CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
21-344

Microbiology Review(s)

Product Quality Microbiology Review
Review for HFD-150

29 JAN 2002

NDA: **21-344/N/BI**

Name of Drug: Faslodex (Fulvestrant) 250/5ML Injection

Review Number: 2

Submission Date: 10-DEC-2001

Applicant: AstraZeneca Pharmaceuticals

Name of Reviewer: David Hussong, Ph.D.

Review Recommendation: Approve (see page 4)

Product Quality Microbiology Data Sheet

A. 1. **NDA: 21-344**

2. **REVIEW NUMBER: 2**

3. **REVIEW DATE: 29-JAN-2002**

4. **TYPE OF SUPPLEMENT:** N/A

5. **SUPPLEMENT PROVIDES FOR:** N/A

6. **APPLICANT/SPONSOR:**

Name: AstraZeneca Pharmaceuticals
Representative: E. Jane Valas, Ph.D.
Telephone: (302) 886-2122

7. **MANUFACTURING SITE:**
iPR Pharmaceuticals
Carolina, Puerto Rico

8. **DRUG PRODUCT NAME:**
Proprietary: Faslodex™ Injection
Non-proprietary: fulvestrant
Drug Priority Classification: Standard

9. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** 250 mg/5 ML

10. **METHOD(S) OF STERILIZATION:** [redacted]

11. **PHARMACOLOGICAL CATEGORY:** Anti-estrogen receptor agent that inhibits the growth of estrogen sensitive breast cancer cells.

B. 1. **DOCUMENT/LETTER DATE:** 28-MAR-2001 (initial submission)
2. **RECEIPT DATE:** 28-MAR-2001
3. **CONSULT DATE:** N/A
4. **DATE OF AMENDMENTS:** 10-DEC-2001 (subject of this review)
5. **ASSIGNED FOR REVIEW:** 13-DEC-2001
6. **SUPPORTING/RELATED DOCUMENTS:** N/A

C. **REMARKS:** The original submission was reviewed in Microbiologist's Review #1 (06-NOV-2001), which produced six comments that were provided (by FAX dated 19-NOV-2001) to the applicant from that review. The applicant

replied to these comments in their amendment dated 10-DEC-2001, which is the subject of this review.

APPEARS THIS WAY
ON ORIGINAL

Executive Summary

I. Recommendations

A. Recommendation on Approvability - APPROVE

B. Recommendation on Phase 4 Commitments and/or Agreements, if Approvable - n/a

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology - The product is manufactured in two strengths by preparing 2 fill volumes in [redacted] syringes. The solution is non–aqueous and is filtered through [redacted] membranes, then processed by [redacted]

B. Brief Description of Microbiology Deficiencies – n/a

C. Assessment of Risk Due to Microbiology Deficiencies – n/a

III. Administrative

A. Reviewer's Signature /S/

B. Endorsement Block
David Hussong/29-JAN-2002
Peter Cooney/Date

C. CC Block
cc:
Original NDA 21-344
HFD-150/Division File/NDA 21-344
HFD-150/CSO/Amy Baird

D. File Name:
d:\NDA\21-344rv2.doc

Product Quality Microbiology Assessment

Deficiencies and Comments from Microbiology Review #1 were conveyed to the applicant in a FAX dated November 19, 2001. Comments are copied into this review and followed by a review of the applicant's reply.

Comment #1. Process flow descriptions did not indicate which fill line was used and could not be linked to specific rooms or processing areas. Please identify the building and rooms where [redacted] is done. The [redacted] line should be described so it can be associated with the lines that are validated in the process simulations (media fill [redacted]

Review of Response #1: The [redacted] of FASLODEX is performed in the filling suite, [redacted] at Vetter Pharma-Fertigung GmbH [redacted] Ravensburg Germany. The only filling line [redacted] syringe filling and [redacted] machine [redacted] the floor plan). [redacted] is shown on the site plan for the [redacted] facility (Appendix 1(a) on page 25). A floor plan for the production area was provided in Appendix 1(b), on pages 4 and 5. [redacted] of FASLODEX) and the support rooms [redacted] were outlined on the floor plan to show the processing areas for this product. A copy of the manufacturing process flow diagram (page 6) identifies the rooms where [redacted] manufacturing [redacted] are carried out.

The process flow describes preparation of the bulk solution [redacted]

The bulk is [redacted]
Filtration is done by a [redacted] filter and the filtrate is received in [redacted]
The sterile bulk is then [redacted] where [redacted] (sterilizing) is done at the point of syringe filling [redacted] The filled syringe barrels are closed with plunger stoppers and seals.

ACCEPTABLE

Comment #2. Please summarize methods and acceptance criteria for environmental microbiology tests conducted in the sterile facility. Emphasis should be placed on the critical [redacted] area. Fill and support rooms should be identified.

Review of Response #2. Environmental microbiology monitoring of the FASLODEX manufacture areas was described in SOPs provided in Appendix 9. These SOPs are listed below.

Redacted 4

pages of trade secret and/or confidential commercial information

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/s/

David Hussong
2/14/02 09:35:01 AM
MICROBIOLOGIST

Peter Cooney
2/14/02 10:37:33 AM
MICROBIOLOGIST

REVIEW FOR HFD-150
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #1 OF NDA

November 6, 2001

A. 1. NDA 21-344

APPLICANT AstraZeneca Pharmaceuticals
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

AGENTS FOR iPR Pharmaceuticals
Carolina, Puerto Rico

2. PRODUCT NAMES: Faslodex™ (fulvestrant) Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: There are two presentations: both are prefilled syringes of 50 mg/mL. One is a single 5 mL syringe containing 5 mL of drug solution. The other is a single package of 2 syringes (5 cc capacity) containing 2.5 mL of drug solution. Both are for intramuscular injection.

4. METHOD(S) OF STERILIZATION: [redacted]

5. PHARMACOLOGICAL CATEGORY: Anti-estrogen receptor agent that inhibits the growth of estrogen sensitive breast cancer cells.

6. DRUG PRIORITY CLASSIFICATION: Standard

B. 1. DATE OF INITIAL SUBMISSION: March 28, 2001

2. DATE OF AMENDMENT: none

3. RELATED DOCUMENTS: none

4. ASSIGNED FOR REVIEW: May 22, 2001

C. REMARKS: The applicant has submitted this NDA on behalf of iPR Pharmaceuticals in Puerto Rico. The NDA was submitted with a request for expedited review, but the administrative management system reports it has a standard review (S) classification.

The submission was provided as two introductory jackets with summary information. Technical information was electronically transmitted and reviewed.

D. CONCLUSIONS: The application is approvable pending resolution of microbiology issues. Specific deficiencies are provided in "List of Microbiology Deficiencies and Comments," at the end of this review.

/S/

David Hussong, Ph.D.

cc:

HFD 160/Consult File
HFD 150/Division File
HFD 150 /CSO/Amy Baird
HFD 805/D. Hussong

Drafted by: D. Hussong, 11/06/2001
R/D initialed by: P. Cooney

Filename, d:\nda\21-344rv1.DOC

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/s/

David Hussong
11/6/01 02:49:30 PM
MICROBIOLOGIST

Peter Cooney
11/6/01 02:58:54 PM
MICROBIOLOGIST

Safety Update

See pages 90-99 of MOR dated 3/28/02