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Adding Study Details to Public Databases

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Version 1.0	31 May 2007	Annual review
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Version 3.0	08 Feb 2010	Formation of Joint Research Compliance Office
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Version 5.0	03 Dec 2012	Annual review
Version 6.0	18 Feb 2015	Scheduled review
Version 7.0	25 Oct 2017	Annual review
Version 8.0	31 Jul 2019	Administrative changes and clarifications to the process
Version 9.0	19 March 2020	Clarifications to the process.
Version 10.0	19 Oct 2020	Scheduled review Template removed and administrative changes to SOP JRCO name change to RGIT.
Version 11.0	07 Jan 2021	Amendments due to leaving the EU from 1st January 2021
Version 12.0	01 Feb 2022	Amendments due to the partnership between the HRA and ISRCTN registry commencing from 1st January 2022
Version 13.0	02 Dec 2024	3-year SOP review

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1 PURPOSE

This standard operating procedure (SOP) provides an overview of the regulatory framework and processes for registering research studies, maintaining (as well as adding information in) study registry records, and reporting on public registries the study results of Imperial College (IC) and Imperial College Healthcare (ICH) NHS Trust studies.

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, f*or 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 (world health organisation), current declaration of Helsinki and the UK policy framework for health and social care. Please see that registration should occur before the first patient is recruited.

Clinical trial registration and reporting help 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

Although the WHO, ICMJE and the American national institute of health (ANIH) are all primary 'players' when it comes to defining interventional clinical trials internationally, the local clinical trial definitions only are reported for clinical research purposes in this document.

In the UK, the definition of clinical trial is detailed by the HRA in line with the above (see Appendix 8.1 for additional guidance). However, the IRAS framework is usually referred to on study application. That is, within the IRAS application system, 'clinical trials' are simply defined as those studies that fall under the first categories on question 2 of the IRAS form (including CWOW but not those purely for ionising radiation purposes). These categories can be taken as:

- Clinical trial of an investigational medicinal product.
- Clinical investigation or other study of a medical device.
- Combined trial: an investigational medicinal product & 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.

In addition, to help improve research transparency, the HRA publish the full research summaries they collect from the clinical trials they have approved, and whether these have been publicly registered.

2.2 Applicable Studies

All clinical trials must be registered on a publicly accessible database, and, locally, the IRAS framework defines definitions and responsibilities in line with the above expectations.

The study chief investigator (CI), as defined in the IRAS form, has a few options for which database to choose. However, irrespective of the database selected, there are general guidelines that need to be followed (and requirements that need to be conformed to), 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 from it 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 trial 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 participant; otherwise you may not be able to publish.

When registering your study, it is necessary to pre-specify all outcomes that will be measured (e.g. weight, blood pressure, survey measurements) on the public database chosen. Once the trial is complete, all pre-specified outcomes should be reported. Where reported outcomes differ from those pre-specified, this must be declared, along with an explanation of the timing and reason for the change. This ensures a fairer picture of the trial results. Also, the writing style to be used when reporting study results on clinical trial public registries needs to be simple: that is to say, it needs to conform to the relevant guidelines by the individual registries as well as those by the WHO and the EMA, (Cited on 27 Mar 2023).

N.B. For IC (Imperial College) **and ICH NHS Trust sponsored studies only, RGIT reserves the right not to issue sponsorship if a Chief Investigator still has outstanding record sections and/or final reporting to undertake after the 12-month deadline from the study completion.**

2.3 Recommended Registries

A ‘public registry’ is defined as any registry on the WHO list (Cited 23 June 2020) of primary registries or the ICMJE list (Cited 23 June 2020) of registries.

There are several registries that meet the ICMJE criteria as an acceptable trial registry, but the RGIT predominantly works with and tracks the ClinicalTrials.gov, ISRCTN and for CTIMPs running in the EU, EudraCT. Therefore, it is recommended that one of the registries mentioned above is used, depending on the situation. The appropriate registry for a study should be selected by the CI based on the study requirements and their own preferences.

Additionally, the funding body or the research ethics committee for a study may have their own requirements or preferences about which registry to use.

> **ClinicalTrials.gov** is a registry for publicly or privately supported research studies with sites in the United States, though it is often used also for local studies (with or without sites around the world).

ISRCTN is broadly used for any type of study as it accepts studies involving human subjects with outcome measures assessing a broad range of effects on human health and well-being (including studies in healthcare, social care, education, workplace safety and economic development).

