

CLINICAL TRIALS REGISTRIES

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Introduction

In response to the growing public concern about the timely and complete reporting of clinical trials results and recent policy statements of the The International Conference of Medical Journal Editors (ICMJE), The Endocrine Society has developed this position statement, which establishes a Society policy requiring registration of studies describing clinical trials before they may be considered for publication in Society journals.

Disclosure of the existence of clinical trials has been a controversial issue, requiring balance between the opposing needs for transparency, accountability and access to trials compared to the need for protection of the intellectual property of sponsors and investigators. The position of the ICMJE to require prospective and public registration of clinical trials in order to be considered for publication in key biomedical journals has brought to the forefront the need to address the issue of clinical trials registries and databases. In January 2005, Fordham University convened a Summit on Biopharmaceuticals in the 21st Century: Responsibility, Sustainability and the Public Trust, during which the issue of clinical trials registries and databases was discussed, the summary of which has been published.

The ICMJE defines clinical trials as “any research project that prospectively assigns human subjects to intervention or concurrent comparison or control groups to study the cause-and-effect relationship between a medical intervention and a health outcome.” Phase I¹ trials generally examine safety and/or biomarkers in a small number of healthy volunteers and/or patients; such studies are not included within the scope of the ICMJE document. Generally, early Phase II studies that are hypothesis generating, rather than hypothesis-testing, are small, and are not within the scope of the ICMJE guidelines. However, some Phase II trials may in fact meet the above-mentioned ICMJE definition and, thus, ICMJE

recommends that researchers err on the side of caution and register any Phase II study that aims to collect data on health outcomes.

Background

Clinical trials registries and clinical results databases differ in their purposes.

Clinical trials registries provide the public with access to information on ongoing and completed clinical trials. Ongoing trials may or may not be enrolling additional patients. Clinical trials are entered in the registry at or near the time of trial initiation, and were initially intended for use with studies of interventions for rare and/or life-threatening diseases. The intention was to provide access to experimental therapies through dissemination of limited information on such studies. More recently, the scope of registries has changed to include all therapeutic areas and types of interventions.

Results databases were created in an effort to provide transparency in presenting results of clinical trials in response to concerns that publication of clinical trials results was selectively biased toward “positive” trials in which the tested hypothesis was proven. Databases were designed to assure full disclosure of positive and negative trial results. The presumed result of such disclosure is to provide a more complete view of the data available for a particular drug or intervention, and to allow the use of existing data to better determine the need for, and guide the design of, subsequent clinical trials. Databases address concerns that investigators or sponsors may be less inclined to publish negative trial results, and that journal editors may also be less inclined to accept manuscripts describing negative studies for publication.

This position statement focuses on issues related to clinical trials registries.

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- ¹ Phase I studies are usually performed in a small number of normal volunteers to test tolerability and safety of a drug, to assess the effects on a specific physiologic endpoint, or an interaction with another drug or with food
 - Phase IIa studies are usually performed in a relatively small number of patients, generally include a placebo or active control group, and are designed to demonstrate proof of concept for a mechanism of action
 - Phase IIb studies are performed in a somewhat larger number of patients, generally to determine the optimal dose or doses of a drug
 - Phase III studies are large, multicenter, placebo or active controlled definitive clinical trials designed to provide sufficient data for registration of a new drug or a change in the label of a drug.

Considerations

There is general consensus that clinical trials registries fulfill an important need to provide access to, and disclosure of the existence of, clinical trials for the greater public good. However, there are also a number of key considerations for such registries.

Intellectual property and competitive advantage

Both academic and industry sponsors understand that the fact that a study is being performed may be regarded as important intellectual property. Further, key aspects of study design and timing may be proprietary and could provide competitive advantage. To that end, the data fields to be disclosed in registries are critical, and should be selected based on the desire to meet the needs of patients and of the public, but while protecting intellectual property to the extent possible. The WHO “agreement,” from April 2005, recognizes this and allows that trial sponsors may have a need to delay disclosure of five data fields that are of competitive importance.

Compliance/ Responsibility for registration

In managing registries, there should be clarity in responsibility for registering clinical trials. There is no advantage (and in fact, potentially great disadvantage due to confusion and duplication of effort) to having the same trials registered multiple times (for instance, in institutional, local, regional, national and international registries). In fact, such proliferation of registries may be confusing to patients and could defeat the purpose of having clear accountability and transparency. As many studies are multi-site and/or multi-national, access to data in a local language remains a challenge, should a single global registry be endorsed broadly.

In this case, local translations should be verbatim and should cross-reference a global listing. In order to avoid duplication, the sponsor (academic, industry or other) should be responsible for registering trials and maintaining relevant data, such as protocol amendments and enrollment dates. At present, compliance with clinical trials registry participation is voluntary, although necessary for publication in ICMJE-compliant journals.

Administrative Issues

Funding and administration of registries is a key issue. The US National Library of Medicine-sponsored registry, clinicaltrials.gov, is becoming the *de facto* standard. Whether it is appropriate for a U.S.-run registry to be selected as the global standard is a topic for resolution, as some constituents may feel that a non-government sponsored registry would be most appropriate to meet global needs. Existing organizations, such as ICH and WHO, might be considered as sponsors, but issues of financial support for administration would need to be resolved. [Clinicaltrials.gov](http://clinicaltrials.gov) is free and globally accessible; it also has a QA function where the NLM validates information for a proportion of protocols being registered, including confirmation that IRB or ERC approval has been obtained.

Position

The Endocrine Society supports the use of clinical trials registries for clinical trials, as endorsed by ICMJE, and recommends the use of clinicaltrials.gov. Prospective registration of studies will be required in order for manuscripts describing clinical trials to be considered for publication in the Society’s journals.