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

5130 '01 NOV 30 P1:52

Date: November 27, 2001

To: Dockets Management Branch (HFA-305)

From: Melissa Lamb
Office of Generic Drugs

Subject: Microbiology/Sterile Products
Review Issues

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: Microbiology/Sterile Products

Presented for: 2001 Fall Technical Workshop

Date Presented: October 29, 2001

Presented by: Andrea High, Ph.D.
Team Leader, Microbiology Review Team
Office of Generic Drugs

Number of Pages: 14

Melissa Lamb

Attachment

90S-0308

m722

FDA/GPhA Fall Technical Workshop

Microbiology/Sterile Products Review Issues

Andrea High, Ph.D.
Team Leader, Microbiology Review Team
Office of Generic Drugs

October 29, 2001

U.S. Food & Drug Administration
Center for Drug Evaluation and Research

OGD Review Microbiologists

- Lynne Ensor, Ph.D.
- Paul DeLeo, Ph.D. (transferred 12/00 to CFSAN)
- Nrapendra Nath, Ph.D.
- Marla Stevens-Riley, Ph.D.
  - New Addition - May 2001
  - ☞Lisa Shelton, Ph.D.

Microbiology/Priority Reviews

- Any ANDA Completed

  All disciplines: Bioequivalence
  Chemistry
  Labeling
  EER, etc.

- Minor Amendments
- Major Amendments/New ANDAs /Supplements

Sterility Assurance Submissions on Queue

ANDAs	10/99	10/00	10/01
Longest Days Waiting	637	355	210
Days Waiting > 500	4	0	0
> 250	72	17	0
> 180	14	20	11
< 180	31	47	23

Sterility Assurance Submissions on Queue

Supplements

	10/99	10/00	10/01
Longest Days Waiting	312	215	209
Days Waiting > 250	6	0	0
> 180	12	7	7
< 180	25	15	34
Bundled Submissions	8(96)	7(174)	9(80)

Aseptic Fill Manufacturing Process

- Description of Facility
  - Diagrams of the Filling Area
  - Flow Patterns
  - Classifications
  - Areas Surrounding the Filling Line
- Location of the Equipment
- Filtration Validation (Drug Product Solution)

Continued

Aseptic Fill Manufacturing Process

- Description of Holding Periods
- Validation Summaries
  - Container/Closure Depyrogenation Sterilization
  - Equipment Sterilization
- Media Fills/Process Simulation
  - Description of Containers
  - Conditions/Duration, etc.
  - Requalification

Terminal Sterilization

- Loading Patterns
- Heat Distribution/Heat Penetration
- Cycle Monitors
- Microbiological Efficacy of the Cycle

Environmental Monitoring

- Bioburden Limits
- Personnel Testing
- Surface and Air Testing
- Water Testing
- Plan of Action, etc.

Other Considerations

- Release Tests
- Stability Protocol
- Antimicrobial Preservative Effectiveness Test (APET) - if applicable
- Container/Closure Integrity Testing
- Labeling/Package Inserts

Changes to an Approved NDA or ANDA

Problems Encountered...

U.S. Food & Drug Administration

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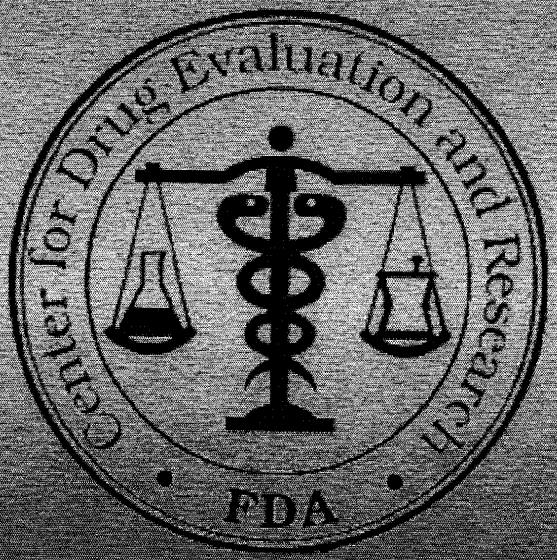
VII. B. Manufacturing Process #2, Bullet 9:

"Changes to aseptic processing methods, including scale, that extend total processing, including bulk storage time, by more than 50% beyond the validated limits in the approved application."

IX B. Package #4, Bullet 6:

"Changes in the size and/or shape of a container for a sterile drug product"

Questions?



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