CTIS and EudraCT make up the current EMA Registry: the use of CTIS is used for to CTIMP studies with at least one site in the European Union. Its use has been recently initiated (since 31, January 2023) for all new studies and ongoing studies transitioned. The EudraCT is only still used for third country CTIMP studies and CTIMP studies that are part of an international Paediatric Investigation Plan (PIP).

Please note that reporting results on ClinicalTrials.gov, ISRCTN or CTIS / EudraCT does not count as prior publication, that is, study results need to be reported within the required timeframe, regardless of the trial outcome and/or potential publications (either planned or pending).

Any researcher's intention to register a study on multiple registries should be first discussed with the RGIT team. Different registries require different levels of information and have different reporting-webpage structures, and a multiple registration would entail maintaining records and post results on all registries on which the study has been registered. **If a study is already registered on one database, it is unlikely that it would need to be registered on others, unless this is necessary to conform to different legislative frameworks.**

2.4 Clinical trials registered after January 1st, 2021

Starting from 1 January 2022, all CTIMPs that are submitted to the Health Research Authority (HRA) using the IRAS combined review service will be automatically registered on ISRCTN. The studies will be registered using data from the HRA's systems, therefore trialists and sponsors will not have to apply for registration separately. There is no charge to sponsors or researchers for automatic registration under an agreement between the HRA, the Department of Health and Social Care and the ISRCTN registry.
Imperial sponsored non-CTIMP clinical trials, beginning on or after January 1, 2022, now have the option to register their studies on either ISRCTN or Clinicaltrials.gov depending on study team preference and funding.
For CTIMPS, studies will be automatically registered with ISRCTN, however they will still need to get a EudraCT number. CTIMPS will need to follow the steps outlined below, in section 3, for acquiring a EudraCT number, but they will not report their results on EudraCT.

For CTIMPs, studies will be automatically registered with ISRCTN. However, if they also need to attain a EudraCT number, they will need to follow the steps outlined below, in section 3, for acquiring a EudraCT number.

2.5 Clinical trials registered before January 1st, 2021

For CTIMPS registered on EudraCT which began before 2021, you will still need to report results on EudraCT. After January 1, 2021, the MHRA will no longer have the ability to update information on EudraCT so you will need to email the MHRA when you have reported results on EudraCT by following the steps below:

- You must send a short confirmatory email to CT.Submission@mhra.gov.uk. The subject line of the email notification must state 'End of trial : result-related information: EudraCT XXXX-XXXXXX-XX' once the result-related information has been uploaded to the public register and provide a link. If your clinical trial is not on a public register, summary results should be submitted by email to

CT.Submission@mhra.gov.uk. An acknowledgement letter will not be sent for this submission.

- You should also submit a final report to the Research Ethics Committee within the same timeframe for reporting the summary of results.

3 CTIS and EUDRACT

As per above, the CTIS and EudraCT are currently the European clinical trial databases of all CTIMP studies with at least one site in the European Union. Since January 31st, 2023, the CTIS has been primarily used to share information and facilitate a regulated interaction between sponsors, European Union (EU) member states, European Economic Area (EEA) countries and the European Commission (EC). If an EudraCT number is required, the steps outlined in the below sections at 3.1 and 3.2 need to be followed. For CTIMP studies (with sites in the EU) that have begun before January 31st, 2023 and have an EudraCT number associated already, a record migration to CTIS would be necessary for result reporting purposes. That is, for studies that have been registered after January 1st, 2021, international registers such as the ISRCTN or ClinicalTrials.gov registries are generally recommended to ensure that the public is aware of any progress in the trial. However, if the trial has been registered on the EudraCT registry it will also have to be migrated to the CTIS system when updating results. More details on reporting results on CTIS can be found in sections 3.3 and 3.4.

3.1 Attaining a EudraCT Number

If a EudraCT number is required for your trial, and this form of registration does not take place within the CTIS system, please contact the RGIT CTIMP team for support and guidance.

3.2 Reporting Results and Maintaining EudraCT Records

Results reporting on EudraCT is for CTIMP studies only and it still is a legal requirement for CTIMP studies that began before 2021. Results reporting should be within 12 months of study completion (and within 6 months of study completion for paediatric trials). Uploading a summary of the results in a document form is only allowed under certain circumstances, such as when the trials ended on or before July 21st, 2013; all trials that ended after 21st, July 2013 need to complete a full result table.

