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January 6, 2003

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

Re: Docket No. 2003D-0497, CDER 2003163. Draft Guidance for Industry on Pharmacogenomic Data Submissions; 68 Federal Register 62461-62463 (November 4, 2003)

Dear Sir/Madam:

The following comments on the above draft guidance are submitted on behalf of Eli Lilly and Company. In preparation of the final guidance, the following comments are submitted for Agency consideration.

General Comments

Lilly commends FDA for taking the initiative with this draft Guidance to work with sponsors and the academic community to facilitate scientific progress in the field of Pharmacogenomics as it relates to future regulatory decisions and policy-making.

Lilly welcomes the draft guidance's intent to facilitate the proper framework for Voluntary Genomic Data Submission (VGDS) and feels the goal for such submissions could be successful with further clarification within the guidance.

To help facilitate VGDS, the draft guidance should emphasize that proprietary interests of the sponsor's data submitted under the VGDS will be protected and under what defined systems.

Lilly feels the role of the Interdisciplinary Pharmacogenomic Review Group (IPRG) needs to be better described within the guidance. The relationship between the IPRG and the sponsor needs to be defined, along with the individuals who will make up this review group. Clarification on how the IPRG will communicate with each component of FDA, including the Review Divisions, on decisions, cross-learning, and policy-making is needed. Lilly understands FDA's intent to state that VGDS would not be the basis for regulatory-decision

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making within the draft guidance. On the other hand, the guidance goes on to state that if evidence is collected across companies to indicate a potential valid biomarker, some action could take place. The guidance should be worded appropriately as to not sound contradictory in this intent to take possible action, when appropriate, when collective knowledge is known.

Lilly agrees with the FDA's suggestion of a flexible format for VGDS and FDA's intention not to make the process overly burdensome.

FDA should consider how the guidance will impact other regions and should collaborate in the near future with global regulatory agencies.

Specific Comments

Within the introduction, the guidance specifically states it does not address data submitted for proteomics. However, it does not indicate that a new guidance will be issued for pharmacoproteomics. Because much work is conducted in this area and the intent of the data submissions should be similar to this draft guidance, a comment to address pharmacoproteomics is warranted.

Definitions

Decision-making: The guidance uses *decision-making* and *regulatory decision-making* throughout the document. A consistent use of the terminology should be adopted or better clarification should be made within the guidance. Regulatory decision-making is quite different from clinical/drug development decision-making. Each could result in GDS.

The NDA/BLA algorithm clearly outlines when a data submission would be required under current regulations. However, when *Decision-making for clinical trials* under the IND is made, it is less clear what meets current regulatory requirements. It would be helpful if the guidance would emphasize *impactful drug development decision-making* from PG research that would require a data submission versus submissions under VGDS.

Biomarkers: Lilly generally agrees with the approach FDA has taken regarding consideration of a valid versus probable biomarker. Because it will be increasingly difficult to always state what is widely accepted in the scientific community as a valid biomarker, or what defines "well-established characteristics", it would be helpful for the guidance to be up front in stating that the FDA will be open to work with the sponsor on its proposed known or probable biomarker while working under the framework proposed in the guidance.

Co-development

The guidance states that an additional guidance will be issued to address co-development of diagnostic tests and drugs in the near future and encourages sponsor's to proactively collaborate with the appropriate Center (lines 207-215).

The new guidance should address which Center at FDA will lead the initiative for a true coordination of efforts for the final drug product. This information will be critical to enable sponsors to collaborate appropriately with the Agency early in the drug development process.

IPRG

With the introduction of the IPRG (lines 236-242), additional effort needs to be placed here in describing the true role of this group. A description of who will make up this review board and how they will interact with the sponsors for questions or consultations related to PG data submissions are needed. It is also difficult to grasp how the IPRG will interact with the drug product's FDA Review Division. Specifically, the guidance discusses that the IPRG will have serve in an advisory capacity to the Review Divisions. Lilly suggests that the guidance further clarify what this role entails and in what situations might a consultation be warranted. Furthermore, the guidance should specify how any outcomes from a consultation would be communicated to the sponsor. Finally, the guidance should specifically address how cross-learning will continue between Divisions and the IPRG by gathering and reviewing information on voluntary submission data.

Data Submissions

The guidance repeatedly states VGDS will not be used for regulatory decision-making. To ease sponsors' concerns about voluntary submissions, it would be useful for FDA to be explicitly state in the guidance their intent to render required submissions or additional work to the sponsor when additional information becomes available. It would be helpful to know who at FDA will be communicating to the sponsor and what type of communication the sponsor will receive.

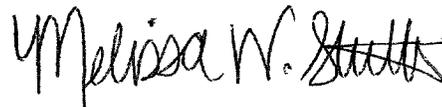
The guidance should generally address what expectations, if any, are required regarding the quality of the VGDS, specifically regarding the use of data generated from non-GLP studies.

Eli Lilly and Company thanks the FDA the opportunity to comment on this draft guidance. Furthermore, we are prepared to respond to any question the Agency might have regarding our response.

Sincerely-



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