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<h1>Adding Study Details to Public Databases</h1>	
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Version 6.0	18 Feb 2015	Scheduled Review
Version 7.0	25 Oct 2017	Annual Review
Version 8.0	12 June 2019	Administrative changes and clarifications to the process.
Version 9.0	19 March 2020	Clarifications to the process

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1. PURPOSE

This Standard Operating Procedure (SOP) describes the process for registering, adding study details, maintaining study records and reporting results on public access databases.

2. INTRODUCTION

The World Medical Association Declaration of Helsinki states that “Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject” and the International Committee of Medical Journal Editors (ICMJE) considers clinical trials for publication only if registered in an appropriate registry.

It is a best practice expectation that all research should be registered in a publicly accessible database. *However, for clinical trials, it is a condition of a favourable ethical opinion to do so.* Since September 2013, the registration of clinical trials has been a formal condition of NHS Research Ethics Committee (REC) approval, in line with researcher and sponsor duties as set out by the WHO, current Declaration of Helsinki and the Research Governance Framework. EU legislation also requires that clinical trials of investigational medicinal products (CTIMPs) are entered in a public register (with limited exemptions for healthy volunteer studies). Registration should occur before the first patient is recruited.

Clinical trial registration and reporting helps to prevent selective publication and selective reporting of research outcomes, to prevent unnecessary duplication of research effort, and to help patients and the public know what trials are planned or ongoing.

2.1 Definition of a Clinical Trial

‘Clinical trials’ are defined as all studies which fall into the first four categories of question two on the [Integrated Research Approval System \(IRAS\)](#) filter page. These are:

- Clinical trial of an investigational medicinal product
- Clinical investigation or other study of a medical device
- Combined trial of an investigational medicinal product and an Investigational medical device
- Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice.

Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration.

2.2 Applicable Studies

All clinical trials must be registered on a publicly accessible database, however there are a few options for which database to choose. Irrespective of the database selected, there are general guidelines that need to be followed, most importantly that the results need to be reported within 12 months from the submission of the end of study notification (or within 6 months for paediatric trials). **Results need to be reported within this timeframe regardless of the study outcomes and regardless of the publication status.**

The International Committee of Medical Journal Editors (ICMJE) requires and recommends that all medical journal editors require registration of clinical trials in a public trials registry at or before the time of first patient enrolment as a condition of consideration for publication. If your research falls into the definition of a clinical trial, you must make sure you register your study **BEFORE enrolment of the first patient**; otherwise you may not be able to publish.

The JRCO reverses the right not to issue sponsorship if a CI currently has outstanding final reporting to undertake after the 12-month deadline.

2.3 Recommended Registries

A 'public registry' is defined as any register on the [WHO list](#) of primary registries or the [ICMJE list](#) of registries.

There are a number of registries that meet the ICMJE criteria as an acceptable trial registry, but JRCO predominantly works with and tracks EudraCT and ClinicalTrials.gov.

- EudraCT (European Union Drug Regulating Authorities Clinical Trials) is the European Clinical Trials Database of all clinical trials of investigational medicinal products with at least one site in the European Union.
- ClinicalTrials.gov is a registry and results database of publicly and privately supported research studies conducted in the United States and around the world.

If a study is registered on EudraCT, it does not need to be registered on ClinicalTrials.gov as well, unless any of the following applies:

1. The study has a site in the USA.
2. The study is evaluating a drug, biological, or device product which is regulated by the United States Food and Drug Administration.
3. You would like to publish in a journal which requires that the trial has been registered on ClinicalTrials.gov prior to the enrolment of the first patient (the ICMJE stated that member journals will only consider a trial for publication if it has been registered before the enrolment of the first patient).

If you do decide to register on both databases, you will need to maintain both records and post results on both sites (which require different levels of information and have different reporting templates).

Reporting results on ClinicalTrials.gov or EudraCT does not count as prior publication, thus results need to be reported within the required time frame regardless of the outcome of the trial and regardless of potential planned or pending publications.

3. EUDRACT

EudraCT (European Union Drug Regulating Authorities Clinical Trials) is the European Clinical Trials Database of all clinical trials of investigational medicinal products with at least one site in the European Union.