A study needs to be registered following the assignment of an EudraCT number on the EudraCT registry as per section 3.1. That's is, the researcher has to register the trials by opening an EMA account and asking the QA Facilitator to become a results user (though, this may be done through different procedures, depending on whether the new user's email contact has been included in the trial agreement (CTA); more instructions on this are detailed in Appendix 8.2). Once the results user status has been achieved, an email to the QA Facilitator including the relevant EudraCT number and EMA account username needs to be sent out to request reporting-access (that is, a back-up user status for that trial). Access to the EudraCT registry to create the CTA and/or post results will be this way granted. Also, once all result-related information has been uploaded on to the record, a confirmatory email must be sent to the MHRA at CT.Submission@mhra.gov.uk as per section 2.5 of this SOP: it takes at least 14 days for the record to become public after the results have been posted. Additional guidance and definitions on posting results on EudraCT are available in Appendix 8.3.

With respect to the maintenance of CTIMP study records that were created prior to January 1st, 2021, as these EudraCT entries have been created/completed by the national competent authority (which in the UK is the MHRA)**, any changes to this information (including changing the study end dates or reporting a patient recruitment failure and data unavailable) need to be done through the national competent authority that originally authorized the trial.** Also, as explained in the previous section, since January 31st, 2023 all records may also need to be migrated to the CTIS system, where results/information can be added by the researcher. However, for certain trials and for the addressing of information related to certain changes, the researcher may still need to act through the national competent authority.

Studies that fail to post results on time are monitored and tracked on a variety of publicly accessible websites, including those 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.

- EU Trials Tracker for Imperial College London (Cited 23 June 2020)
- EU Trials Tracker for Imperial College Healthcare NHS Trust (Cited 23 June 2020)
- EU Trials Tracker for Imperial College London and Imperial College Healthcare NHS Trust (Cited 23 June 2020)

3.3 CTIS – Becoming a User

Since January 31st, 2023, if a CTIMP study has sites in the EU and needs to be registered on the CTIS registry, the researcher has to register the trial by opening an EMA account and asking the CTIMP Manager to become a user to access the CTIS registry.

3.4 CTIS Migration from EudraCT – The Timeline

The recent introduction of the Clinical Trial Information System (CTIS) has been to facilitate the exchange of information between the sponsors and the different European regulatory bodies. The CTIS registry is currently actively used by the sponsor to apply for (and record) clinical trials in up to 30 EEA countries and engage in communication with the regulatory bodies of the individual countries. Similarly, the individual national regulatory bodies can use CTIS for authorization, evaluation, oversight, assessing as well as monitoring of EU based clinical trials. Since its institution, sponsors have been given 3 years to migrate all clinical trials from the EudraCT registry to CTIS.

In order to enable the migration of study records from the EudraCT registry to the CTIS registry, it is necessary to initiate a CTIS account as detailed in section 3.3 and create an initial clinical trial application (CTA) marked as a 'transitional trial' in CTIS (and submit it). The new CTA must be such that the 'transitional trial' checkbox on the relevant webpage shows ticked: this will enable the user to use the 'transition trial' sub-section to make note of the transitional trial EudraCT number. Subsequently, the trial in question must be also accessed on the EudraCT registry so that the trial can be marked as a transitioned trial on the other registry too. More information on this can be found in Appendix 8.4.

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 the study on ClinicalTrials.gov, please note the following conditions:

1. **If the CI wants to register a study on ClinicalTrials.gov, they will need to post the study results on the website within one year of study completion, regardless of the outcomes of the study and regardless of the publication status**. Once the study has been entered onto ClinicalTrials.gov, it becomes part of the public domain and the CI needs to ensure that results are reported, in accordance with best practice and in light of increased awareness and scrutiny around transparency.
2. **Once the study has been registered, the CI must log into ClinicalTrials.gov and verify that the information on record is still accurate at least every 6 months.**
3. **If the 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.*
4. If the study is automatically registered with ISRCTN by the HRA, it does not need to be registered on ClinicalTrials.gov unless the CI needs to do so to meet requirements set by other organisations or regulatory bodies for that trial.
5. If the CI does decide to register on multiple registries including ClinicalTrials.gov, they will need to maintain all records and post results on all the sites (which require different levels of information and have different reporting templates).

4.1 Registering a study on CT.gov

The Research Governance and Integrity Team is the designated 'Administrator' for registering users on ClinicalTrials.gov.

