

Frequently Asked Questions (FAQ) About The International Committee of Medical Journal Editors (ICMJE) Clinical Trials Registration Requirement

What is the requirement?

This requirement states that “all clinical trials must be entered in a public registry *before the onset of patient enrollment* as a condition of consideration for publication” in member journals.

What is the purpose of this requirement?

Recent scandals regarding drug safety and lack of disclosure have resulted in public mistrust and increased scrutiny of the clinical research enterprise. The ICMJE established this policy in an effort to promote transparency of the clinical trials process, prevent selective reporting, and “promote the public good by ensuring that everyone can find key information about every clinical trial whose principal aim is to shape medical decision making.”

It is hoped that this requirement will lead to a uniform international standard for the disclosure of clinical trial information. The requirement is supported by the governments of many countries as well as the World Health Organization (WHO). The WHO also plans to certify registries that meet agreed standards and is in the process of developing a clinical trials portal that will link national registries, thereby providing an international resource on clinical trials.

What is the ICMJE?

Initially known as the “Vancouver Group,” this group first met in 1978 to establish formatting guidelines (known as the Uniform Requirements for Manuscripts) for manuscripts submitted to their journals. As it began to respond to issues beyond the scope of manuscript preparation, the group expanded and became more formalized and is now known as the International Committee of Medical Journal Editors (ICMJE).

Which journals are enforcing this requirement?

Although this policy was formulated and signed by representatives from eleven journal members of ICMJE, it is anticipated that publishers of most medical journals will begin to require prospective public registration of clinical trials as a condition for publication. Currently, the 11 journals that have adopted this requirement are:

- Annals of Internal Medicine
 - Croatian Medical Journal
 - Canadian Medical Association Journal
 - Dutch Journal of Medicine (Nederlands Tijdschrift voor Geneeskunde)
 - Journal of the American Medical Association
 - Journal of the Danish Medical Association
 - The Lancet
 - The Medical Journal of Australia
 - The New England Journal of Medicine
 - The New Zealand Medical Journal
 - Norwegian Medical Journal
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When does this requirement take effect?

This requirement applies to clinical trials that begin recruiting subjects on or after **July 1, 2005**. Ongoing trials that were not registered at inception must be registered before **September 13, 2005**, in order to be considered for publication in an ICMJE journal.

What is the definition of “clinical trial?”

The ICMJE defines **clinical trial** as “any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause and effect relationship between a medical intervention and a health outcome. The trial must have at least one prospectively assigned concurrent control or comparison group in order to trigger the requirement for registration.”

How is “medical intervention” defined?

The ICMJE defines a **medical intervention** as “any intervention used to modify a health outcome.” This term can include “drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like.”

Are any clinical trials excluded from this requirement?

Because the focus of this policy is to ensure public access to “clinically directive” trials (that is, trials that test a clinical hypothesis about health outcomes), certain trials are excluded. An example would be phase I trials where the primary goal is to assess a major unknown toxicity or to define pharmacokinetics. Trials designed to examine the biology of disease or provide preliminary data to direct further clinically-directive research fall into a gray area, and the investigator must have a sound rationale for a decision to not register their trial. The journal editor will review these trials on a case-by-case basis.

What if I'm unsure about whether to list a trial?

If you are in doubt as to whether or not your trial should be listed, you can:

- review the ICMJE editorial statements (www.icmje.org/clin_trial.pdf, www.icmje.org/icmje_response.pdf, www.icmje.org/clin_trialup.htm)
 - contact the journal editor, or
 - err on the side of listing the trial.
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Who is responsible for registering trials?

Registration of multi-site trials should be coordinated among the sites and be registered by the lead sponsor. The lead sponsor is defined as "...the entity with primary responsibility for initiating and conducting the trial. For trials associated with IND or IDE applications with the FDA, the IND/IDE holder is the lead sponsor." Regardless of who holds responsibility for actually registering the trial, the PI should ensure that registration requirements are met. This can be done searching on www.ClinicalTrials.gov.

Can any registry be used to list a trial?

Although the ICMJE does not endorse a specific registry, an acceptable registry must meet the following minimal requirements:

- The registry must be open to all registrants.
- The registry must be not for profit.
- The registry must be accessible to the public at no charge.
- The registry must be electronically searchable.
- The registry must have a mechanism to ensure the validity of the registration data.

