

Guidelines for Registering in a Clinical Trials Registry

Why register?

Tri-Council Policy Statement (TCPS) 2 –Ethical Conduct for Research – Article 11.10

“All clinical trials shall be registered before recruitment of the first trial participant in a publicly accessible registry that is acceptable to the World Health Organization (WHO) or the International Committee of Medical Journal Editors (ICMJE).

TCPS 2 discusses several compelling ethical reasons for the registration of all clinical trials:

- Registration improves researchers’ awareness of similar trials so that they may avoid unnecessary duplication and thereby reduce the burden on participants.
- Registration also improves researchers’ ability to identify potential collaborators and/or gaps in research so that they may pursue new avenues of inquiry with potential benefits to participants and to society.
- Perhaps of most concern is the danger that some researchers or sponsors may only report trials with favourable outcomes. Failing to report the outcome of a trial or withholding negative findings is more difficult when all trials must be registered.

Obligation to register clinical trials by International Committee of Medical Journal Editors (ICMJE)

- The International Committee of Medical Journal Editors (ICMJE) announced that in order for clinical trial results to be considered for publication in journals that adhere to ICMJE standards, **all clinical trials** that start recruiting patients or volunteers **on or after July 1, 2005** must be registered with a public registry before the enrolment of the first participant. Ongoing trials not registered at inception will be considered by the ICMJE for publication if they are registered before September 13, 2005. All trials with recruitment completed before July 1, 2005 need not register.
- Details of the ICMJE requirement are described at the [ICMJE website](#)

Do I need to register my Clinical Trial?

Yes, if as described below, your clinical trial:

- Meets the definition of a clinical trial.
- You meet the requirement of the “responsible person” for registering the trial

What is the Definition of a Clinical Trial for Registration Purposes?

Three similar definitions of a “**clinical trial**” are provided below. If your study meets any one of these definitions, the trial must be registered.

TCPS 2 defines a clinical trial as:

- *A form of clinical research (also known as patient-oriented research), is any investigation involving participants that evaluates the effects of one or more health-related interventions on health outcomes. Interventions include, but are not restricted to, drugs, radiopharmaceuticals, cells and other biological products, surgical procedures, radiologic procedures, devices, genetic therapies, natural health products, process-of-care changes, preventive care, manual therapies and psychotherapies. Clinical trials may also include questions that are not directly related to therapeutic goals – for example, drug metabolism – in addition to those that directly evaluate the treatment of participants.*

ICMJE definition of a clinical trial includes:

- "Any research study that prospectively assigns human participants or groups of humans to one or more **"health-related interventions"** to evaluate the effects of health outcomes."
- **"Health-related interventions"** include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events.

FDA (Food and Drug Administration) requires registration of applicable "clinical trials" defined as follows:

- For any trials of drugs and biologics: controlled clinical investigations, other than Phase I investigations, of a product subject to FDA regulations
- For trials of biomedical devices: controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric post market surveillance.

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

Which Trial Registries are acceptable to the ICMJE?

The ICMJE accepts registration in the following

registries: www.anzctr.org.au (Australia)

www.clinicaltrials.gov (US)

www.ISRCTN.org (UK)

www.umin.ac.jp/ctr/index/htm (JAPAN)

www.trialregister.nl (Netherlands)

<https://eudract.ema.europa.eu/> (new registrations after June 20, 2011)

In addition to the above registries, starting in June 2007 the ICMJE will also accept registration in any of the primary registries that participate in the WHO International Clinical Trials Portal (see <http://www.who.int/ictrp/network/primary/en/index.html>). Because it is critical that trial registries are independent of for-profit interests, the ICMJE policy requires registration in a WHO primary registry rather than solely in an associate registry, since for-profit entities manage some associate registries. Trial

registration with missing or uninformative fields for the minimum data elements is inadequate even if the registration is in an acceptable registry.

Who is Responsible for Registering a Trial?

The “**responsible party**” must register a clinical trial. The responsible party is defined as:

- The *sponsor* of the clinical trial

OR

- The **principal investigator (PI)** of the clinical trial if so designated by a sponsor grantee, contractor, or awardee.

