

Editorial

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International clinical trial registration: Any progress?

Clinical trial registration has been a popular theme in clinical research for the past two years. Following the lawsuit against GlaxoSmithKline in New York in 2004, the pharmaceutical industry [1], journal editors [2], academia [3], consumer organizations, governments and WHO [4] have all expressed support for more transparency in research. The pharmaceutical industry has made attempts to improve transparency and access to research information. Some larger companies are putting the results of their trials in a non-promotional format on their web sites and these are important developments. However, as long as it is not known whether those are selected trials or all of their trials there will continue to be less than full public trust in the clinical trial research system.

Trial registration is a complex area with multiple facets that can be best tackled with international collaboration. Many important trials are multinational and are conducted increasingly in low-income and middle-income countries. With unprecedented advances in science, the demand for such trials is likely to increase dramatically in the near future. Low and middle-income countries need to be prepared to respond to such increasing demands on their health and health-research systems, and to ensure protection of their citizens who participate in research. Strengthening coordinated global capacity for trial registration is necessary if we are to maximize access to research information globally and improve the ethical foundation and the efficiency of the research enterprise.

In January 2005 the WHO initiated a project called The International Clinical Trials Registry Platform. The main objectives are to set international norms and standards on trial registration, improve efficiency through linking existing registers meeting certain standards, promote compliance and build capacity where needed. Following several informal consultations a stakeholders meeting was convened in April 2005 [5]. There was agreement on which trials should be registered, the minimum data set required for each trial and when and how trial results should be disclosed. However, the pharmaceutical industry representatives argued that the disclosure of certain fields at the start of a trial may result in exposing their clinical development programme and thus loss of competitive advantage. Others argued that those fields constitute the core information about a trial and if that information is not made available the registration is meaningless. Research funders and systematic reviewers want to know

exactly which research is ongoing to improve efficiency and reduce unnecessary duplication. The WHO Secretariat suggested solving that issue through discussions with all stakeholders and this was agreed. The WHO Secretariat is currently working with all stakeholders on several options proposed and will hold an open process to resolve this issue by April 2006.

On less controversial issues, the Registry Platform has several immediate goals [6]. We are defining which trials need to be registered. We are clarifying and finalizing the WHO Registration Data Set, which is the information to be registered about each trial. We are establishing standards for registers worldwide, and establishing a cooperative network of these registers. We are defining a globally unique Universal Trial Reference Number, which only WHO-qualifying registers will be able to apply for. In addition, we are establishing data interchange standards that all WHO-qualifying registers will have to adhere to. These interchange standards will facilitate our development of a one-stop portal for searching registers worldwide. The WHO does not have any current plans to offer a WHO-administered register. Plans are for the register network and the unique trial reference number to be operational by the first quarter of 2006, and the search portal to be operational by May 2006. To achieve these goals, the Registry Platform is consulting broadly with stakeholders worldwide to produce consensus-based policies that uphold scientific and ethical principles but that are also practical and feasible.

After working on the coordination of efforts and mediating between different stakeholders for over a year, can we be optimistic? We believe that all the stakeholders are genuinely interested in reaching a compromise that would increase transparency and accountability for clinical trials. The WHO project provides the appropriate forum with international support and legitimacy for stakeholders to move ahead with optimism for building a strong foundation for trial registration and reporting worldwide.

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Draft Trial Registration Data Set⁺

Item	Field Value	Definition/Explanation
1. Primary Register and Trial ID #	<input type="text"/> Trial ID # <input type="text"/>	Select name of Member Register in which this trial was first registered (the trial's "Primary Register"), and that register's registry-specific unique ID assigned to this trial.
2. Date of Registration in Primary Register	<input type="text"/> <input type="text"/> <input type="text"/>	Date when trial was officially registered in the Primary Register DD/MM/YYYY.
3. Secondary ID#s	Issuing Authority <input type="text"/> ID Number <input type="text"/> Click to add more ...	Other identifying numbers and issuing authorities besides the Primary Register, if any. Include the sponsor name and sponsor-issued trial number (e.g., protocol number) if available. Also include other member and non-member trial registers that have issued a number to this trial. There is no limit on the number of Secondary ID numbers that can be provided.
4. Source(s) of Monetary or Material Support	Name <input type="text"/> Click to add more ...	Major source(s) of monetary or material support for the trial (e.g., funding agency, foundation, company).
5. Primary Sponsor	Name <input type="text"/>	The individual, organisation, group or other legal person taking on responsibility for securing the arrangements to initiate and/or manage a study (including arrangements to ensure that the design of the study meets appropriate standards and to ensure appropriate conduct and reporting). The primary sponsor is normally the main applicant for regulatory authorisation to begin the study. It may or may not be the main funder.
6. Secondary Sponsor(s)	Name <input type="text"/>	Additional individuals, organisations or other legal persons, if any, that have agreed with the primary sponsor to take on responsibilities of sponsorship. A secondary sponsor may have agreed <ul style="list-style-type: none"> o to take on all the responsibilities of sponsorship jointly with the primary sponsor; or o to form a group with the primary sponsor in which the responsibilities of sponsorship are allocated among the members of the group; or o to act as the sponsor's legal representative in relation to some or all of the trial sites o to take responsibility for the accuracy of trial registration information submitted.

