

PHARMACIA

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September 13, 2000

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

Re: ICH Q3A(R) Impurities in New Drug Substances, Step 2 Document
(Docket No. 94D-0325)

Pharmacia Corporation would like to take the opportunity to comment on the referenced document. In general, we find the draft-revised document to be a very useful guide and agree with many aspects of it. There are a few areas that we believe need to be modified or clarified. Please find enclosed two copies of our comments for your consideration.

We thank the agency for the opportunity to provide comment.

Respectfully submitted,



Patrick Blacha
Director, Technical Services (Searle)
Pharma Global Quality & Compliance

Attachment

94D0325

C8

ICH Q3A(R) STEP 2 DOCUMENT
(Docket No. 94D-0325)

Reporting Impurity Content of Batches (page 45087)

- In the first paragraph, sixth sentence, modify the sentence “All impurities at a level greater than (>) the reporting threshold should be summed and reported as Total Impurities.”

All impurities at the reporting threshold level or greater should be summed and reported as Total Impurities.

Specifications for Impurities (page 45087)

- In the third paragraph, second sentence, clarify the sentence “Where there is no safety concern, impurity specifications should be based on data generated on batches of the new drug substance manufactured by the proposed commercial process, allowing sufficient latitude to deal with normal manufacturing and analytical variation, and the stability characteristics of the new drug substance.”

The attempt to clarify the expectation for new drug substance impurity specifications when there is no safety concern is appreciated. However, the use of the terminology “sufficient” and “normal” may lead to inconsistent interpretation.

- In the third paragraph, third sentence, clarify the sentence “Although normal manufacturing variations are expected, significant variation in batch-to-batch impurity levels may indicate that the manufacturing process of the new drug substance is not adequately controlled and validated (see ICH Q6A guidance on specifications).”

The attempt to clarify the expectation for new drug substance impurity specifications when there is manufacturing variation is appreciated. However, the use of the terminology “normal” and “significant” may lead to inconsistent interpretation.

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Docket No. 94D-0325

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