As administrator, the RGIT will create a user account for the CI (upon request), giving access to register trials on the system. We will check and release records for ClinicalTrials.gov to review once the dedicated users have completed them properly. If any study team member would like a user account, they should send the QA Facilitator an email requesting an account to register the trial.

Once the QAF has created an account for the CI, the study-team representative's login details will be sent out automatically from ClinicalTrials.gov via email and the dedicated user will be able to register the trial.

4.2 Maintaining your ClinicalTrials.gov Record

Once the user account is created, they will be able to enter information about clinical trials online.

To Log In:

- Visit the PRS registration site (Cited 23 June 2020)
- 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** (depending on which organisation is sponsoring the study)

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 the members of the public. The users are required to update each clinical trial record every 6 months.

Please ensure to update the 'Record Verification' to that day's date every time the user logins or updates the record.

4.3 Reporting results & maintaining records on CT.gov

These procedures are based on those provided by ClinicalTrials.gov. For more information on procedures and on the database's data fields, please use the help section after logging into the ClinicalTrials.gov website. Please see appendix 8.5 for general tips and other results reporting guidance.

Steps for Results Reporting:

- Review and make any necessary changes indicated by the messages below the data fields on the Edit Protocol Record screen.
- After you have completed the data entry for a record you need to submit the record. Once the record has been submitted, the RGIT Administrator will be notified by email that the record is ready for review. The RGIT Administrator will check the record and either confirm that it is ready to release to the ClinicalTrials.gov team for their review or they will contact the study team to make the 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 RGIT Administrator who will release it back to the ClinicalTrials.gov team. If you have not made the needed corrections, the ClinicalTirals.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.**

Please note that the record needs to be marked as complete for you to be able to submit it to the RGIT administrator. Once ClinicalTrials.gov confirms that all issues have been resolved the record should be published within two working days.

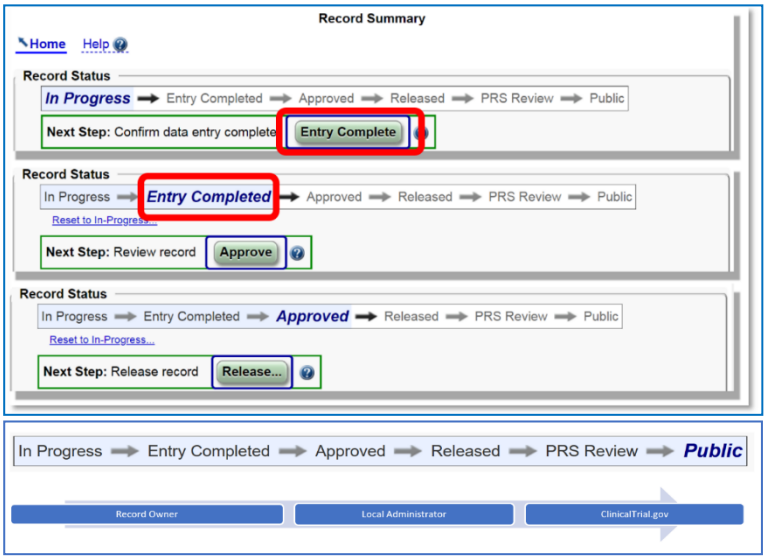

Figure 1 - Reviewer Stages & Responsibilities: CT.gov - ADDRESSING COMMON MAJOR ISSUES & SUBMITTING RESULTS.pdf

5 ISRCTN

ISRCTN is a publicly accessible clinical trial registry which accepts all research studies; both prospective and retrospective registrations are accepted. It is officially recognised by the World Health Organisation (WHO) and the International Committee of Medical Journal Editors (ICMJE) as a primary clinical trial registry.

On 20th October 2021, the Health Research Authority (HRA) announced their partnership with ISRCTN registry, leading to a service which will automatically register all clinical trials of investigational medical products (CTIMPs), beginning on or after 1st January 2022. There is no charge to sponsors or trialists for automatic registration under an agreement between the HRA, Department of Health and Social Care and the ISRCTN registry. This service is only applicable to registration of CTIMPs but the HRA has stated this service will be rolled out to other types of clinical trials in the future.

The partnership is part of the HRA's Make it Public strategy (Cited on 02 December 2024) and supports the UK's commitments to the G7 Therapeutics and Vaccines Clinical Trials Charter. (Cited 02 December 2024)

Studies registered on ISRCTN should have either a results publication or a basic results summary added within 12 months of the overall end date.