Item	Field Value	Definition/Explanation
7. Contact for Public Queries	Email, telephone number, or address <input type="text"/>	Email address, telephone number, or address of the contact who will respond to general queries, including information about current recruitment status.
8. Contact for Scientific Queries	Email, telephone number, or address <input type="text"/> Affiliation <input type="text"/>	Email address, telephone number, or address, and affiliation of the person to contact for scientific inquiries about the trial (e.g., principal investigator, medical director for the study at the sponsor). For a multi-center study, enter the contact information for the lead Principal Investigator or overall medical director.
9. Public Title	<input type="text"/>	Title of the study intended for the lay public in easily understood language.
10. Scientific Title	<input type="text"/> Acronym <input type="text"/>	Scientific title of the study, including the intervention name, health problem, and primary outcome name. Example: "A Randomized Controlled Trial of Chocolate on Beck Depression Scores in Patients with Seasonal Affective Disorder." Include trial acronym if available.
11. Countries of Recruitment	<input type="text"/>	The countries from which participants will be, are planned to be, or have been recruited (as last reported to the Primary Register).
12. Health Condition(s) or Problem(s) Studied	<input type="text"/>	Primary health condition(s) or problem(s) studied (e.g., depression, breast cancer, medication error). Enter one term per line in the field.
13. Intervention(s)	Intervention name <input type="text"/> Other details (e.g., dose, duration, etc.) <input type="text"/> Click to add more experimental interventions ... Control Intervention name <input type="text"/> Other details of control (e.g., dose, duration, etc.) <input type="text"/> Click to add more control interventions ...	Enter the specific name of the intervention(s) and the comparator/control being studied, one at a time. Use the International Non-Proprietary Name if possible (not brand/trade names). For an unregistered drug, the generic name, chemical name, or company serial number is acceptable. If the intervention consists of several separate treatments, list in one line separated by commas (e.g., "low-fat diet, exercise"). For multi-armed studies, describe the intervention(s) for each arm in separate entries. The control intervention(s) is/are the interventions against which the study intervention is evaluated (e.g., placebo, no treatment, active control). If an active control is used, enter the name(s) of that intervention, else enter "placebo" or "no treatment" as applicable. For each intervention, describe other intervention details (dose, duration, mode of administration, etc.).
14. Key Inclusion and Exclusion Criteria	Inclusion Criteria <input type="text"/> Exclusion Criteria <input type="text"/>	Key inclusion and exclusion criteria for participant selection, including age and sex.
15. Study Type	Single group study? <input type="text"/> If a multiple group study, is it randomized? <input type="text"/>	A single group study is one in which all participants are given the same intervention. Trials in which participants are assigned to receiving one of two or more interventions are NOT single group studies. Crossover trials are NOT single group studies.

Item	Field Value	Definition/Explanation
		For multiple group studies (2 or more study groups), a trial is “randomized” if participants are/were assigned to intervention groups by a method based on chance.
16. Date of First Enrollment	<input type="text"/> <input type="text"/>	Anticipated or actual date of enrollment of the first participant (MM/YYYY).
17. Target Sample Size	<input type="text"/>	Number of participants that this trial plans to or had planned to enroll as last reported to the Primary Register.
18. Recruitment Status	<input type="text"/>	Recruitment status of this trial as last reported to the Primary Register. <ul style="list-style-type: none"> o <i>Pending</i>: participants are not yet being recruited or enrolled at any site o <i>Active</i>: participants are currently being recruited and enrolled o <i>Temporary halt</i>: there is a temporary halt in recruitment and enrollment o <i>Closed</i>: participants are no longer being recruited or enrolled.
19. Primary Outcome(s)	<p>Outcome Name</p> <input type="text"/> <p>Timepoints</p> <input type="text"/> <p>Click to add more outcomes ...</p>	<p>Outcomes are events or experiences that trial investigators measure because it is believed that they may be influenced by the intervention or exposure. The Primary Outcome should be outcome used in sample size calculations, or the main outcome(s) used to determine the effect of the intervention(s).</p> <p>Enter the names of all primary outcomes of the trial, one at a time. Be as specific as possible (e.g., “Beck depression score” rather than just “depression”). For each outcome measure, also provide all the timepoints at which it is to be measured. Examples: Outcome name: all cause mortality, Timepoints: one year; or Outcome name: Beck depression score, Timepoint: 6,12, and 18 weeks.</p>
20. Key Secondary Outcomes	<p>Outcome Name</p> <input type="text"/> <p>Timepoints</p> <input type="text"/> <p>Click to add more outcomes ...</p>	<p>Outcomes are events or experiences that trial investigators measure because it is believed that they may be influenced by the intervention or exposure. Secondary outcomes are events or experiences other than the primary outcome(s) that will be used to evaluate the intervention(s), and that are specified in the study protocol.</p> <p>Enter the name of each secondary outcome of the trial, one at a time. Also provide all the timepoints at which this outcome is to be measured. Examples: Outcome name: cardiovascular mortality, Timepoint: 6 months; or Outcome name: functional status, Timepoint: 4 and 8 weeks.</p>

* All entries should accurately reflect the study protocol. If the study was approved by an ethics review board, entries should reflect the study protocol that received final approval from the ethics board.

+ Draft Trial Registration Data Set as of 15 December 2006. For the latest on the data set and trial registry project visit www.who.int/ictrp.