



**ABBOTT LABORATORIES**  
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September 18, 2000

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

RE: International Conference on Harmonisation; Draft Revised Guidance on  
Impurities in New Drug Products  
Docket No. 96D-0009

Dear Sir:

Abbott Laboratories is pleased to have the opportunity to provide comments on the revised draft guidance entitled "Q3B (R) Impurities in New Drug Products" published on July 19, 2000, in the Federal Register. We propose the attached modifications to the text to help clarify some ambiguities and suggest that the glossaries for both ICH Q3A and Q3B are reviewed to insure harmonization between the documents.

On behalf of the 54,000 Abbott employees who help produce healthcare products marketed in more than 130 countries worldwide, we thank you for your consideration of our comments. Please contact Dr. Gopi Menon, of Abbott Laboratories, should you have any questions (847-937-7437 phone, 847-938-6092 fax).

Sincerely,

Douglas L. Sporn

cc: Gopi Menon, Abbott Laboratories  
Thomas White, PhRMA

96D-0009

CS

**SPECIFIC COMMENTS**

- (1) Clarification is needed between a statement in the ICH Q3B Scope and Section 2.4 dealing with the reporting of Total Impurities and Total Degradation Products.

**EXAMPLE**

Section 1.0 Scope, p.5 (ICH Q3B)

"Impurities present in the new drug substance need not be monitored or specified in drug products unless they are also degradation products (see ICH Q6A guidance for specifications)."

Section 2.4 Specification Limits for Degradation Products, p. 7 (ICH Q3B)

"All impurities at a level greater than (>) the reporting threshold should be summed and reported as Total Impurities."

**DISCUSSION**

The ambiguity between the Scope statement and the Section 2.4 requirement may be eliminated with the addition of the intended exception as stated in the Scope statement. Therefore the following proposal is made:

**PROPOSED CHANGE**

2.4 Specification Limits for Degradation Products (p. 7)

"All ***degradation product impurities***, at a level greater than (>) the reporting threshold should be summed and reported as Total ***Degradation Products***."

- (2) Clarification and harmonization of rounding rule applications as they apply to ICH Q3A and ICH Q3B is needed. An example:

EXAMPLE

Section 2.6 New Degradation Products. P.8 (ICH Q3B)

"In this event, these new degradation products should be identified and/or Qualified. Such changes call for qualification of the level of degradation Product unless it is present at a level of not more than (ls-thn-eq>) the threshold values as set out in Attachment 1."

DISCUSSION

The need for qualification can be impacted by where the rounding of threshold values takes place. For example, a new degradant product value of 0.149 could be rounded to 0.1. If the specification is 0.1, and the threshold is 0.1 (in the case where the dose is > 2 g), there would not be the need to qualify. In this case we believe the rounding of values should be performed prior to the determination of the need to qualify- these changes should be considered and applied to both Q3A and Q3B.

PROPOSED CHANGE

Section 2.6 New Degradation Products. P.8 (ICH Q3B)

"In this event, these new degradation products should be identified and/or qualified. Such changes call for qualification of the level of degradation product at a level, after rounding, of not more than (ls-thn-eq>) the threshold values as set out in Attachment 1."

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402