5.1 Registering CTIMP studies on ISRCTN

For CTIMPs that are automatically registered by the HRA, researchers and sponsors will not have to apply for registration separately. Registration will be free for CTIMPs using combined review, via the new part of IRAS, that are submitted on or after 1st January 2022. The HRA will not be registering any CTIMPs that are submitted prior to this date.

For studies that are automatically registered by the HRA, researchers and sponsors are not required to create an account under ISRCTN since the records are automatically created using the data submitted in the IRAS application (Cited on 26 November 2024). Upon

confirmation of a registration, the ISRCTN will generate a unique registration number which will be passed on to the HRA and shared with the trialists and sponsors.

5.2 Registering non-CTIMP studies on ISRCTN

If the CI would like to register a non-CTIMP clinical trial on ISRCTN, please note that this will be subjected to a registration fee + *tax when applicable.* Since these studies will also not be automatically registered by the HRA, the dedicated study team member will have to create themselves an account on the ISRCTN website which will give them access to register their trials on the system[1].

To register a new study:

- Go to isrctn.com and click on 'Register your study' (Cited on 26 November 2024).
- Create an account or go to the 'login section'.
- After login, the application has four stages: trial details, contacts, sponsors/funders, payment agreement.
- Navigate through the sections by clicking on the circles and click on 'Save' to save your progress.
- Complete all the required fields and once all the sections are complete, click on 'Submit'.

Once the application has been received, a member of the editorial team at ISRCTN will contact the user by email within 1 working day for any supporting information/clarification needed. If the study details are in line with their editorial policies and the payment has been successfully processed, the study will be assigned a registration number, and the record will be immediately added to the registry.

Please be aware that a study will permanently remain on the registry and cannot be deleted once it has been registered on the ISRCTN registry. If two or more ISRCTN records have been assigned to the same trial, the ISRCTN editorial team should be notified immediately.

5.3 Maintaining an ISRCTN study record

For CTIMPs beginning on or after 1 January 2022, entries will be made up of information submitted to IRAS via the combined review service. Any amendments in IRAS will be automatically fed into the ISRCTN update process so the Principal Investigator and/or the sponsor will not have to update both systems.

If the CI would like to make any other changes to a record that is not automatically fed into the system by IRAS, please follow the instructions below:

- Go to isrctn.com and click on 'Update your record' (Cited on 26 November 2024).
- This will lead to an online form where you can quote the ISRCTN number of the record you wish to update; there is no need to log in.
- Edit any fields in the study record that you wish to update.
- Click on 'Choose files' to upload any related files e.g., study protocol document, participant information sheet.
- Click on 'Submit' once you have confirmed all the changes needed.
- Alternatively, you can also contact the ISRCTN via email requesting any changes that you would like to update on your record.

[1] Please note that some studies from the NIHR portfolio may be entitled to free ISRCTN registration.

A member of the editorial team at ISRCTN will then review and record the changes and contact the study contact for confirmation via email. A link to the record will also be provided to ensure that the study team is happy with the changes made. The record will usually be updated within two working days; however, this may vary depending on the size of the update.

Once a draft record has been submitted, only ISRCTN editors have administrative access to modify or update the record. Please be aware that the ISRCTN editorial team cannot remove information from a record, or overwrite previous information, and is only any information that has been added is enclosed with a date stamp detailing the date on which the record has been changed.

When updating non-CTIMP studies, the researcher may wish to rely on the fact that ISRCTN sends automated reminders to the study record owners to prompt record updates at predefined key study-life-cycle milestones (e.g., recruitment start/end, completion, results overdue) to update a record, to report any study amendments (such as delays to the trials) or to update the funder and sponsor details (if for example the previous funding has run out).

If a registry record has not had either a results publication or a basic results summary added within 12 months of the overall end date of the study, the editorial team at ISRCTN will be in touch with the sponsor of the study.

5.4 Reporting results on ISRCTN

All study records on ISRCTN must be updated to include information about the results within 12 months of study completion.

The steps for results reporting on ISRCTN are:

- Go to isrctn.com and click on ‘Report your results’ and complete all the required fields (Cited on 26 November 2024).
- Click on ’Choose File’ to upload basic results. If you have already published your study, please also provide a link to the publication on PubMed or as a DOI (Digital Object Identifier).
- The basic results should consist of four sections: Flow, Baseline Characteristics, Outcome Measures and Adverse Events.
- Once you have finished completing all the four sections, click on ‘Submit’.

