Registering Clinical Trials

Moderator:
Drummond Rennie
Journal of the American Medical Association and University of California, San Francisco
Jacksonville, Oregon

Speakers:
An-Wen Chan
Canadian Institutes of Health Research and University of Toronto
Toronto, Ontario

John R Hoey
Canadian Medical Association Journal
Ottawa, Ontario

Jocalyn P Clark
BMJ
London, England

Hélène Faure
Current Controlled Trials
London, England

Reporter:
Ellen M McDonald
University of Texas
M D Anderson Cancer Center
Houston, Texas

Some scientists tend to publish only their positive findings, and information about some clinical trials is not available at all. A move is therefore under way to have information about all clinical trials listed in a comprehensive register so that information will be complete, unbiased, and free. Drummond Rennie opened this session on registering clinical trials with a historical perspective, from the 1948 publication of the first randomized controlled trial of streptomycin to the recent allegations of the suppression of negative studies about Vioxx. With the weight of this history behind them, Kay Dickersin and Rennie, in a 2003 article in the *Journal of the American Medical Association*, urged journals to publish clinical trials only if they had been registered at inception.

After offering a rationale for trial registration that emphasized the ethical obligations to participants and future patients, An-Wen Chan compared two current proposals for registration: the Ottawa Statement and the World Health Organization (WHO) International Clinical Trials Registry Platform. Although similar in intent, the two initiatives differ in some key recommendations. For example, whereas the Ottawa Statement calls for the registration of all trials, the WHO platform excludes exploratory trials without defining "exploratory" precisely. In addition, each defines a minimal dataset differently and uses its own criteria to determine when to release protocol items publicly and register results. Overall, the Ottawa Statement is more inclusive but currently less complete with regard to implementation; Chan noted that making it operational would not be formally discussed until a meeting after his presentation. He concluded by stressing the role of journal editors in defining and implementing their own standards.

John R Hoey presented the International Committee of Medical Journal Editors (ICMJE) position on clinical-trial registration: for trials starting on or after 1 July 2005, member journals will consider publishing only trials registered before enrollment of the first patient. Hoey outlined ICMJE criteria for registration, including assignment of a unique identifying number to a trial and clearly stating the interventions planned, the study hypothesis, and the primary and secondary outcomes. Hoey noted that the North American editors in ICMJE had met with representatives of the pharmaceutical industry to discuss concerns about proprietary interests that might be revealed in a registry; ICMJE's response to the concerns was under embargo at the time of Hoey's presentation. (In its new statement, ICMJE has maintained the implementation date and stated its willingness to consider harmonizing its requirements about data fields with the WHO position once it is final.) Hoey also reviewed some unpublished data showing that *www.ClinicalTrials.gov* lacks crucial information on many trials despite US laws requiring disclosure.

Jocalyn P Clark described the five principal ways that journal editors might use trial registration data. First, the peer-review process could be optimized with the additional information available. Second, articles could be viewed in the context of the larger trial, making them part of a continuum of data rather than solitary pieces of information. Third, editors could improve the commentary on trials (such as editorials) and check interpretations, reining in excessive ones. Fourth, the accessibility of all trial registration data could make it easier to detect possible ethical problems in articles, including duplicate publication and selective reporting of data. Fifth, and perhaps most important, trial registration data could benefit patients by increasing accountability and fostering the recruitment of better-informed participants into trials. Clark concluded with some unresolved future questions, including whether journals will eventually become unnecessary to clinical trials.

Hélène Faure outlined the strengths and weaknesses of some of the clinical-trial registries now available (*www.ClinicalTrials.gov*, the International Standard Randomised Controlled Trial Number [ISRCTN] Register, Eudra CT/EuroPharm, pharmaceutical registers, TrialsCentral, CenterWatch, and Current Controlled Trials' metaRegister), many of which are interactive. She described PubMed's initiative to use a trial ID meta tag to link abstracts with registration data. Faure concluded by citing the legislative initiatives in the United States, the United Kingdom, France, Australia, and other countries to mandate national public registers.