A EudraCT number is required in order to apply to the Medicines and Healthcare products Regulatory Agency (MHRA) for a Clinical Trial Authorisation (CTA) and to apply for Research Ethics Committee (REC) approval of your clinical trial.

3.1 Registering on EudraCT

Application for EudraCT Number:

You need to email the Research Integrity Officer, Elizabeth Magnusson at e.magnusson@imperial.ac.uk providing the information requested below:

- Requestor's organisation name: **Imperial College** or **Imperial College Healthcare NHS Trust**
- Contact information:
- Sponsor's protocol code number:
- Is it anticipated that this EudraCT Number will be used for a Clinical Trial contained in a Paediatric Investigation Plan (PIP)?
- Is it anticipated that this EudraCT Number will be used for a Clinical Trial conducted in a third country (outside of the EU/EEA)?
 - If so, which Member States is it anticipated that the trial will be run?
 - If not, which EU/EEA member states do you expect the trial to run in?

You should receive a response within three working days. Once the EudraCT number has been created, it will be forwarded to you. When the EudraCT number is forwarded to you, you will also receive a template which shows you the type of information that will need to be collected in order to report the results. Reviewing this template and making a plan to record the needed information will help you to report results in the future. The template can also be found in appendix 6.1.

3.2 Maintaining your EudraCT Record

Entries on EudraCT are made up of information uploaded by the national competent authority (NCA) in EU member states. In the UK the competent authority is the MHRA. This means that if your trial is of a medicinal product covered by EU law, your trial will automatically be registered onto **EudraCT once you have submitted your application to the MHRA and it has been accepted.**

If you need to make changes to this information, including changing the study end dates or reporting a failure to recruit patients (so that a note can be added to the register entry to explain that no results should be expected), **it needs to be done through the national competent authority that originally authorized the trial.** Results information is the only information a researcher can add to EudraCT directly. For everything else the information must go through the national authority.

3.3 Reporting Results on EudraCT

Reporting results on EudraCT within one year of study completion (and within six months for paediatric trials) is a legal requirement.

Prior to the reporting deadline, the person responsible for uploading the study results should do the following:

1. Create an account on EudraCT (instructions for creating this account can be found in appendix 6.2)
2. Become a results user (instructions on becoming a results user can be found in appendix 6.3)

Once the account has been created and results user status has been received, you will need to email the Research Integrity Officer, Elizabeth Magnusson at e.magnusson@imperial.ac.uk requesting reporting access for your trial. Please include your EudraCT number and EudraCT account username in the email. Once the Research Integrity Officer has this information, they will designate you as the back-up user for the trial and you will be able to log in and post results. Once the results have been posted, it takes at least 14 days until the record becomes public.

The Research Integrity Officer will remain the primary user in order to help troubleshoot issues if needed.

In some circumstances it is possible to upload a summary of the results in document form, for example a journal article or the synopsis section of a Clinical Study Report. This is only an option for trials that ended on or before 21 July 2013. Trials ending after July 21, 2013 will need to fill in the full table of results information.

EudraCT has created guidance on posting results, please see appendix 6.4.

The JRCO has created a template of the type of information required for results reporting, which may be useful to review. Please see appendix 6.1 or request a copy to be sent to you via email.

Studies that fail to post results on time are monitored and tracked on a variety of publicly accessible websites, including those with links below. **Not posting study results on time has a negative effect on Imperial as a sponsor** and goes against Imperial's commitment to research best practice and transparency.

- <https://eu.trialstracker.net/sponsor/imperial-college-london>
- <https://eu.trialstracker.net/sponsor/imperial-college-healthcare-nhs-trust>
- <https://eu.trialstracker.net/sponsor/imperial-college-healthcare-nhs-trust-and-imperial-college-london>

4. CLINICALTRIALS.GOV

ClinicalTrials.gov is a publicly accessible database, which is free to register details of your clinical trials. It will accept any trial that meets the ICMJE definition of a clinical trial, regardless of where the trial is to take place. Before registering your study on ClinicalTrials.gov, please note the following conditions:

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1. If you want to register a study on ClinicalTrials.gov, you will need to post the study results on the website within one year after completion, regardless of the type of study and regardless of the outcome of the study. Once the study has been entered onto ClinicalTrials.gov it becomes part of the public domain and we need to ensure results are reported, in accordance with best practice and in light of increased awareness and scrutiny around transparency.
2. **Once your study has been registered, you must log into ClinicalTrials.gov and verify that the information on record is still accurate at least every 6 months.**
3. **If your study is registered on EudraCT, it does not need to be registered on ClinicalTrials.gov as well, unless any of the following applies:**
 - The study has a site in the USA.
 - The study is evaluating a drug, biological, or device product which is regulated by the United States Food and Drug Administration.
 - You would like to publish in a journal which requires that the trial have been registered on ClinicalTrials.gov prior to the enrolment of the first patient (the ICMJE stated that member journals will only consider a trial for publication if it has been registered before the enrolment of the first patient).
4. **If you do decide to register on ClinicalTrials.gov in addition to EudraCT, you will need to maintain both records and post results on both sites** (which require different levels of information and have different reporting templates).

4.1 Registering on ClinicalTrials.gov

The Joint Research Compliance Office is the designated 'Administrator' for registering users on ClinicalTrials.gov.

As Administrator, we will create a user account for you (upon request), giving you access to register trials on the system. We will check and release records for National Library of Medicine review once you have completed them properly. If you would like a user account, please email the Research Integrity Officer, Elizabeth Magnusson at e.magnusson@imperial.ac.uk requesting an account to register your trial.

- Once the Research Integrity Officer has created an account for you, your log in details will be sent to you automatically from ClinicalTrials.gov via email.

The Research Integrity Officer can serve as the contact point for the ClinicalTrials.gov team and will help resolve any questions associated with trial information.

4.2 Maintaining your ClinicalTrials.gov Record

Once your user account is created, you will be able to enter information about clinical trials online at register.clinicaltrials.gov.

To Log In:

- Go to <https://register.clinicaltrials.gov>.
- Complete the three fields on the login screen (as provided to you in the automatic email notification after your account was created):
 - Organisation: **ImperialC** or **ImperialNHSTrust**
 - Username: user login name
 - Password: (case-sensitive)

To Create a Record:

A record may be created at a single session or created and saved for completion later. To create a record during a single session:

- Follow [Create] from the Main Menu screen. Choose "New Record"
- To create a record and save for completion later, use [Quit] to stop data entry after step b (above), or any other successive screen. Then use [Save Protocol Record] to keep your data. The record will be saved for later.

Information must be correct and readily understood by members of the public. **You are required to update each clinical trial record every six months.**

Please update the "Record Verification" to that day's date every time you login or update your record.

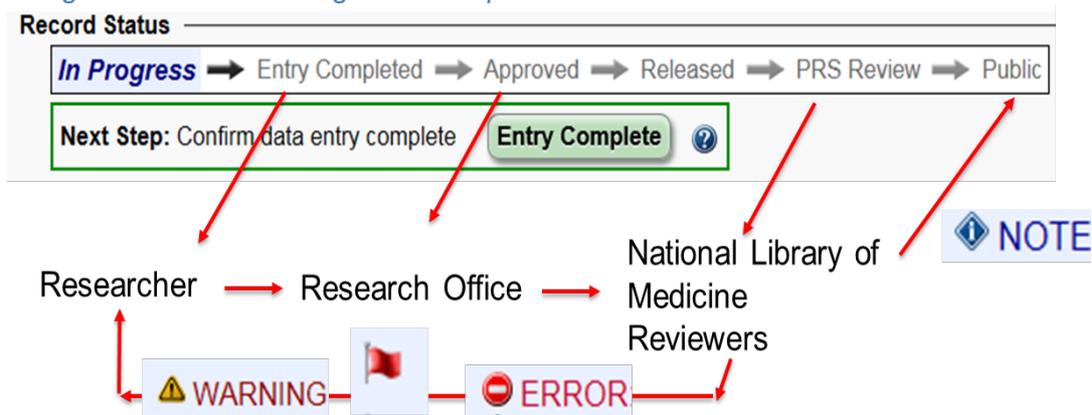
4.3 Reporting Results on ClinicalTrials.gov

These procedures are based on those provided by ClinicalTrials.gov. For more information on procedures and the database's data fields, please use the help section once you have logged into ClinicalTrials.gov website. Please see appendix 6.5 for general tips and other results reporting guidance.

