M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: March 6, 2001

To: Dockets Management Branch (HFA-305)

From: Melissa Lamb
Office of Generic Drugs

Subject: AAPS Workshop on Successful US and EU Registrations

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

Title of Presentation: Specifications for Simple Dosage Forms

Presented for: AAPS Workshop on Successful US and EU Registrations

Date Presented: May 3, 2000

Presented by: Devinder S. Gill, Ph.D.
Team Leader

Number of Pages: 20

Melissa Lamb

Attachment

90S-0308

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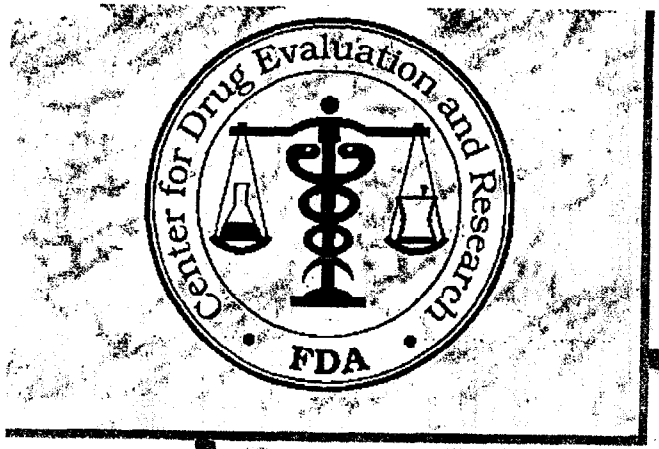

AAPS Workshop on Successful US and EU Registrations

SPECIFICATONS FOR SIMPLE DOSAGE FORMS

FDA Point of View

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May 3, 2000

ICH Q64

- Specifications

Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances

INTRODUCTION(Cont'd)

- Conformance to Specifications

  It means that the drug substance and/or drug product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria.

  Specifications are critical quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities as condition of approval.

TOTAL CONTROL STRATEGY

- For products, give relevant technical specifications, using as many slides as necessary.
- For services, detail the terms and conditions under which the service is offered.

SCOPE OF THE GUIDELINE

- Specifications assuring the quality of the new drug substance and the new drug product at release and during shelf life
- Addresses only the marketing approval of new drug products
- Universal acceptance criteria
- Specific acceptance criteria
- Application of new technologies if justified

SCOPE OF THE GUIDELINE Cont'd

- Covers solid oral dosage forms, oral liquids, and parenterals
- Does not address:
  - Clinical research
  - Biologicals
  - Biotechnological products
  - High molecular weight peptides and polypeptides
  - Oligonucleotides
  - Radiopharmaceuticals
  - Fermentation products
  - Herbal products
  - Crude products of animal or plant origin

UNIVERSAL TESTS AND CRITERIA

- Description
- Identification
- Assay
- Impurities

SPECIFIC TESTS AND CRITERIA

- Drug product testing based on dosage forms
  - Solid orals
  - Oral liquids
  - Parenterals

SOLID ORALS

- Specifications
  - Dissolution
  - Disintegration
  - Hardness/Friability
  - Uniformity of dosage units
  - Water content
  - Microbial limits

SPECIFIC TESTS AND CRITERIA

- Dissolution:

  Immediate-release Products: Single-point dissolution

  Extended-release Products: Multiple time sampling

  Delayed-release products: Two stage testing

- Disintegration testing may be sufficient where the drug product is rapidly dissolving (>80% in 15 minutes) and the drug substance is highly soluble throughout the physiological range

  and

  A relationship to dissolution is established or disintegration is shown to be more discriminating than dissolution

SPECIFIC TESTS AND CRITERIA

- Hardness/friability are normally performed in-process and are not needed at release unless they have a critical impact on drug product quality
- Uniformity of dosage units includes both uniformity of content and uniformity of mass. In-process testing may be possible; the acceptance criteria should be in the specification
- When weight variation is applied to new drug products, applicant should verify that the homogeneity of the product is adequate
- Water content should be included when appropriate
- Microbial testing of components

SPECIFIC TESTS AND CRITERIA

- Oral Liquids
  - Uniformity of dosage units
  - pH
  - Microbial limits
  - Antimicrobial preservative content
  - Antioxidant preservative content
  - Extractables

SPECIFIC TESTS AND CRITERIA

- Oral Liquids (Cont'd)
  - Alcohol content
  - Dissolution
  - Particle size distribution
  - Redispersibility
  - Rheological properties
  - Reconstruction time
  - Water content

SPECIFIC TESTS AND CRITERIA

- Parenterals
  - Uniformity of dosage units
  - pH
  - Water content
  - Antmicrobial preservative content
  - Antioxidant preservative content
  - Extractables

SPECIFIC TESTS AND CRITERIA

- Parenterals (Cont'd)
  - Particle size distribution
  - Redispersibility
  - Reconstitution time
  - Sterility
  - Endotoxins/Pyrogens
  - Particulate matter
  - Functionality testing of delivery systems
  - Osmolarity

INTRODUCTION

- Specification

A list of tests, references to analytical procedures, and appropriate acceptance criteria, which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a drug substance or drug product should conform to be considered acceptable for its intended use.

GENERAL CONCEPTS

- Release vs. shelf-life acceptance criteria
- Periodic/Skip testing
- Pharmaceopoeial tests and acceptance criteria
- Parametric release
- In-process tests
- Design and development considerations

GENERAL CONCEPTS (Cont'd)

- Limited data available at filing
- Alternative procedures
- Evolving technologies
- Impact of drug substance on drug product specifications
- Reference Standard