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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Re: PhRMA Comments on Draft Guidance for Industry on Information Program on Clinical Trials for Serious or Life-Threatening Diseases: Implementation Plan
Docket No. 00D-1033, 66 Fed. Reg. 35798 (July 9, 2001)

Dear FDA:

On behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA), the PhRMA Clinical Trial Data Bank Work Group is providing comments on the above-referenced draft "Implementation Plan" guidance that was published in the July 9, 2001 issue of the *Federal Register*. That guidance provides the logistical and reporting instructions that will enable the private clinical research community, once it and the other outstanding draft "Information Program" guidance are finalized, to submit information on human clinical trials to the NIH/FDA Clinical Trial Data Bank authorized by Section 113 of the FDA Modernization Act (FDAMA §113, as codified in the Public Health Service Act at 42 U.S.C. §282(j)). As stated in our previous comments to NIH and FDA on other components of the Data Bank program (e.g., PhRMA May 30, 2000, comments on the March 29, 2000 draft "information Program" guidance), we feel the public health can benefit from giving patients increased access to clinical trials, with appropriate safeguards and procedures.

PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer, healthier and more productive lives. Investing over $30 billion this year in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures. Our member companies are a leading source of new drug research and development, and they look forward to participating in the Data Bank program following issuance by FDA of the final Implementation and Information guidances.

The anticipated benefits of the Data Bank include increased patient access to clinical trials, together with, it is hoped, more patients enrolling in investigational drug trials, more efficient development of new and innovative therapies and ultimately more options and improved quality of life for patients.

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While seeking to achieve these benefits, it remains important for NIH/FDA to take care to ensure that the information disseminated to the public is of a rigorous nature (relevant, timely and accurate, as well as useful and beneficial to patients), and that any program that facilitates increased access neither compromises sponsor data that is proprietary (and should not be required to be reported in the data bank), nor creates administrative burdens that delay the drug development process.

The proposed approach, including the Draft Web-based Protocol Registration System (PRS; see http://prsinfo.clinicaltrials.gov/), provides a promising and workable framework for achieving all of these benefits and goals. Following are a number of questions and concerns that need to be addressed to assure that the final implementation plan guidance and overall Data Bank program address the needs of patients, consistent with the statutory scheme outlined by Congress in FDAMA §113.

Startup Issues

The final guidance needs to specify a startup compliance date for the completion of initial information submission to the PRS. The initial reporting of any covered, and presumably ongoing, studies will present a considerable one-time administrative burden that largely cannot be addressed until the final guidance becomes available. 60 days following publication of the final guidance in the Federal Register would provide a minimally reasonable period.

The draft guidance is helpful in specifying that the deadline for submission of information to the PRS is "no later than 21 days after the trial is first open for enrollment." The final guidance should also specify which, if any, clinical trials are required to be included if, as of the startup compliance date, trials are beyond the '21 days after the trial is first open for enrollment' stage. At a minimum, the final guidance should specify that trials where enrollment has closed are not subject to reporting.

Only U.S. Trials Are Covered

Only clinical trials with U.S. trial sites can be required to be reported under FDAMA §113, in keeping with the Congressional purpose – to facilitate enrollment of subjects in clinical trials in the United States. The guidance document should clarify that clinical trials conducted outside the U.S., and foreign sites of U.S. clinical trials, are not required to be included.

Clearly Identify Mandatory v. Optional Data Elements In The PRS

The PRS website (and any hard-copy materials) should more clearly identify which data elements are optional (or, if more easily accomplished, which elements are mandatory). This is particularly important for any fields that

preclude completion or submission if left blank. If not resolved, this could result in the improper rejection of submissions by sponsors who are offering data that satisfies the statutory requirements.

Updating and Removing Data

The final guidance should specify a timeframe of no less than 30-day intervals for required updating of information. The final guidance should also specify how quickly information entered into the PRS will be available on the public web site.

The final guidance should also specify how and when information will be removed from the PRS.

Providing Information To The PRS

To help assure the security and integrity of the data, no submissions from unauthorized sources/individuals should be allowed. Organizations reporting data should be required to specify whether single or multiple individuals will be authorized to enter data, either with regard to all of the organization's trials, or specific trials.

In addition to direct web-based input, there should also be provision for direct computer-to-computer transfer of information (to accommodate and facilitate automation of the process).

Multiple Trial Sites

Sponsors should have a clearly identified option for identifying a central contact for large trials with multiple sites. Provision should be made in such cases for more generally identifying the location of the various sites (e.g., cities where institutions are involved in the study), while alerting interested patients to obtain detailed information from the central contact. This would also help minimize the administrative burden in keeping the data current (allowing one central site to be updated, rather than individually maintaining multiple sites with similar information, such as completion of enrollment). If sponsors are given the option of maintaining multiple trial data sites, provision should be made to allow single-input changes to multiple PRS sites without having to navigate the individual screens of each site.

Need To Clarify Coordination With Other Data Banks

The draft guidance states that until the final guidance document is available, sponsors should continue to follow current procedures for the AIDS Clinical Trials Information Service (ACTIS). This implies that sponsors who submit clinical trial information to the FDAMA §113 Data Bank need not provide duplicative submissions to ACTIS and other HHS clinical trial websites. The final

guidance should specify that provision has been made to avoid duplicative submissions.

Particular Data Elements

Status page; "Verification Date." The guidance should clarify the definition of this term (presumably the date information was last updated by the sponsor).

Status page; "Start Date." This optional element would be better styled "Estimated Start Date."

Status Page; "Completion Date." This optional element would also be better styled "Estimated Completion Date."

Design page; "Control." This data field should allow for multiple selections/entries (e.g., study containing both placebo and an active control).

Design page; "Endpoints." This data field should allow for multiple selections/entries, or if this is required to be a single entry, additional guidance should be given such as "Please select the most appropriate endpoint for this study."

Locations page. This page does not currently seem to allow for the identification of a central contact person for all trial sites. Additionally, the navigation to add additional sites is not clear in the tour. The application should provide for the easy addition of new sites/locations. (See also discussion above, re "Multiple Trial Sites").

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The PhRMA Clinical Trial Data Bank Work Group appreciates the opportunity to comment on the draft Implementation Plan guidance. The Work Group is available at your convenience to discuss these comments, and to provide any additional support and information that would be useful for completing the implementation of the FDAMA §113 Clinical Trial Data Bank.

Sincerely Yours,

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