ClinicalTrials.gov, established by the National Institutes of Health's National Library of Medicine, meets these criteria and is the most widely used vehicle at this point. Trials can be listed on this website via the Protocol Registration System (PRS) at <http://prsinfo.clinicaltrials.gov>.

What information must be included when a trial is registered?

The ICMJE specified the minimal information required for trial registration. In addition, there is information that is required when you list a trial on clinicaltrials.gov. A list and description of these required data fields can be obtained at <http://prsinfo.clinicaltrials.gov/trial-reg-requirements.html>.

How do I know if my trial is registered?

Check with the person responsible for actually registering the trial to identify if/where the trial has been registered. Investigators should search the registry to ensure that the clinical trial has been registered, regardless of whether or not they hold responsibility for registering a trial. To avoid duplicate registration, investigators who hold responsibility for registering a trial should search the registry to ensure that the trial has not already been entered.

How do I register a trial?

Investigators at the University of Pittsburgh who are responsible for registering a qualified clinical trial should take the following steps.

- Search www.clinicaltrials.gov to ensure that the trial is not already listed. NIH-sponsored clinical trials and many industry-sponsored trials have already been registered on this site. If the trial is not listed, continue.
- Establish an account with the ClinicalTrials.gov Protocol Registration System (PRS) by sending an e-mail message to the University's PRS administrator, Laurel Yasko, at lyasko@hs.pitt.edu. The subject line should state "Protocol Registration" and the body of the message should contain your name, telephone number, and e-mail address.
- Within 24-48 hours, you will receive an e-mail message from ClinicalTrials.gov containing your login name, temporary password, and login instructions.
- Once you have received your login information and instructions, register the trial. This process will take approximately 1 hour, and it will be helpful to have the protocol, informed consent document, and IRB approval on hand. Note that this system offers the option to save data if you do not have time to complete the entire process.
- To begin the registration process, go to the ClinicalTrials.gov registration website (<https://register.clinicaltrials.gov/>). Complete the login fields. In the "Organization" field, enter "University of Pittsburgh."
- The "Main Menu" page will appear. The "User Account" link provides information on changing your temporary password, and this should be done as soon as possible. This link also has a helpful "User's Guide."
- To complete the protocol template, return to the "Main Menu" page, go to "Protocol Record" and select "Create." The information that you will be required to enter will be variations of the following.
 - **Unique trial number**
Use the University of Pittsburgh IRB number that was assigned to the trial
 - **Trial registration date**
 - **Secondary trial ID**
Optional, but usually not applicable
 - **Funding source**
 - **Primary sponsor**
 - **Secondary sponsor(s)**
 - **Responsible contact person**
 - **Research contact person**
 - **Title of the study**

- **Official scientific title of the study**
- **Research ethics review**
Include the following information:
IRB Approval Number
Board Name: University of Pittsburgh Institutional Review Board
Board Affiliation: University of Pittsburgh
Board Chair: Richard Guido, MD (if needed- phone: 412-383-1480;
Email: rguido@upmc.edu)
- **Medical condition studied**
- **Intervention(s)**
- **Key eligibility criteria**
- **Study design**
- **Anticipated trial start date**
- **Target sample size**
- **Recruitment status**
- **Primary outcome**
- **Key secondary outcomes**

- When the template is complete, hit "Submit." The template will be forwarded to the University's PRS administrator who will review it and release the approved content to ClinicalTrials.gov.
- The PI must review and make necessary changes to the protocol listing every six months or more frequently if a significant protocol change occurs.

IMPORTANT: The PI is responsible for ensuring that the information provided is complete, accurate, and updated as outlined in the requirements.

Where can I obtain more information?

Additional information is available from the following sources:

- ClinicalTrials.gov
 - www.clinicaltrials.gov
- ICMJE Editorial Statements
 - www.icmje.org/clin_trial.pdf
 - www.icmje.org/icmje_response.pdf
 - www.icmje.org/clin_trialup.htm
- University of Pittsburgh Office of Clinical Research, Health Sciences (OCR)
 - Laurel Yasko, RN, BSN, CCRC, PRS Administrator
 3550 Terrace Street, Suite 401 Scaife Hall
 Pittsburgh, PA 15261
 412-648-9756
lyasko@hs.pitt.edu
www.clinicalresearch.pitt.edu
- University of Pittsburgh Office of Research
 - 412-624-7400