

# PhRMA Clinical Study Results Database Proposal

## **Background**

The PhRMA *Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results* (the *Principles*) express the commitment of PhRMA member companies to communicate the results of clinical studies (clinical trials), both positive and negative:

“We commit to timely communication of meaningful results of controlled clinical trials of marketed products or investigational products that are approved for marketing, regardless of outcome.”

While publication of study results in a peer-reviewed medical journal is the preferred method of communication, the *Principles* recognize that not all studies will merit publication in such a journal and thus provide for alternate methods of communication, such as “abstract submission with a poster or oral presentation at a scientific meeting or making results public by some other means”

PhRMA believes an appropriately designed electronic database will also fulfill our members' commitment to communicate meaningful clinical study results. By providing a central, widely accessible repository for clinical trials results and a standardized format for the reporting of such results, a clinical study results database will serve the valuable function of making clinical study results on marketed products more transparent. PhRMA thus supports the establishment of a focused database as described below.

## **Proposal**

### **A. Elements of the Database**

The database should consist of three major elements:

- (1) a link to the electronic version of the drug label, where available;
- (2) a bibliography of articles on the drug in question that have been published in peer-reviewed medical journals together with a link to the actual article wherever possible; and
- (3) a complete summary of each hypothesis-testing trial (as defined below), regardless of outcome, that has not been published in a peer-reviewed medical journal.

The summary should be presented in a standardized, industry-accepted format (see Section B for details). It should provide scientific information in a non-promotional manner consistent with applicable regulatory requirements. This will both facilitate posting to the database and present the data clearly and concisely to those who might use the database. Additionally, given the importance of FDA approval and the FDA-approved drug labeling, the database should contain a

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<sup>1</sup> The PhRMA *Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results* can be downloaded from [www.phrma.org](http://www.phrma.org).

conspicuous notice referring users to the most current FDA-approved prescribing information on the drug in question, as well as the link to the drug label itself, where available.

### ***Results of Hypothesis-Testing Trials***

PhRMA believes that, consistent with the PhRMA *Principles*, the database should consist of the results of all hypothesis-testing clinical trials for products that are approved by the FDA for marketing in the U.S., regardless of the outcome of the trial or where the trial is conducted. Additionally, trials that are posted will have been sponsored by the drug manufacturer, and trials for which the sponsor was responsible for the study data.

Hypothesis-testing trials are defined in the PhRMA *Principles* as follows:

“Hypothesis-testing (also known as “confirmatory”) clinical trials are always well-controlled and are intended to provide meaningful results by examining pre-stated questions (i.e., hypotheses) using predefined statistically valid plans for data analysis, thereby allowing firm conclusions to be drawn to support product claims” (Question and Answer to PhRMA *Principles* p. 30)

The PhRMA *Principles* further explain that “[h]ypothesis-testing trials may occur at any stage of drug development, and include all phase III trials, some earlier phase trials and many trials of marketed products” Specific examples of hypothesis-testing trials are provided in the PhRMA *Principles* (see Question and Answer to PhRMA *Principles* p. 31).

Thus, PhRMA member companies are committed to submitting the results of all hypothesis-testing clinical trials on marketed drugs in the U.S. to a database regardless of whether the results are positive or negative. Furthermore, PhRMA commits to assessing this model for future expansion to a global database to include products marketed outside the U.S.

The principal focus of this database is to improve the transparency regarding clinical studies on marketed pharmaceuticals. It is the information on these products and studies that is of most use to physicians, patients, and other users and should be the primary focus of this database.

### ***The Current Approved Labeling***

The package insert provides the FDA-approved prescribing information and thus should be the physician’s initial focus of attention. Consequently, the database should contain a conspicuous notice referring database users to the most current FDA-approved prescribing information and a link to the electronic version of the prescribing information on the drug in question, where available (if the database later is expanded to apply internationally, the notice can be revised to refer people to the most current, locally approved prescribing information). In addition, the notice should state that the database is being made available for informational purposes only and that prescribing decisions should be made based on the approved package insert.

