



September 15, 2000

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

RE: Content and Format of the Adverse Reactions Section of Labeling for Human Prescription Drugs and Biologics

Docket No. 00D-1306

Dear Ms. Jones:

On behalf of ALZA Corporation, I am submitting comments to the Draft Guidance on the Content and Format of the Adverse Reactions Section of Labeling for Human Prescription Drugs and Biologics published in the Federal Register dated June 20, 2000. ALZA Corporation (ALZA) commends the Food and Drug Administration (FDA) for proposing to revise the ADVERSE REACTIONS section of the approved product labeling. ALZA agrees with FDA that the approved product labeling could be clearer, more informative, and more accessible. Avoiding long and exhaustive lists of every reported adverse event should help in that regard. The presentation of data that are infrequent and minor or not plausibly related to drug therapy makes it difficult for the health care professional to discern the meaningful information from the current labeling format. By restricting the information presented in this section to what is pertinent to the safe and effective use of the drug, FDA will enhance the usefulness of this section for the health care professional and the patient.

II. ADVERSE REACTIONS SECTION – CONTENT AND FORMAT

A. Overview—Content and Format

Although conceptually appealing, this subsection seems redundant and summarizes information presented elsewhere, making the document more difficult to use. This subsection would highlight information presented later in a drug’s adverse reaction profile, as well as information presented in other sections of the labeling, but it would not summarize all information contained in the ADVERSE REACTIONS section. According to the Draft Guidance, these listings should cross-reference more detailed discussions of the listed reactions in other sections of the labeling or elsewhere in the ADVERSE REACTIONS section.

Furthermore, this Overview subsection would highlight select information contained elsewhere in the labeling. Highlighting some adverse events or some select information concerning AEs may increase the risk that health care professionals may not read all the

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information necessary for the care of a particular patient. The health care professional could assume that the most important information is presented in the Overview and ignore the references to the more detailed information presented in other sections of the labeling. Therefore, ALZA recommends against the selective presentation of information concerning the adverse events associated with the use of a pharmaceutical product in an Overview of the ADVERSE REACTIONS section.

B. Discussion of Adverse Reactions Information – Content and Format

ALZA agrees with FDA that describing the database before presenting the adverse reaction data is important. Providing the health care professional with information concerning the overall exposure, composition of control groups, and the basis for including adverse reactions in the table is critical to evaluating the risk associated with the use of the product. We also agree that to obtain more precise adverse reaction rates, it is often important to pool data from studies that are not identical in design. Because an overall pooling of data is probably the most clinically useful representation of a drug's adverse reaction profile, ALZA recommends that the data pool include all relevant clinical trials, not merely the placebo-controlled and/or dose-response trials suggested in the guideline.

IV. PRESENTING DATA IN THE ADVERSE REACTIONS SECTION OF LABELING

Comparative Safety Claims

ALZA agrees with FDA that “adverse reaction rates from placebo or other comparator arms (e.g., active control, different dosage groups) should be included in the table unless inclusion of such rates would be misleading (for example, if a suboptimal or excessive dose of an active comparator was used).” We believe further that any study that compares comparable doses of active agents and is adequately powered to compare adverse events should be included in the ADVERSE REACTIONS section of the labeling. In many cases, this type of information would be very useful to the health care professional because it provides a benchmark with a drug currently in use, and allows an evaluation of the new drug based on substantial evidence with an active comparator. The omission of these types of data would be a disservice to health care professionals. ALZA supports having sponsors describing the type of comparison made between the new drug and the active comparator, including the doses used for each drug and the duration of therapy. Such a presentation would not be misleading, but would provide health care providers with additional valuable information concerning adverse events. Therefore, ALZA recommends including comparisons of adverse events for both the new drug and an active comparator with a complete description of the conditions under which the products were compared.



If you should have any further questions or comments, please contact me by telephone at (650) 528-3056 or by facsimile at (650) 237-2851.

Sincerely,

A handwritten signature in black ink that reads "Stephen W. Sherman". The signature is fluid and cursive, with the first and last names being more prominent.

Stephen W. Sherman
Director, Advertising and Labeling
Regulatory Affairs

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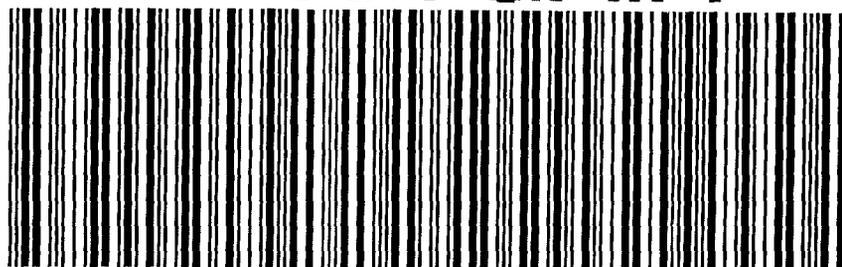
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