Clinical Trial Registration
A Statement From the International Committee of Medical Journal Editors

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Trial Registration
A Great Idea Switches From Ignored to Irresistible

Drummond Rennie, MD

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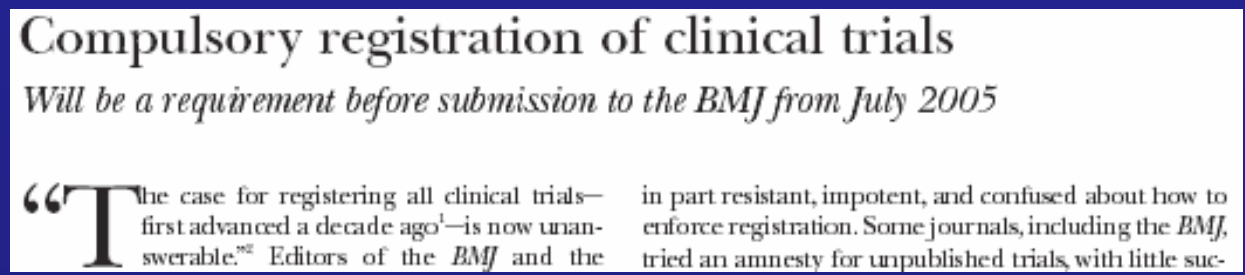
Registration of Clinical Trials

and

Resources for Clinical Trial Registration



Compulsory registration of clinical trials

Will be a requirement before submission to the BMJ from July 2005

"The case for registering all clinical trials—first advanced a decade ago[1]—is now unanswerable."[2] Editors of the *BMJ* and the

in part resistant, impotent, and confused about how to enforce registration. Some journals, including the *BMJ*, tried an amnesty for unpublished trials, with little suc-

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EDITORIALS

Clinical Trial Registration: A Statement from the International Committee of Medical Journal Editors

Altruism and trust lie at the heart of research on human subjects. Altruistic individuals volunteer for research because they trust that their participation will contribute to improved health for others and that researchers will minimize risks to participants. In return for the altruism and trust that make clinical research possible, the research enterprise has an obligation to conduct research ethically and to report it honestly. Honest reporting begins with revealing the existence of all clinical studies, even those that reflect unfavorably on a research sponsor's product.

The Journals Involved:

Members of ICMJE

(International Committee of Medical Journal Editors)

Catherine De Angelis, M.D., M.P.H.
Editor-in-Chief, *JAMA*

Jeffrey M. Drazen, M.D.
Editor-in-Chief, *New England Journal of Medicine*

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Editor-in-Chief, *Norwegian Medical Journal*

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Editor, *The Lancet*

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Editor, *Croatian Medical Journal*

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Executive Editor, *Nederlands Tijdschrift voor Geneeskunde (Dutch Journal of Medicine)*

Torben V. Schroeder, M.D., D.M.Sc.
Editor, *Journal of the Danish Medical Association*

Hal C. Sox, M.D.
Editor, *Annals of Internal Medicine*

Martin B. Van Der Weyden, M.D.
Editor, *The Medical Journal of Australia*

Summary

- Altruism and Truth lie at the heart of human subject research.
- Researchers have an obligation to conduct research ethically and report it honestly.
- Ethically, must reveal “the existence of *all* clinical studies, even those that reflect unfavorably…”.
- Ethical arguments in favor of registration far outweigh any proprietary interests or concerns.

Summary

- "…trial results that place financial interests at risk are…likely to remain unpublished and hidden."
- Concealed and unreported trials do not become part of the body of literature or evidence that might affect clinical practice
- Comprehensive trial registration addresses the issue of selective publication.
- Full transparency will enhance public confidence.

Summary: The Requirements

- All clinical trials starting enrollment after July 1, 2005 must register *prior* to commencing enrollment.
- For studies enrolling prior to July 1, 2005, registration must be complete by Sept 13, 2005.
- Includes cause and effect studies
- Excludes phase 1 trials, toxicity studies

Summary: Registry Characteristics

- Open and freely accessible to public
- Managed by non-profit organization
- Validity of data ensured
- Searchable
- Unique identifying number
- Statement of intervention and comparison studied
- Statement of hypothesis, definition of primary and secondary outcomes, eligibility criteria, trial dates, target number of subjects, funding source, and contact information for PI.

Additional Resources : http://www.clinicaltrials.gov

- Run by US National Library of Medicine
- http://www.clinicaltrials.gov/ct/info/about for submitting new studies or taking a tour of the Protocol Registration System (PRS)
- http://www.niddk.nih.gov/patient/clinical_trials/reginfo.htm for registration instructions

Additional Resources : http://www.clinicaltrials.gov

- **Pros**: Run by a non-profit organization; each study assigned a unique registration number; National Library of Medicine verifies accuracy of information and provides quality control; electronically searchable.
- **Cons**: Registration is only open to federal agencies sponsoring clinical trials and private sponsors who submitted an IND to the FDA (i.e. pharmaceutical and biotech companies). Excludes trials from low and middle-income countries. Information about results is not required.
- In 2002, 91% gov't-sponsored trials were registered vs 49% industry-sponsored trials. Until now, no enforcement.

Additional Resources : http://www.clinicaltrials.gov

- FDA guidance document: What information must be submitted?
- IND clinical trial information must be submitted, "if it is for a drug to treat a serious or life-threatening disease or condition and it is a trial to test effectiveness (42 U.S.C.282 (j)(3)(A)). ***If you wish***, you can also provide information about non-effectiveness trials or for drugs to treat conditions not considered serious or life-threatening."

Guidance for Industry Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions. US DOHHS, FDA, CDER, CBER March 2002

Additional Resources:

www.controlled-trials.com

- Run by Current Controlled Trials Ltd, part of the Current Science Group of Biomedical publishing companies.
- Other members of the group: www.biomedcentral.com

  www.biomedcentral.com/openaccess
- Launched controlled-trials.com in 1998 to, “increase availability and promote exchange of information about ongoing randomized controlled trials worldwide”

Additional Resources:
www.controlled-trials.com

- Have an International Advisory Group, although some criticism of the registry as it is run by a private, for-profit company.
- Trials registered by International Standard Randomized Controlled Trial Number (ISRCTN)
- Other support:

  www.controlled-trials.com/links/support.asp
- Free Access

Additional Resources:
http://www.clinicalstudyresults.org

- Phrma Database: **Ph**armaceutical **R**esearch and **M**anufacturers of **A**merica
- www.phrma.org/whoweare - mission statement, member companies
- "commitment…to communicate the results of clinical studies, both ***positive*** and ***negative***."

Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results is available on www.phrma.org

Additional Resources: www.clinicalstudyresults.org (cont'd)

- Purpose: to make "clinical study results for US-marketed pharmaceuticals more ***transparent***."
- Will contain results from all "hypothesis-testing" clinical studies i.e. mainly phase III and IV, completed since October 1, 2002.
- Free, public access. Available as of October 1, 2004?