to ensure the validity of the registration data, and the registry should be electronically searchable.

Use of the ISRCTN register fulfils all the criteria for the ICJME.

Other acceptable registries for ICMJE are listed here: http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/

Alternatively, clinical research may be registered at http://www.clinicaltrials.gov (a register of world-wide studies where there are US sites or the IMP being used is from a US company).

For other types of research, registration is also encouraged wherever possible. It may be possible to register a study through an NHS organisation or a register run by a medical research charity or publish the study protocol through an open access publisher.

In general, registration is not expected for projects undertaken entirely for educational purposes below doctoral level.

4. Procedure

4.1 Responsibilities

Chief Investigator (CI) (or delegate)	• Registering study on a publicly accessible database • Ensuring the register is kept up to date • Publication of results within the required timelines

	• Ensuring results are made available to participants • Stating plans for future data sharing in the trial/study protocol
Sponsor	• Ensuring appropriate arrangements are in place

4.2 When?

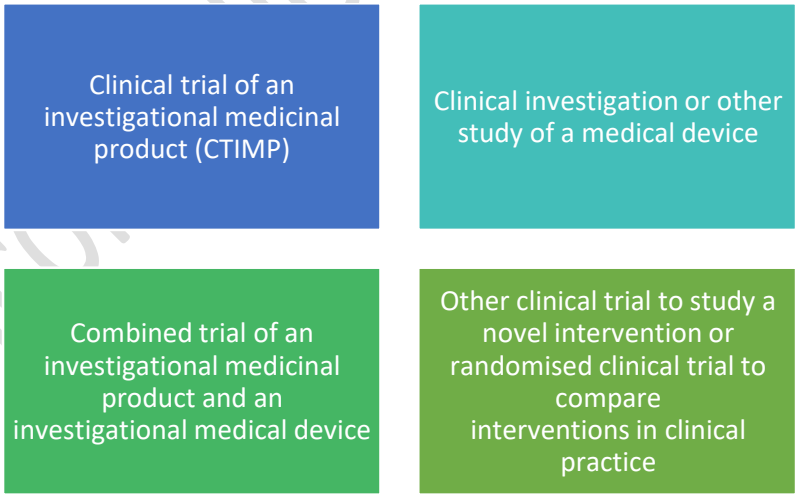
The UK Health Research Authority (HRA) expects registration of all clinical trials before the first participant is recruited, in line with researcher and sponsor duties as set out by the World Health Organisation (WHO), current Declaration of Helsinki and in the UK Framework for Health and Social Care.

The HRA has identified trial/study registration as a specific ethical expectation within the existing duties of the sponsor, and it has been a condition of the REC favourable opinion, and hence a requirement, to ensure clinical trials are registered.
Failure to do so within **6 weeks** of the recruitment of the first UK participant is therefore a breach of the favourable ethical opinion unless a request to defer registration has been granted by the HRA and is still valid.

The sponsor is responsible for ensuring appropriate arrangements are made for making information about the research publicly available before it starts. If a trial is already registered when completing the IRAS application, the registration number should be included. If registration occurs after submitting the IRAS application, email the REC with your registration number as soon as possible.

The ICJME states that they will only consider a trial/study for publication if it was registered before the enrolment of the first participant. Failure to do so may prevent publication in key journals, such as the BMJ, which actively implement this requirement.

The mandatory requirement to register will apply to clinical trials which fit the definition of at least one of the first four categories listed on the Integrated Research Application System (IRAS) question:



All registration records must be kept up to date during the conduct of the study and summary results must be uploaded within twelve months of the Notification of the End of the Study to the authorities.

4.3 How?

4.3.1 Study Registration

4.3.1.1 Non-CTIMPs

A study can be registered on the ISRCTN website via: http://www.isrctn.com/ where full guidance is provided. It is necessary to create an account in order to log in to the system. (If the trial has been adopted onto the National Institute of Health and Care Research (NIHR) Clinical Research Network (CRN) Portfolio of clinical trials, it is not necessary to create a registration as this will be done by the relevant CRN).

Guidance on the completion of the form is available from this website. The application can be saved at any point and returned to at a later time for completion.

Please note that all study registers are publicly accessible and there is a requirement to ensure the text used is in lay-persons terms, so it is easily understandable.

Contact details are required but note that Sponsors and CIs may request that telephone and email addresses are not displayed in their records. Details are required for administration purposes. Use of a study resource email account is acceptable rather than a personal account.

A fee is usually required to cover the costs of assigning each number. It is a one-off payment and in return the trial record will be hosted permanently in the ISRCTN Register. The ISRCTN website has details of the current rates.

However, the NIHR Clinical Research Network CRN Coordinating Centre has developed a process which enables free ISRCTN registration for all eligible new NIHR CRN Portfolio studies. For more information and to see if your trial is eligible for free registration see the NIHR CRN website.

Once confirmation that the study has been adopted onto the Portfolio, the CRN will contact the trial manager/CI with instructions on how to complete the ISRCTN information. The CI or their delegate must then complete the registration and file the email response to confirm the registration details. Trial registration details can be subsequently accessed via: https://www.isrctn.com/

Ongoing maintenance and updates to the information held in the register is required throughout the duration of the trial to ensure the details remain correct.

The ISRCTN website has instructions on the practicalities of how to update ISRCTN records.

4.3.1.2 Clinical Trials of Investigational Medicinal Products (CTIMPs)

From 1 January 2022 the Health Research Authority (HRA) will automatically register CTIMPs that are submitted through combined review in the new part of IRAS with the ISRCTN Registry as one of the steps to ensure research transparency.

