Clinical Trials FAQs

1. Why should clinical trials be registered?

Registration ensures that all clinical trials that are being conducted are in the public domain, although it does not guarantee that sponsors will publish their results in a publicly available site, or that published results are complete and accurate. Public knowledge that a trial is being conducted, however, should engender interest in its eventual results. Thus, at the least, it will be much more difficult for results of unsuccessful trials, or trials with adverse effects or harmful results, to be hidden.

If the trial demonstrates a sufficient benefit in treating the disease under investigation, and if there is an acceptable minimum of adverse effects, then a clinical trial can change the standards of medical therapy.

However, clinical trials can also have negative outcomes. Results of a clinical trial can show no statistically significant benefit of a new therapy over the previous standard or even a statistically significant worsening. Or, and this may only be apparent after a very large number of subjects have been exposed to the therapy, the new therapy may produce serious adverse effects in a small number of subjects, insufficient to halt its prescription for specifically indicated conditions, but sufficient to place substantial caution on its more indiscriminate use.

It is evident that investigators will want the positive results of their clinical trials to be widely announced. However, past experience has shown that sponsors of clinical trials, whether they are corporations, other institutions, or individual investigators, may not wish to make public the negative results of their clinical trials. Because biomedical investigators and clinicians, as well as the public, should have a right to know both the positive and negative results of clinical trials, registration of clinical trials before they begin recruiting subjects is required.

2. What kinds of trials should be registered?

- Any research study that prospectively assigns human participants or groups of humans to two or more health-related interventions to evaluate the effect on human outcomes.
- Prospective interventional studies of one or more patients where there is a concurrent comparison to untreated, placebo-treated or alternatively treated controls. This is the type of study that has required registration since 2006.
- The WHO definition of a clinical trial is: Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. This would include traditional Phase 1 Studies or interventional case series (which often use historical controls). Studies such as this would require registration according to the most recent WHO guidelines. ARVO recommends, but does not currently require registration of such studies. However, because the ARVO

policy could change to conform to the WHO guidelines, it is prudent to register these trials.

- Prospective clinical studies investigating the use in human subjects of therapies pharmaceuticals already on the market and/or comparisons with other therapies or pharmaceuticals on or being introduced to the market.

3. What is the deadline for registration?

Registration before the first patient is enrolled has been required since July 1, 2006 for clinical trials of 2 or more groups submitted to ARVO journals or educational meetings sponsored or co-sponsored by ARVO.

4. Where can I register my clinical trial?

The following sites are recognized primary registries by the World Health Organization and the International Committee of Medical Journal Editors.

http://www.anzctr.org.au/ (Australia/New Zealand)

http://www.chictr.org/ (China)

http://www.clinicaltrials.gov/ (US)

http://www.ctri.in/Clinicaltrials/index.jsp (India)

http://www.irct.ir (Iran)

http://isrctn.org/ (UK)

http://rctportal.niph.go.jp (Japan)

http://www.umin.ac.jp/ctr/ (Japan)

http://www.clinicaltrials.jp/user/cte_main_e.jsp (Japan)

http://www.trialregister.nl/trialreg/index.asp (The Netherlands)

http://www.slctr.lk/ (Sri Lanka)

https://eudract.emea.europa.eu/ (Europe)

5. What kinds of clinical studies would be required by the new WHO guidelines that did not previously require registration?

- Preliminary tests by an investigator of a medical or surgical therapy, even if there is no control group.
- Experimental treatments or other interventions that are compared to non-simultaneous (e.g. "historical") control groups.
- Prospective collection of data where there is an intervention.

6. What clinical studies do not need to be registered?

- Retrospective individual case reports or case series (retrospective studies do not require registration).
- Prospective data collection where there is no intervention (observational studies).

7. Does registration of clinical trials add an extra administrative burden to investigators and institutions?

Registration of a clinical trial on one of the sites listed above is a relatively straightforward process that is not excessively time-consuming. The World Health Organization (WHO) registration advisory group, cited in the New England Journal of Medicine, (see DeAngelis CD, Drazen JM, Frizelle FA, et al. Is this clinical trial fully registered? – A statement from the International Committee of Medical Journal Editors. N Engl J Med, 2005;293:2927-9), and on line at http://www.lillytrials.com/docs/ictrp_sag_meeting_april2005_conclusions.pdf, lists the series of 20 items that investigators will able to provide easily.

8. Who has responsibility for registering clinical trials?

The principal investigator (PI) of a trial is responsible for registering the trial. In a multi-institutional trial, the responsibility rests with the sponsor or trial organizers.

9. What happens if an investigator is unaware of the requirement?

Ignorance of the law is not an excuse." ARVO published the original registration policy on its Web site in November 2005, in the ARVO Winter Newsletter in January 2006, and in both IOVS and JOV. Updates to the policy will be published in IOVS, ARVONews, the call for abstracts publication and on the ARVO Web Site, as well as distributed to all annual meeting submitters. However, investigators, who feel that their unregistered studies are being unfairly penalized may appeal to the Editors-in-Chief of ARVO journals, or if appropriate, to the Annual Meeting Program Committee or Professional Development and Education Committee for abstract or program topic selection for educational meetings sponsored or co-sponsored by ARVO.

10. Will requiring registration of clinical trials make the reporting of data from such trials more transparent?

That, of course, is the hope of the ARVO Board of Trustees. No set of regulations is flawless, but

we strongly believe that by making the conduct of clinical trials and the reporting of their results available to the public we will reduce the possibility that negative and harmful results will remain hidden, to the detriment of all.

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Contact us at clinicaltrials@arvo.org with additional questions.