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May 5, 1999

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5600 Fishers Lane, Rm. 1061  
Rockville, MD 20852

0550 '99 MAY -6 09:10

SUBJECT: Docket 98D-1168  
DRAFT Guidance for Industry: ANDAs: Impurities in Drug Products

Dear Sir or Madam:

We refer to your January 5, 1999 Federal Register notice requesting comments on the draft guideline "ANDAs: Impurities in Drug Products," Docket No. 98D-1168. We appreciate this opportunity to provide comments, which include input from our colleagues at our world headquarters in Beerse, Belgium. In general, the guidance is in line with the ICH Q3B document, "Impurities in New Drug Products." In addition, we note the following comments (in **bold face type**) for your consideration.

Line 84-85, "... identification should be attempted for those degradation products that are suspected to be unusually potent, producing toxic or significant pharmacologic effects at levels lower than indicated."

**Although this text is identical to the Q3B text, we question how information about unusual potency or toxicity can be obtained without identifying the degradant. That is, identity must be known before conclusion or suspicion of abnormal toxicity.**

Line 225-231 and 275-278, "A degradation product present in the generic drug product would be considered qualified if the amount of identified degradation product in the generic drug product is no more that two times the amount of the corresponding degradation product in the RLD..... (2) the safety studies to qualify the RLD generally are carried out at significantly higher levels that the acceptance criteria."

**From a scientific and safety perspective, we see no rationale to apply a looser qualification requirement for a generic product. Further, the assumption of justification (2), that higher levels are qualified in RLD safety studies, cannot be substantiated for every case. In addition, this assumption implies an added burden on the RLD sponsor.**

We again thank the Agency for the opportunity to comment on this draft guideline and look forward to a continuing dialog as the Agency finalizes its guidance on this topic. Please contact me at (609) 730-3081 if you have any questions.

Sincerely,

Sheila Alexander

Asst. Director, Technical Regulatory Affairs

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98D-1168

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