In most cases, registration will be the **responsibility of the Sponsor** and will not require the researcher to complete any extra work. For clinical trials that do not have a Sponsor or are funded by a grant, the **lead PI** is responsible for registering. If the trial is a single study site, this responsibility will fall to the **local PI**. In general the following applies:

- **Industry-sponsored trials** should be registered by the sponsor. These are trials in which there is a contract between the industry sponsor, the host institution, and the PI. Before enrolling study participants, every PI should ensure the industry sponsor has registered the trial. The PI should also check the registry to ensure that all ICMJE minimal data set elements are included in the registration.
- **Investigator-initiated trials**, whether or not there is industry funding or, in fact, if there is no funding, the PI is considered the sponsor and is responsible for registering the clinical trial.
- For **clinical trials that are being performed at multiple institutions**, the lead sponsor should take responsibility for registering the trial. If the University of Alberta PI is not the lead sponsor, he or she should work with the other investigators and sponsors to ensure that the trial is registered only once for the entire project.
- **CIHR-funded randomized controlled trials**- The PI is advised to contact CIHR. CIHR may prefer the trial be registered in the ISRCTN registry rather than ClinicalTrials.gov.
- **NIH sponsored trials** are usually registered by the Institute that is funding the research. They may delegate this responsibility to the lead PI.

When Does a University of Alberta PI Register a Trial?

When Do I Register my Clinical Trial?

- **Register a trial before any participants are enrolled.** TCPS 2 and ICMJE require registration be completed before the first participant is enrolled to avoid publication restrictions
- You can expect each registration to take approximately 1 to 2 hours.

Does the local Research Ethics Board need to grant final approval of the study before it is registered?

- The ClinicalTrials.gov registry allows for trials to be registered '**pending**' ethics final approval. However, once a trial has been approved by the REB, the registry must be updated with the REB approval number.
- In most instances it is suggested that you wait to register the **trial following receipt of your letter of the conditional approval** from the initial review of the study by the University of Alberta Research Ethics Board.

Most clinical trials are registered on **ClinicalTrials.gov** via a web-based entry system called the **Protocol**

What are the Steps to Register a Study in Clinicaltrials.gov?

Registration System (PRS). The University of Alberta has an organizational account and recommends this registry as they are most familiar with processes involved with this registry.

1. **Obtain and User Account:** Following the initial review of your clinical trial by the University of Alberta Research Ethics Board please send an e-mail to the University of Alberta Protocol Registration system (PRS) Administrator, Lori Anderson at lori.anderson@ualberta.ca, with the following information:
 - Ethics reference # and study title;
 - *PI's name; and*
 - *telephone contact number to be used by Clinical Trials.gov staff to contact your site.*

An account will be created for the PI in ClinicalTrials.gov. The PI will receive an **e-mail confirmation from Clinical Trials.gov** within **two business days** when the user account has been created.

NOTE: If you already have already have a User Account you can register a new study by creating a new **PROTOCOL RECORD** in your Clinicaltrials.gov User Account

2. **Login to PRS:** Once your account has been created go to <https://register.clinicaltrials.gov/> Complete the three fields on the Login screen. See example below:
 - **Organization:** UAlberta as provided in e-mail
 - **Username:** *as provided in e-mail from Clinicaltrials.gov*
 - **Password:** *you will receive a password in the e-mail from clinical trials.gov that you can reset.*

3. **Create a Protocol Record:** A trial is registered in the system by creating a “**protocol record.**” Click on the **Create** link under **Protocol Records** on the Main Menu and fill in a series of data entry screens. Clicking on the various fields will allow you to access instructions for that field. If you still have questions, mail to: register@clinicaltrials.gov.

IMPORTANT NOTE: Using an electronic version of your protocol, you can copy and paste information into the requested data fields.

4. **Review the Protocol Record:** After filling in the last data entry screen, the **Edit Protocol** screen will appear. Review the information for accuracy and completely and address any **ERRORS, ALERTS, WARNINGS, or NOTES** in the protocol record. **If you fail to do so, you cannot complete the registration process.**

5. **Mark the Protocol Record as Complete:** If you fail to mark your record as complete, it will not be approved and released for publication and your trial will not be properly registered.

6. **Releasing and Approving the Record:** The “**responsible party**” (i.e. PI) may assign the work of completing/updating the record to another study team member (a separate account may be created for this individual). However, **the PI must** “approve” and “release” the record on receipt of the e-mail from Clinical Trials.gov

7. **Keep your Protocol Record Up-To-Date:** An **affirmative verification** or update of the data in the protocol records that have not been closed or terminated is required every six months. **Failing to login to the PRS and confirm or update your record(s) every six months, regardless of whether there has been a change to the trial or not, may result in a loss of funding and/or the inability to publish the results of a trial in an ICMJE associated journal.**

IMPORTANT NOTE: You should receive a reminder e-mail notification from clinicaltrials.gov once every six months to update your study information.