A member of the editorial team at ISRCTN will update the study record with the results and contact the user by email to confirm.

If you have not published your study or are not planning to publish, you can upload only the basic results summary to your record. Please find below the checklist of items that are required to upload the basic results summary to the record:

- **Participant Flow:** A CONSORT flow diagram showing participants involved at each stage of the study (primarily enrolment, intervention allocation, follow-up and data analysis.
- **Baseline Characteristics:** A tabular summary of the baseline demographic and clinical characteristics of the participants.
- **Outcome Measures:** A tabular summary of the outcome measures listed in your ISRCTN record. If possible, it is recommended that you present the primary outcome measures separate to the secondary outcome measures, both in the tabular format.

- **Adverse Events:** A tabular summary of all the anticipated and unanticipated serious adverse events (life-threatening) and anticipated and unanticipated non-serious adverse events (non-life threatening) with a description of the adverse event and the total number of participants affected. If there were no adverse events associated with your trial, please include this statement instead: 'There were no adverse events associated with this trial'.

The ISRCTN has also provided examples of basic results summaries, which can be accessed in Appendix 8.5.

6 DEFERRING A REGISTRATION

Please note that, any intention to defer a registration should be in line with the related policy/procedure as published on the HRA website and emailed by the CI/Study Team to the HRA at study.registration@hra.nhs.uk by copying the RGIT QAF in any of the related correspondence.

7 REFERENCES

ISCTR (International Standards for Clinical Trial Registries) WHO, 2018
(Cited on 16 Mar 2023).

WHO: International Clinical Trials Registry Platform (ICTRP)
(Cited on 15 Mar 2023).

Primary Clinical Registries: WHO list & ICMJE list
(Cited on 16 Mar 2023).

Health Research Authority: Research Registration and Research Project Identifiers
(Cited on 15 Mar 2023).

Joint Letter by the European Commission of the EMA
(Cited on 27 Mar 2023).

IRAS: Integrated Research Approval System
(Cited on 16 Mar 2023)

International Committee of Medical Journal Editors: Clinical Trial Registration
(Cited on 15 Mar 2023).

Health Research Authority: transparency in health & social care research
(Cited on 15 Mar 2023).

Health Research Authority: clinical trial registration requirements
(Cited on 07 Jun 2023).

Department of Health & Social Care: G7 Policy Paper - Clinical Trials Charter
(Cited on 15 Mar 2023).

EudraCT Registry (European Union Drug Regulating Authorities Clinical Trials)
(Cited on 15 Mar 2023).

CTIS Clinical Trials Information System (Cited on 25 Jul 2024).

EU Trials Tracker
(Cited on 15 Mar 2023).

ClinicalTrials.gov Registry
(Cited on 15 Mar 2023).

ISRCTN Registry (International Standard Randomised Controlled Trial Number)
(Cited on 15 Mar 2023).

ISRCTN Account Webpage
(Cited on 24 Mar 2023).

Health Research Authority: HRA data sharing criteria with ISRCTN Registry
(Cited on 22 Mar 2023).

Guidelines for Reporting Medical Research on Clinical Registries by the WHO and the EMA,
(Cited on 27 Mar 2023).

Instructions on results reporting: the EMA registry (Cited on 12 Jul 2023).

American National Institute of Health,
(Cited on 22 Mar 2023).

8 APPENDICES

The following appendices list the additional advice associated with this SOP, a copy of which can also be found at the SOP, Associated Documents & Templates webpage
(Cited on 24 Mar 2023).

8.1 Additional guidance on defining a clinical trial:

'A 'clinical trial' (Cited on 07 Jun 2023) is defined as a clinical trial of an investigational medicinal product, clinical investigation or other study of a medical device, combined trial of an investigational medicinal product and medical device, any other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice, such as trials of surgical interventions radiotherapy, imaging investigations, mental health investigations or therapies, physiological investigations trials of products not defined as medicines or medical devices, that is, including nutritional, complementary or alternative therapies'.

8.2 Additional guidance on registering and becoming a result user on EudraCT

The European Medicines Agency (EMA) has created a PowerPoint presentation explaining how to register and/or become a result user to report results on EudraCT (Cited on 20 Mar 2023).

8.3 Additional guidance on reporting results on EudraCT

The EMA has created an Excel spreadsheet, called the Data Dictionary, with results related data definitions which can be found at the relevant webpage links of the EMA website, where tutorials about results reporting can also be found (Cited on 20 Mar 2023).