Steps for Results Reporting:

- Review and make any necessary changes indicated by messages below the data fields on the Edit Protocol Record screen.
- After you have completed data entry for a record you need to submit the record. Once the record has been submitted, the JRCO Administrator will be notified by email that the record is ready for review. The JRCO Administrator will check the record and either confirm that it is ready to release to the ClinicalTrials.gov team for their review or it will contact the PI to make needed changes before it can be released.
- Once the record has been released to ClinicalTrials.gov for review it may take a few weeks before their team returns with comments. You will receive an automatic email once the ClinicalTrials.gov team have completed their review. You will need to log in and address any issues highlighted and correct the record. Once you have done this you will submit the record again and it will go to the JRCO Administrator who will release it back to the ClinicalTrials.gov team. If you have not made the needed corrections, the ClinicalTrials.gov team will not allow the record to be made public. **Errors are denoted by red flags in the entry. If there are any errors the entry will not be made public. You are responsible for correcting and replying to all comments and corrections from ClinicalTrials.gov reviewers until they are satisfied with the quality of your entry.**
- Once ClinicalTrials.gov confirms that all issues have been resolved the record should be published within two working days.

Figure 1: Reviewer stages and responsibilities



5. REFERENCES

- Health Research Authority: <https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/>
- International Committee of Medical Journal Editors: <http://www.icmje.org/>
- World Health Organisation: <https://www.who.int/ictrp/network/primary/en/>
- EudraCT website: <https://eudract.ema.europa.eu/>
- ClinicalTrials.gov: www.clinicaltrials.gov
- EU Trials Tracker: <https://eu.trialstracker.net>

6. APPENDICES

6.1 Reporting Results on ClinicalTrials.gov

Please see embedded template below:



EudraCT_Results_re
porting_template.xls

6.2 How to Register on EudraCT

Please see embedded PowerPoint presentation which explains how to register on EudraCT below:



EudraCT
registration guidanc

6.3 How to Become a Results User on EudraCT

Please see embedded PowerPoint presentation which explains how to become a EudraCT results user below:



EudraCT how to
become a results usi

6.4 Guidance on Reporting Results for EudraCT

Please see embedded Excel document with definitions of data fields in results reporting below:



EudraCT result
related data Diction.

Further guidance on individual steps can be found here:

https://eudract.ema.europa.eu/multimedia_tutorials.html

6.5 Reporting Results on ClinicalTrials.gov

Definitions: <https://prsinfo.clinicaltrials.gov/definitions.html>

General tips:

- Written language for lay public
- Brief Title – information on the participants, condition being evaluated, intervention, do not include study design terms as double blind or randomized!
- Official Title – study title
- Unique Protocol ID – DOCUMAS number
- Secondary ID – EudraCT if you have registered there

Study Status:

- Anticipated – planned number, Actual – final number
- Actual Study Completion Date is when the final participant has been examined or received an intervention for the purposes of final collection of data for the Primary Outcome Measure
- When a study is terminated, Study Status - Terminated (enrolling participants

has halted prematurely and will not resume), update Primary Completion Date and Study Completion Date to reflect when data collection ended, Change Type to Actual for both dates.

- Study Status - Withdrawn (study halted prematurely, prior to enrolment of first participant)
- If the study is suspended, then it is still a requirement to specify the Primary Completion day
- Update the Verification Date at least once per year

Oversight:

- Board affiliation - official name of the organization
- The report also includes the FDAAA column which indicates if a record is a probable Applicable Clinical Trial (pACT) or an Applicable Clinical Trial (ACT) that appears to be subject to the requirements of Section 801 of the Food and Drug Amendments Act (FDAAA 801) or 42 CFR Part 11.
- More information about FDA: <https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/fdas-role-clinicaltrials.gov-information>

Study Description:

- No references, complete sentences
- Brief summary: Study's hypothesis or purpose, 5000 characters
- Detailed Description: More technical information, 32000 characters

Study Conditions:

- Condition names should be taken from the National Library of Medicine's Medical Subject Headings (MeSH) vocabulary when possible
- Keywords - Help users to find studies in database

Study Design:

- Interventional studies are those in which participants are assigned prospectively to an intervention or interventions according to a protocol to evaluate the effect of the intervention(s) on biomedical or other health-related outcomes.
- In observational studies, the investigator does not assign participants to interventions, but instead observes (for example) patients who have been given interventions in the course of routine clinical care.
- Expanded Access records are limited to situations in which procedures are available for obtaining an experimental drug or device outside of a clinical trial.
- Study Phase is defined by the US FDA for trials of drug products (including biological products). Select "N/A" for trials that do not involve drugs or biological products.
- For active studies, set Enrolment Type to Anticipated and specify the target number of participants. Update the number as needed over the course of the study. Upon study completion, change Type to Actual and update the enrolment if necessary.
- For Bio specimen Description list all types of bio specimens to be retained, if any.
- Some observational studies have one Group/Cohort; case control studies typically have two.