Some suggestions when completing the “Protocol Record Template”:

As a **PRS user** you are responsible for ensuring that the information you provide on your trial is correct, complete readily understood by the public, and updated in a timely manner.

- **Pertinent Source Information:** It will be helpful to have the protocol, the informed consent document, the REB application and the REB approval letter on hand
- **Data definitions:** are available by clicking on the element. Please be clear and specific and choose appropriate and meaningful key words
- **Unique protocol ID:** We suggest using the **REB Ethics Reference Number** as your unique protocol identifier (e.g. Pro000XXXXX)
- **Review Board Approval Number:** using the REB Ethics Reference Number(e.g. Pro000XXXXX)
- **Oversight Authorities:** Generally this should be Country: Canada: Research Ethics Board
- **Sponsor:** This will be the organization for which you register through.
- **Research Ethics Board Affiliation:** University of Alberta
- **Research Ethics Board Chair:** Indicate “Susan Babcock” rather than the name of the person currently serving as the Chair. This will ensure that all queries regarding ethics approval are responded to quickly and consistently.
- **Research Ethics Board Phone:** (780) 492-0459
- **Research Ethics Board Email:** reoffice@ualberta.ca
- **Research Ethics Board Address:** #308 Campus Tower, 8625 112 Street, Edmonton, AB, T6G 1K8
- **Records Verification Date:** The date the record has been verified/approved by the “*responsible party*” (i.e. PI). This date requires updating with each change and at a minimum every 6 months. We also suggest it is **updated** with each **annual approval**. This serves as a date alert for the public as to whether the information is being kept current, particularly with reference to recruiting status and contact information.
- **Study Start Date:** Use date enrollment began- not the date of REB approval
- **Last Follow-up Date:** Actual date that the last participant was examined or treated or anticipated date when expected last follow-up will occur.

Are updates required?

Tri-Council Policy Statement (TCPS) 2 –Ethical Conduct for Research – Article 11.11

“Following registration of their study in accordance with [Article 11.10](#), researchers are responsible for ensuring that the registry is updated in a timely manner with:

- *new information ([Article 11.8](#));*
- *safety and, where feasible, efficacy reports ([Article 11.6](#));*
- *reasons for stopping a trial early; and*
- *the location of findings.”*

- Clinicaltrials.gov requires that the “**responsible party**” must also verify, review and update the study record when **any changes** are made to a study protocol and/or at a **minimum every 6 months**. The records must also be updated when the trial is completed.

What are the Consequences of not Registering a Trial?

There are penalties for responsible parties who fail to register clinical trials, keep the information up to date, or submit false or misleading information.

- The inability to publish the results of a trial in an ICMJE associated journal.
- For US federally-funded trials, the penalties could include withholding or recovery of grant funds.

What is the Specific Wording Required in the University of Alberta Consent Forms?

In the section titled “**Questions**” include the following wording:

FDA regulated research:

Public Information about this Study

ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on <http://www.ClinicalTrials.gov> as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.”

NON FDA regulated research

Public Information about this Study-

ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.”

How do I register a trial with ISRCTN?

If you wish to register through ISRCTN, access the on-line application at ControlledTrials.com. You can log-in immediately and register your trials. Once the form has been submitted, you will get an email confirming receipt of your application, which you may print out for your records if you wish. The ISRCTN editorial office will then check whether the application is eligible. An administrative charge will then be requested – the 2007 rate is

£132 per trial (US\$255/€195 based on April 2007 exchange rates). All users will have permanent free access to the information in the ISRCTN Register. If you have any questions about the registration process, please feel free to email infor@isrctn.com

References

Clinical Trials.gov Registry



[ClinicalTrials.gov Protocol Registration System](#)

[ClinicalTrials.gov Fact Sheet](#)

ICMJE Initiative

Ottawa Statement on Trial Registration

The Ottawa Statement aims to establish internationally recognized principles for trial registration.

Health Canada – Drugs and Health Products - Clinical Trials: Registration and Disclosure of Information

Canadian Institutes of Health Research (CIHR) Registration Requirements

International Clinical Trials Registry Platform (ICTRP)

The mission of the WHO International Clinical Trials Registry Platform is to ensure that a complete view of research is accessible to all those involved in health care decision making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base.