November 16, 2001

GlaxoSmithKline

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

Re: Docket No. 01D-0269
Draft Guidance for Industry on the Clinical Studies Section of Labeling for Prescription Drugs and Biologics – Content and Format

Dear Sir/Madam:

GlaxoSmithKline (GSK) appreciates the opportunity to comment on the *Draft Guidance for Industry on the Clinical Studies Section of Labeling for Prescription Drugs and Biologics – Content and Format* and applauds the Agency's efforts to make prescription drug labeling a better information source for health care practitioners. In the Background document, the Agency acknowledges that the clinical studies section of the labeling typically contains large amounts of important and complex information and that the Agency is striving for consistency in format and content across product classes and individual medical products. To improve the likelihood of this outcome, the guidance document should be explicit and unambiguous. To this end, GSK recommends additional clarification on the following points in the final guidance document.

Scope

The draft guidance document is unclear as to whether it applies to all existing labeling or only labeling for those NDAs approved after the issuance of the final guidance. GSK would strongly recommend that the final guidance clearly state that it only applies to original New Drug Applications for new chemical entities. Previously approved products have undergone comprehensive reviews by the Agency. Any revision of the clinical studies section subsequent to approval of labeling would potentially alter the intent of the original reviewers. Therefore, to avoid any misrepresentation of the original review, the effect of this guidance should not be retroactive.

Limitations of Effectiveness

The final guidance should clarify the Agency's expectations around "clinical studies that provide important information about the limitations of effectiveness." As limitation of effectiveness are often addressed in the INDICATIONS and USAGE section, redundancy in the Clinical Studies section would unnecessarily lengthen the labeling.

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Comparative Data

GSK notes the Agency's stated desire to raise awareness of the implications for product promotion of information contained in the Clinical Studies section. Therefore it is important that the sections that address this issue are consistent and unambiguous. Section III.A.4, *Comparative Data*, attempts to delineate when a comparator should be identified and respective results provided. The guidance recommends inclusion only when the comparator information is "essential to a clinician's understanding of the drug's effects" or "when an active control, non-inferiority trial is critical to establishing effectiveness of a new drug". In contrast, Section III.C.3, *Describing Results Within Treatment Groups*, advises results for both the study drug and comparator *should be* (emphasis added) presented, because the comparison between treatment groups is critical to an understanding of the treatment effect. Additional discussion about inclusion of comparative data should be provided in the final guidance.

Quality of Life

The introduction to the guidance indicates the overriding objective in labeling is to provide the information that is most useful to prescribers in treating patients. In the treatment of some diseases (e.g., cancer) the impact of a drug on quality of life is an important consideration for both the patient and the prescriber. For this reason, the guidance document should delineate the type and extent of data from quality of life studies that would be allowable in the Clinical Studies section.

Graphs Most Commonly Used (Section II.B., APPENDIX)

The examples included in the guidance are beneficial; however, to reinforce section II.C, the features of a good graph could be incorporated in all sample graphs in section II.B. of the appendix. Alternatively, several examples containing the appropriate features could be provided in section II.C.

Cumulative Distribution Plot (Section II.B., APPENDIX)

Because individual patient data cannot be readily viewed in the graph, consideration should be given to changing the first sentence of the description of the cumulative distribution plot to "summarizes population data". To ensure accuracy, several modifications should be made to the remainder of the text. The second sentence should read, "The *data line* represents a cumulative percentage of subjects with a response less than or equal to the effect shown on the x-axis." The last sentence in the paragraph should read, "A response of *x or less* was seen by a percent of the patients on New Drug and b percent of the patients on Placebo.

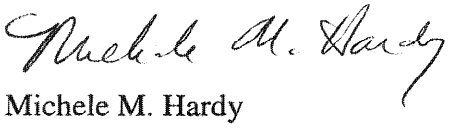
Features of a Good Graph (Section II.C., APPENDIX)

- In bullet four, "Axis Scale," the guidance discourages differences in scales for labels of drugs in the same class, to avoid misleading comparisons. Consideration should be given to eliminating this statement in the final guidance. Comparisons between drugs are inappropriate and potentially misleading unless the comparison is within the same study. The inclusion of this statement would appear to support inappropriate comparisons between studies.

- In "Uncertainty of Treatment Effect," the guidance provides for use of confidence interval or p-valve as appropriate measures of uncertainty. However, Section III.C.2, Treatment Effect, Uncertainty of Treatment Effect, considers use of a p-value alone potentially misleading. This discrepancy should be resolved in the final guidance document.

In summary, GSK supports the Agency's efforts to make prescription drug labeling a better information source for health care practitioners. We would be happy to discuss our comments on this guidance and other labeling documents with the Agency.

Sincerely,



Michele M. Hardy
Director, Strategic Product Labeling
Regulatory Affairs

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