## **B. Overview of Reporting Format for Clinical Study Results**

PhRMA supports the posting of a summary that provides clear and accurate scientific information in a standard, non-promotional presentation format to those who use the database. PhRMA believes that the synopsis described in the E3 Guideline issued by the International

Conference on Harmonization (ICH) addresses this<sup>2</sup> ICH represents the pharmaceutical regulatory authorities and industry from the United States, European Union, and Japan. Its guidelines are developed via a consensus process and are incorporated into the regulatory requirements of those regions. The E3 synopsis is concise and should contain numerical data illustrating results, not just text or p-values.

### **C. Timing of Submission**

The FDA annual report regulations call for a “summary of completed unpublished clinical trials”<sup>3</sup> to be submitted to the Agency one year after completion of the trial(s).<sup>4</sup> PhRMA believes that this is a reasonable target for submitting study summaries to the database. References to scientific papers should be posted when they are published. It must be noted that the posting of any results of a clinical study may be delayed for those studies that have been or will be submitted to a journal for publication. Premature disclosure of results may compromise peer-reviewed publication, and pharmaceutical companies have no control over journal publication schedules which can involve lengthy review processes. The database will indicate those studies that have been submitted for publication following their conclusion. However, if a paper on the study in question has not been published within 1 year of the announced intent to publish (as indicated in the database), a summary will be posted to the database.

### **D. Location and Operation of Database**

PhRMA supports the creation and administration of an electronic clinical study results database by an independent, non-governmental third-party. The database should provide free access to posted clinical trials results by interested healthcare professionals, patients and others. The database should accept and post information about clinical study results sponsored by the company that holds the New Drug Application (NDA)/Biologics License Application (BLA) for the drug when presented in the template described above. In this way, the database administrator and company can assure users that the information is current and accurate.

However, the initial establishment of the database will be undertaken by PhRMA to bring this information forward in a timely manner as a service to the medical community.

### **E. Proposal Effective Date**

PhRMA member companies are encouraged to submit the above information on marketed products to the database as soon as possible following the October 1, 2004 implementation date. The goal of this industry effort is to have substantial information on all trials completed after October 1, 2002 (the effective date of the PhRMA *Principles*) by the 1 year anniversary of the establishment of the database. Companies would have the option to post information on studies of marketed products generated prior to the effective date of the *Principles*.

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<sup>2</sup> Structure and Content of Clinical Study Reports: Guideline approved by the International Conference on Harmonization; July 1996. This Guideline is available electronically on the FDA Internet Site at: <http://www.fda.gov/cder/guidance/iche3.pdf>.

<sup>3</sup> A trial is considered completed upon the last visit of the last patient enrolled in the trial.

<sup>4</sup> 21 C.F.R. §314.81(b)(2).

**Appendix – Illustrative Data Fields for the Summary (based on ICH E3 template)**

<i>These results are supplied for informational purposes only. Prescribing decisions should be made based on the approved package insert</i>		
<b>REFERENCEDIRECTING USERS TO APPROVED DRUG LABEL FOR PRESCRIBING INFORMATION</b> Link to drug label, where available		
Proprietary Drug Name	Generic Drug Name	Therapeutic area and FDA approved indications
Name of Sponsor/Company:		
Title of Study:		
Principal Study Investigators		
Study centre (s):		
Publication (reference, if applicable)		
Studied period (years): (date of first enrolment) (date of last completed)	Phase of development:	
Objectives		
Methodology:		
Number of patients (planned and analyzed):		
Diagnosis and main criteria for inclusion:		

Test product, dose and mode of administration, batch number:								
Duration of treatment:								
Reference therapy, dose and mode of administration, batch number:								
Criteria for evaluation: Efficacy: Safety:								
Statistical methods								
<p>SUMMARY –</p> <table> <tr> <td>CONCLUSIONS</td> <td>EFFICACY RESULTS:</td> </tr> <tr> <td></td> <td>SAFETY RESULTS:</td> </tr> <tr> <td>CONCLUSION:</td> <td></td> </tr> <tr> <td>Date of the report:</td> <td></td> </tr> </table>	CONCLUSIONS	EFFICACY RESULTS:		SAFETY RESULTS:	CONCLUSION:		Date of the report:	
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