8.4 Additional guidance on migrating study records to CTIS

More information on the timeline and procedure to migrate study records from the EudraCT website to the CTIS website can be found on the EMA informative-leaflet-1, EMA informative-leafleat-2 and EMA informative-leaflet-3 (Cited on 25 Jul 2024).

8.5 Additional guidance on reporting results on ClinicalTrials.gov

General advice:

- *Written language: use language for the lay public.*
- *Brief Title: comprises information on the participants, condition evaluated, and intervention; do not include study design terms (e.g., double blind/randomized).*
- *Official Title: the study title as per protocol.*
- *Unique Protocol ID: the Local Reference Number or Edge number.*
- *Secondary ID: the EudraCT if it is registered also on that.*
- *Study data: data that can be also uploaded as XML-formatted data directly from the Sponsor Organization's computer system.*

Oversight advice:

- *Board affiliation: refers to the official name of the organisation.*
- *The FDAAA acronym: indicates whether a record is a probable applicable clinical trial (pACT) or an applicable clinical trial (ACT): that is, subject to the requirements of Food and Drug Administration Act Section 801 (FDAAA 801) or 42 CFR Part 11.*
- *The FDAAA role in shaping CT.gov definitions: this is better explained on the FDA's website (Cited on 24 Mar 2023).*
- *For ACTs, reporting-timeline extension certifications/requests may be submitted via the protocol registration system (PRS): for each provision 30-day extension from the earliest event comprised in it are allowed, with a maximum result submission delay of 2 years after the certification submission date.*

Advice on the study status:

- *Anticipated: planned number.*
- *Actual: final number.*
- *Actual study completion date: that is, when the final participant has been examined or received an intervention for the primary-outcome-measure final data collection.*
- *Study status – Terminated: enrolling has halted prematurely and will not resume, that is, the primary/study completion dates become the data collection end-dates and the date type becomes actual for both dates.*
- *Study status – Withdrawn: the study has halted prematurely (that is, prior to the enrolment of the first participant).*
- *Study status – Suspended: in so a case, it is still a requirement to specify the primary completion date.*
- *Record verification date: this should be updated at least every 12 months.*

Advice on the study description:

- *No references: means use only complete sentences.*
- *Brief summary (study hypothesis or purpose): means 5000 characters.*
- *Detailed description (more technical information): means 32000 characters.*

Advice on the study conditions:

- *Condition names should be taken from the Medical Subject Headings (MeSH) vocabulary when possible (Cited on 24 Mar 2023).*
- *Keywords must be used to help the users to find studies in the registry.*

Advice on the study design:

- *Interventional studies are those in which participants are assigned prospectively to one or more interventions as per protocol to evaluate their effect on biomedical (or other health-related) outcomes.*
- *Observational studies are studies where participants are not assigned to interventions, but are only observed (for example, after that they have been given interventions in routine clinical care).*
- *Expanded access records are records for which procedures are in place to obtain an experimental drug or device outside of the clinical trial (that is 'provide information about investigational products/devices that are made available through expanded access for patients who do not qualify for enrolment in a clinical trial').*
- *A study phase is defined (as per US FDA definition) only for trials of drug products (including biological products). 'N/A' should be selected for trials that do not involve drugs and/or biological products.*
- *For active studies, the enrolment type should be set to anticipated and the target number of participants should be specified: that is, the number of participants should be amended over the course of the study and both this number and the enrolment type should be both set to the actual number after study completion.*
- *The bio-specimen description list should comprise all bio-specimen types to be retained, if any.*
- *Some observational studies may have one group (cohort studies) while case-control studies generally have two groups (the terms arm, cohort and group are used interchangeably).*

Advice on the study arms/groups/interventions:

- *Arm (or group/cohort): one arm might present concurrent interventions, so its name should be informative/specific (avoid using terms such as Arm1/Intervention1).*
- *Arm description: this should list the intervention name(s), dosage form, dose, frequency/duration.*
- *Intervention: it may mean drug, device, procedure or dietary supplement.*
- *Intervention name: if this is a drug, it refers the generic name of a drug (that is, brand names, serial numbers and code names should be annotated in the other intervention names list).*

Advice on the study outcome measures:

