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International Clinical Trials Registry Platform
World Health Organization
Avenue Appia
CH-1211 Geneva 27
Switzerland

RE: PhRMA Second Round Comments on International Clinical Trials Registry Platform (ICTRP) Disclosure Timing

Dear Sir/Madam:

The following comments on the World Health Organization (WHO) "International Clinical Trials Registry Platform (ICTRP) Disclosure Timing," are submitted on behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA is a US-based trade association representing the leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. PhRMA's response to the WHO request for comments covers the topics of disclosure timing and the scope of trials to be registered.

Clinical Trial Transparency and Disclosure Timing

PhRMA companies have implemented a number of policies designed to improve the transparency of clinical research. These policies are embodied in the PhRMA "Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results" that were issued in 2002 and updated in 2004¹.

The pharmaceutical industry acknowledges the important public health benefits associated with public access to clinical trial information and is committed to increasing transparency. As noted by the European Federation of Pharmaceutical Industries and Associations (EFPIA), the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), the Japanese Pharmaceutical Manufacturers Association (JPMA) and PhRMA in the "Joint Position on the Disclosure of Clinical Trial Information Via Clinical Trial Registries and Databases²", the pharmaceutical industry is committed to the registry of all clinical trials, other than exploratory trials. This policy statement parallels that of the International Committee of Medical Journal Editors³.

Collectively, the two industry positions, referred to above, establish a firm foundation to evaluate the transparency of pharmaceutical company sponsored research. Transparency can only be assessed by examining the sponsor's commitment to timely posting results of the trial once it is completed and examining the results of the clinical trials in the full context of how they are registered. Registration of a clinical trial alone does not fully meet the full transparency

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objective. This WHO focus on registration and the associated data elements misses this important connection.

As noted in PhRMA's previous comments, sponsors will normally disclose all twenty data elements when registering clinical trials. There may be infrequent instances where companies may regard certain data elements as sensitive for competitive reasons and wish to delay public disclosure. The following five elements were identified as falling into this category: official scientific title of the study, specific mechanism or molecular identifier of the intervention(s), target sample size, primary outcome, and key secondary outcomes. One or more of these five sensitive data elements may be delayed at initial registration. However, if delayed, all data elements will be disclosed when the information is no longer commercially sensitive; generally before product approval, but at the latest, at first product approval.

PhRMA commented in depth during the first round of comments regarding the critical need to delay disclosure in certain instances. The following examples represent instances where certain fields would be considered highly proprietary during the drug development process and whose disclosure would be delayed.

1. A sponsor has a medication whose normal route of delivery is subcutaneous injection. They have developed a new approach that uses a device to administer the drug via inhalation. If a competitor has a similar drug in this therapeutic category, the sponsor may wish to maintain the confidentiality of the delivery technology. The sponsor would amend the title of the study so that the route of administration was not disclosed. (injected vs. inhaled insulin)
2. A sponsor is developing a new surrogate endpoint concurrent with developing a test to measure the surrogate and gain a patent on the new technology. The sponsor envisions the surrogate will reduce the time it takes to get the product approved by the FDA. Therefore the sponsor will delay disclosure of the surrogate as the primary outcome while it develops the novel approach.
3. A sponsor is pursuing an out of therapeutic class new indication for a marketed product. Other drugs in the class may also have a clinical effect on the new indication. The sponsor will delay disclosure of the drug name until later in development (bupropion for depression and smoking cessation).
4. A sponsor is developing a new formulation of a medicine that will permit weekly dosing versus daily dosing. This new dosing regimen will improve patient compliance and in early stage development is highly proprietary. The company will not want to disclose the formulation to potential competitors.

Finally, it is critical for WHO to consider the resource implications of trial transparency on all parties and not just the pharmaceutical industry. In the United States two academic clinical trials are filed with the Food and Drug Administration for every one commercially sponsored trial. This does not count the many observational trials (some of which are quite large with respect to number of patients enrolled) done by the public sector that don't need to be approved by a regulatory authority but would fall under these WHO disclosure requirements. Clinical trial transparency extends to all parties who conduct them. This should be viewed as an adjunct to adherence with Good Clinical Practice guidelines.

Scope of Trials to be Registered

It appears that WHO is moving toward requiring registration of **all interventional** trials⁴ (thus including, the early Phase 1 and 2 studies previously excluded in agreements with industry trade associations) and open-label (single treatment arm or non-comparator) studies. The addition of these 'interventional' studies adds little information to inform healthcare practice. Furthermore, PhRMA does not believe there is consensus on the language posted by WHO on this subject.

The inclusion of early phase trials is not in the best interests of the stakeholder community. The registration of Phase 1 trials may stifle pharmaceutical innovation, resulting in fewer new products reaching the market. Phase 1 trials are largely focused on the safety of new compounds in humans; are designed as dose toleration, ADME studies in healthy volunteers; and are not interventional, as they do not evaluate health outcomes. These trials do not result in information that can inform clinical practice. Therefore, we recommend that the WHO ICTRP register only those trials that inform health and healthcare practice and exclude exploratory trials as agreed upon at the April 2005 WHO Technical Committee meeting.

PhRMA supports this ongoing technical consultation as a means to establish a common approach to the registration of clinical trials and trusts that these comments are useful to the WHO consultation. In order to achieve a consensus, decisions regarding the Registry Platform should include industry representation and input. We look forward to continuing to work with the WHO in this process, which we trust will continue with full stakeholder involvement.

Sincerely,



1. <http://www.phrma.org/publications/publications//2004-06-30.1035.pdf>
2. Joint Position on the Disclosure of Clinical Trial Information Via Clinical Trial Registries and Databases, pg. 2:
http://www.ifpma.org/Documents/NR2205/joint%20position_clinical%20trials.PDF
3. DeAngelis, C, Drazen, JM, Frizelle, FA, et al. Clinical trial registration a statement from the International Committee of Medical Journal Editors, N Engl J Med 2004; 351: 1250-1
4. The language in the comment solicitation currently reads: "This responsibility extends to *all* trials, including early and late phase trials, trials of marketed and non-marketed interventions, randomized and non-randomized trials, etc." As noted in the text, PhRMA does not believe that there is consensus on this point and it is deserving of further discussion.
<http://www.who.int/ictrp/comments4/en/print.html>