Arms/Groups/Interventions:

- Arm (or Group/Cohort) might have a mix of interventions, name should be informative and specific – don't use Arm1, Intervention 1
- Arm Description, include the intervention name(s), dosage form, dose, frequency and duration
- Intervention = Drug, Device, Procedure, Dietary supplement
- For Intervention Name enter the generic name of a drug. Include brand names, serial numbers and code names in the Other Intervention Names list.

Outcome measures:

- Outcome Measure information should describe WHAT is to be measured and

- how ("assess by questionnaire, EEG"...), not why it is measured.
- Example: Number of Participants with...", "Concentration of...", "Rate of..."
 - Make each Outcome Measure Title unique and descriptive, indicating the metric to be used. Examples:
 - Change in Systolic Blood Pressure
 - Area under the plasma concentration versus time curve (AUC) of [DRUG NAME]
 - Peak Plasma Concentration (Cmax) of [DRUG NAME]
 - Time Frame is usually a single point in time at which a study participant is assessed for that measure, with these exceptions:
 - Change measures (e.g., "baseline and 8 weeks")
 - Time-to-Event measures (e.g., "up to 100 weeks," "from date of randomization until the date of first documented progression or date of death from any cause, whichever came first, up to 100 months")
 - Pharmacokinetic measures (e.g., "0, 1, 2, 3, 4, 6, 8, 24 hours post-dose")

Eligibility:

- For Age Limits, if there is no minimum or maximum age, select "N/A (No limit)" from the corresponding option menu.

Contacts/Locations:

- Study official – Principal Investigator

IPD Sharing Statement:

- If planning to share individual participant data (IPD), provide a brief description of the data to be shared, availability time frame and access criteria for obtaining the data. Provide a web address (URL) for more information, if applicable.

Study Document Submission:

- Each document must not have tracked changes and must include a cover page with below details:
 - Official title of the study
 - NCT number
 - Date of the document
- [To convert from PDF to ARCHIVE PDF \(https://www.pdf-archive.com/\)](https://www.pdf-archive.com/)
- An uploaded document can be deleted from a ClinicalTrials.gov record even after it has been made publicly available. However, previous versions of the document(s) will remain available in the ClinicalTrials.gov Archive site
- Steps:

To upload a single document for the first time:

- Click on the "+ New Document" button on the Document Section page.
- Select the appropriate document type.
- Enter the Document Date from the document cover page.
- Click on the "Browse..." button and locate the PDF/A file for upload.
- Click on the green "Upload" button.

To upload multiple documents of the same type (for example, separate ICFs for parent and child):

- Click on the "+ Advanced..." button, select document type and click the "Next" button.
- Enter subtitles to indicate the specific contents of each document.
- Enter the Document Date from the document cover page.
- Click on the "Browse..." button and locate the PDF/A file for upload.
- Click on the green "Upload" button.

To update and replace a previously uploaded document:

- Click on the "Update" button under the document to be updated.
- Enter a new Document Date from the document cover page.
- Click on the "Browse..." button to locate the updated PDF/A file to be uploaded.
- Click on the green "Upload" button.

To delete a study document:

- To delete a previously submitted document, click on the "x Delete" button for that document and confirm the operation when prompted. A previously submitted study document can be deleted from a record even after being made publicly available. However, the deleted document(s) will remain accessible on ClinicalTrials.gov, in the record's History of Changes.

Links:

- Study Results Submission
<https://clinicaltrials.gov/ct2/manage-recs/how-report#StepsForSubmittingResults>
https://prsinfo.clinicaltrials.gov/results_definitions.html
- Adverse Events: Video tutorial
<https://prsinfo.clinicaltrials.gov/webinars/module8/index.html>