If you wish to defer registration of a trial (for example if it is an adult phase I trial) contact the HRA at study.registration@hra.nhs.uk for advice.

The registry number, if available, should be included in section A.5. of the application form in IRAS when the application is being prepared. If this is not available at the time of application, email the details to the MHRA at clintrialhelpline@mhra.gov.uk with subject line “Clinical Trial Registration”

within six weeks of recruiting the first research participant. You should also let the REC know your registration number as soon as possible.

4.3.2 Making the results of research public

For CTIMPs other than adult phase I trials, it is mandatory that results are made publicly available within 12 months of study completion (as defined in the study protocol) in the public registry where the study was registered.

Post-Brexit, and prior to the HRA automatically registering all CTIMPs (section 4.3.1.2), researchers were obliged to register their trials onto EudraCT, the European wide trial registry to obtain a reference number to make an application to the MHRA. For UK trials where this was applicable, it is still expected that results are uploaded onto EudraCT.

Results do not need to be submitted to the MHRA as well, but a short confirmatory email needs to be submitted to CT.Submission@mhra.gov.uk to confirm that the results have been uploaded to EudraCT. The subject line of the email should be 'End of trial: result-related information: EudraCT XXXX-XXXXXX-XX'. No acknowledgement email will be sent by the MHRA. A copy of this email should be retained in the Study/Trial Master File.

It is a good practice requirement that results from non-CTIMPs are also made publicly available within 12 months of study completion. This applies no matter whether the results are positive, negative, neutral or inconclusive.

The ICMJE does not consider the posting of trial results in any registry as prior publication if results are limited to a brief (500 word) structured abstract or tables (to include trial participants enrolled, baseline characteristics, primary and secondary outcomes, and adverse events). Further details are available on the ICJME web site.

For studies managed by WCTU, the QA team will alert study teams three months prior to the reporting deadline (with additional prompts as required until the actions are completed). If results are not published in the required timelines, the issue will be escalated to the WCTU Director via the WCTU Governance Committee who will ensure appropriate actions are taken.

Summary results including key outcomes should be posted to the results section of the register(s) where the research project is registered.

Each trial should discuss the requirements for posting of results and delegate the activity to a member of the team. This would usually require input from the study statistician with support from the CI.

If the register used does not have a results section, the results should be posted on a free-to-access, publicly available, searchable institutional website of the sponsor, funder or chief investigator.

Where the main findings are also to be submitted for publication in a journal, this should be done within 12 months of study completion, to be published through an open-access mechanism in a peer-reviewed journal.

Key outcomes of CTIMPs and trial protocols must be made publicly available within 12 months of primary study completion.

4.3.3 Letting research participants know about the results of the research

Information about the findings of the research should be available, in a suitable format and timely manner, to those who took part in it, unless otherwise justified.

The HRA have developed guidance to explain how and what information should be provided to study participants, their legal representatives, consultees, relatives or close friends (as applicable), at the end of a study.

Plans to communicate findings to participants should be detailed in the participant information so participants will be aware of the likely timing of communication about findings so they know when and how to expect this information.

It is important to comply with UK GDPR and data protection legislation. To meet the transparency principle, an explanation should be provided to participants on how you will collect, store and use their contact details, and how and when you will communicate findings.

See SOP 7 'Participant Information and Consent' for further details.

4.3.4 Making data or tissue from studies available for further research.

It is a requirement that the data and any tissue collected for a research project are made accessible for further research with appropriate safeguards.

The ICMJE require the following as conditions of consideration for publication of a clinical trial report in member journals:

- Manuscripts submitted to ICMJE journals that report the results of clinical trials must contain a data sharing statement as described below.
- Clinical trials that begin enrolling participants on or after 1 January 2019 must include a data sharing plan in the trial's registration.
- The ICMJE's policy regarding trial registration is explained at www.icmje .org/recommendations/browse/publishing-and-editorial -issues/clinical-trial-registration.html.
- If the data sharing plan changes after registration this should be reflected in the statement submitted and published with the manuscript and updated in the registry record.
- Data sharing statements must indicate the following: whether individual deidentified participant data (including data dictionaries) will be shared; what data in particular will be shared; whether additional, related documents will be available (e.g., study protocol, statistical analysis plan, etc.); when the data will become available and for how long; by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism).

See SOP 22 'Publication and Dissemination' for more details on data sharing and G27 guidance on data sharing statements.

The UKCRC have created a comprehensive guidance document about making datasets available e.g., reviewing data requests, preparation of the data pack (including anonymisation), secure transfer methods etc.

Before the end of the original project, if the human tissue has continuing value you will need to do one of the following to make it lawful to store the tissue for further research use:

- apply for ethical approval of a new project,
- set up a research tissue bank and obtain a HTA licence,
- transfer the human tissue to a licensed establishment.

List of Abbreviations

CI	Chief Investigator
CRN	Clinical Research Network
CTIMP	Clinical Trial of an Investigational Medicinal Product
EMA	European Medicines Agency
HRA	Health Research Authority
ICMJE	International Committee of Medical Journal Editors
IMP	Investigational Medicinal Product
IRAS	Integrated Research Application System
ISRCTN	International Standard Registered Clinical/soCial sTudy Number
NIHR	National Institute for Health and Care Research
QA	Quality Assurance
R&IS	Research & Impact Services
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SOP	Standard Operating Procedure
WCTU	Warwick Clinical Trials Unit
WHO	World Health Organisation

Template Documents

Guidance on data sharing statements (G27)