- *Outcome measures: this information should describe what is measured (for example, number of participants with…, concentration/rate of..) and how this is measured (for example by questionnaire, EEG…); it should not detail why it is measured.*
- *The outcome measure title should be unique and descriptive and detail the metric used (for example, change in systolic blood pressure, area under the plasma concentration vs time curve of …, AUC, plasma concentration peak of …, Cmax).*
- *The timeframe is generally the time point at which a study participant is assessed for a certain measure, with these exceptions: the change measures (e.g., baseline/8-weeks), time-to-event measures (e.g., 'up to 100 weeks', or '..from randomization date until the first-documented progression-date or death-date from any cause, whichever occurred first, up to 100 months.'), pharmacokinetic measures (e.g., X hours post-dose).*
- *If a study has several secondary or other pre-specified outcome measures, each outcome should be specified separately.*
- *If a given outcome is assessed with different units of measure, it must be presented in separate outcome measures.*
- *If a given outcome is assessed with the same units of measure at different time points should show unique outcome measures for each time point.*

Advice on the study eligibility criteria:

- *Eligibility criteria such as age limit: if there is no minimum/maximum age limit, 'N/A'*

should be selected.

Advice on the contacts/locations:

- *Study Officials: must be the principal investigator.*
- *Central Contact Person: must be the chief investigator.*
- *Central Contact Backup: there is no imposed restriction on this.*

Advice on the IPD sharing statement:

- *Where there is a plan to share individual participant data (IPD), a brief description of the data to be shared (including data availability timeframe and access criteria to data) should be provided, together with a web address (URL) for additional information, if applicable.*

Advice on the study document submission:

- *Each document enclosed must be in pdf format and it must include a cover page with details as follows: the study official title, NCT number, and document date.*
- *There are a number third party websites that can be used to convert documents into PDF format. However, before using these it is necessary to make sure that these are comprised in the college approved software list and no personal data is still available in the documents that will be processed with it (e.g., protocol, statistical analysis plan, and ICFs), (Cited on 04 Apr 2023).*
- *Although uploaded document can be deleted from a CT.gov record (even after that it has been made publicly available) all previous versions of that document(s) will remain stored in the CT.gov archive website.*

Upload steps per upload type:

Upload of a single document for the first time: → click on the 'new document' icon in the document section page; → select the document type; → enter the document date as detailed on its cover page; → click on the 'browse' icon and choose the PDF/A file to be uploaded; → click on the green 'upload' button.

Upload multiple documents of the same type (eg., ICFs parent & child): → click on the 'advanced' icon, select document type and click on the 'next' icon; enter the subtitles indicating the specific document content; → enter the document date as per its cover page; → click on the 'browse...' icon and choose the PDF/A file to be uploaded; → click on the green 'upload' button.

Update and replace a previously uploaded document: → click on the 'update' icon below the document to be updated; → enter a new document date as per its cover page; → click on the 'browse...' icon and choose the PDF/A file to be uploaded; → click on the green 'upload' button.

Deleting a study document: → click on the 'x Delete' icon below the document; → confirm the deletion when prompted (all the deleted document(s) will remain accessible on CT.gov, in the record change history).

Additional guidance on CT.gov result reporting:

- *CT.gov registration & PRS registration webpages (Cited on 20 Mar 2023).*
- *Entering study information (Cited on 31 Mar 2023).*
- *Entering adverse events (Cited on 25 Jul 2024).*
- *Study result submission (Cited on 24 Mar 2023).*
- *Additional NIH Training Materials (Cited on 25 Jul 2024).*

8.6 Reporting results on ISRCTN

The ISRCTN website provides definitions for the reporting of results (Cited on 27 Mar 2023).

General Advice:

- *The writing style should be in plain English, that is, easily understandable by the public. The use of the Cancer Research UK guidance is recommended by ISRCTN (Cited on 27 Mar 2023).*
- *The public title (differently from the scientific title, which is intended for ethics and grant applications) should be in a brief and easily understandable format.*
- *All dates should entered in an 8-digit format (DD/MM/YYYY).*
- *The main reference number should be the IRAS ID (for UK registered studies, that is format IRAS 123456), the Local Reference Number and/or Edge Number reference number.*
- *The application should be completed as per the ISRCTN website examples: example1, example2, and example3, (Cited on 27 Mar 2023).*

Additional Resources on ISRCTN result reporting:

- *How to report study results: Video Tutorial (Cited on 27 Mar 2023).*
- *How to request an update to a study record at the ISRCTN registry: Video Tutorial (Cited on 27 Mar 2023).*
- *Online form to report study results (Cited on 27 Mar 2023).*
- *Online form to request an update to a study record (Cited on 27 Mar 2023).*