



Abbott

Medical, Scientific and Regulatory Affairs

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Division of Dockets Management (HFA-305)
The Food and Drug Administration
5630 Fishers Lane, room 1061,
Rockville, MD 20852

Re. **Docket No. 2005D-0312 - Draft Guidance for Industry on Abbreviated New Drug Applications: Impurities in Drug Products; Chemistry, Manufacturing, and Controls Information.**

Abbott Laboratories (Abbott) is pleased to have the opportunity to comment on the Draft Guidance on Abbreviated New Drug Applications: Impurities in Drug Products: Chemistry, Manufacturing, and Controls Information, published in the Federal Register on August 29, 2005. The following comments on this draft guidance are provided on behalf of Abbott.

Section III. B. Setting Acceptance Criteria for Degradation Products

Lines 119-121. It is stated in the draft guidance, *"If there is a monograph in the USP that includes a limit for a specified identified degradation product, we recommend that the acceptance criterion be set no higher than the official compendial limit."*

Comment: This is not consistent with the FDA typically not allowing companies to raise the limit if their process data supports a lower degradation product limit. We recommend changing the sentence to: "We recommend that the acceptance criterion be set no higher than the official compendial limit or a limit supported by process data, whichever is lower."

Lines 123-125. It is stated, *"If the level of the degradation product is above the level specified in the USP, we recommend qualification. Then, if appropriate qualification has been achieved, an applicant may wish to petition the USP for revision of the degradation product's acceptance criterion."*

Comment: **Attachment 1** in the draft guidance provides a flow diagram for ***“Identification and Qualification of Degradation Products in Generic Drug Products.”***

According to the flow diagram, those degradation products that require genotoxicity studies, general toxicity studies, or other specific toxicity endpoints may be qualified for generic drug products provided no “clinically relevant adverse effects” are found. With respect to this section of the diagram, we have the following comments:

- 1) It is unclear how a determination is made regarding the *clinical relevance* of the results of the toxicology studies described or who (the sponsor or the Agency) makes that determination.
- 2) The conclusion that such degradation products are qualified for generic products under 505(j) appears to be inconsistent with the statutory requirements for ANDA submissions. We agree with the previous iteration of this flow diagram (December, 1998 draft guidance) which described degradation products for which additional toxicity testing is needed as **“qualified but not 505(j).”** We recommend restoring that language to the revised chart.

Line 138. In the sentence, *“Although routine manufacturing variations are expected, significant variation in batch-to-batch degradation...”*, the word “routine” should be changed to “normal” to be consistent with the ICH guideline.

Section IV.B. Qualification Procedures

Lines 206-208. It is stated in the draft guidance, *“A degradation product present in the generic drug product is considered qualified if the amount of identified degradation product in the generic drug product reflects the levels observed in the corresponding approved human drug product.”*

Comment: The wording “reflects the levels observed” is not specific enough. We recommend changing to “the levels are less than or equal to those in the corresponding approved human drug product, adjusted for daily dose.”

Lines 216-218 are a repeat of lines **212-214**.

Line 222. It is stated in the draft guidance, *“Toxicity tests are least preferred method to qualify degradation products.”*

Docket No. 2005D-0312

Comment: This statement makes toxicity tests sound as if they are not technically acceptable, when the opposite is true. A better explanation should be provided for avoiding this type of tests.

We thank the Agency for their consideration of our comments. Should you have any question, please contact Ivone Takenaka, Ph.D. at (301) 255-0080 or by FAX at (301) 255-0090.

Sincerely,



Douglas L. Sporn