



Pharmaceuticals

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

Nutley, June 27, 2000

Re: Docket No. 93D-0139
International Conference on Harmonisation
Draft Revised Guidance on Q1A(R) Stability Testing of New Drug Substances and Products

Dear Sir or Madam:

Hoffmann-La Roche hereby encloses its comments to the referenced draft guidance published in Federal Register April 21, 2000.

Yours sincerely,

Hoffmann-La Roche Inc.

Kathleen Schostack, Ph.D.
Director
Technical Regulatory Affairs

KS/jaw
Attachment

HLR #2000-1622
FEDERAL EXPRESS PRIORITY #7923 4829 1460

93D-0139

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GENERAL COMMENT

FDA should clarify the relation, or lack thereof, between the ICH Draft Revised Guidance on Q1A(R) Stability Testing of New Drug Substances and Products and FDA's Draft Guidance to Industry for Stability Testing of Drug Substances and Products. It has been some time since FDA submitted its' draft guidance for comment. Because there is much overlap in the two draft guidances, it is not clear if the ICH revised guidance is intended to replace the previous FDA draft guidance or if FDA will continue with implementation of its own stability guidance.

SPECIFIC COMMENTS

NOTE: Roche's Comment regarding the current text for certain sections is listed below. Addition of new text under the Suggested Revision has been underlined.

Drug Substance

1.1.1.1.1 Selection of Batches

Comment: The description of batches which may be used for supporting stability data should provide for use of batches from an alternate process for consistency with current practice.

Suggested revision: Supporting stability data may be provided using stability data generated from batches of drug substance on a laboratory scale and/or batches of comparable quality manufactured by alternate processes.

1.1.1.1.2 Test Attributes, Test Procedures, and Test Acceptance Criteria

Comment: The limits for acceptance criteria are derived by considering both safety and the expected commercial quality of the drug substance. Although safety qualification is based on batches used in preclinical and clinical studies, the expected quality of the commercial material is represented by the primary stability batches.

Suggested revision: The acceptance criteria should be derived from batches of the material used in the preclinical and clinical studies and also by the results observed in primary stability studies supporting the application.

1.1.1.1.3 Evaluation

Comment: The retest period for a drug substance is generally determined using long-term stability data for batches stored at the recommended storage condition. Statistical analysis of drug substance stability data is not typically performed when determining the retest period. Addition of this requirement as described in the draft guidance would present an additional regulatory burden and would not provide any added assurance

regarding the quality and stability of the drug substance.

Suggested revision: References to statistical analysis of drug substance stability data should be deleted or clearly marked as optional.

Drug Product

1.1.1.1.4 Test Attributes, Test Procedures, and Acceptance Criteria

Comment: The limits for acceptance criteria are derived by considering both safety and the expected commercial quality of the drug substance. Although safety qualification is based on batches used in preclinical and clinical studies, the expected quality of the commercial material is represented by the primary stability batches.

Suggested revision: It should include specific upper limits for degradation products, the justification for which should be influenced by the levels observed in material used in preclinical and clinical trials and primary stability studies.

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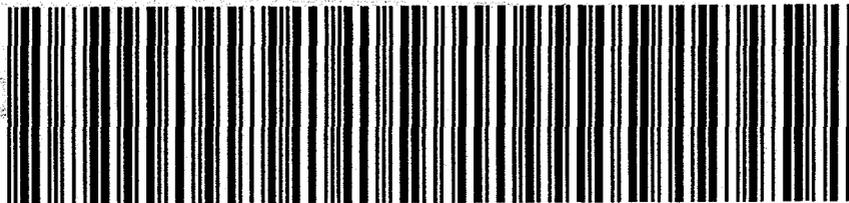
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