CENTER FOR DRUG EVALUATION AND *RESEARCH*

APPLICATION NUMBER:

21-225

MICROBIOLOGY REVIEW

BC51

NOV 1 2000

REVIEW FOR HFD-580
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #1 OF NDA

October 27, 2000

A. 1. NDA 21-225

SPONSOR Berlex Laboratories, Inc.
340 Changebridge Road
P.O. Box 1000
Montville, NJ 07045-1000

2. PRODUCT NAMES: Mirena (levonorgestrel-releasing intrauterine system, LNG IUS)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: Intrauterine system

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: contraceptive

6. DRUG PRIORITY CLASSIFICATION: 3S

B. 1. DATE OF INITIAL SUBMISSION: January 31, 2000

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: DMF —— (Leiras Oy, Turku, Finland 12/15/99)

4. ASSIGNED FOR REVIEW: February 15, 2000

C. REMARKS: The IND for this product (IND —— was held by the Population Council and was transferred to Berlex. The CMC sections of this NDA were submitted in advance of the NDA (presubmission) and amended in the NDA "original" submission.

The product is an intrauterine repository for the slow release of levonorgestrel. The frame of the system resembles a "Tee-shaped" frame of an IUD, but carries a reservoir for the controlled release of the contraceptive drug. The intrauterine system is manfactured by Leiras Oy (Torku, Finland), a subsidiary of Schering AG (Berlin, Germany).

D. CONCLUSIONS: The submission is APPROVABLE for product quality microbiology aspects. Technical problems relating to bioburden counts are noted and included in the "Microbiologist's List of Deficiencies."

/S/ 10-27-2000

David Hussong, Ph.D.

/S/ 11/01/00

cc:

Original NDA 21-225
HFD 160/Consult File
HFD 580/Division File
HFD 580/CSO/J. Best
HFD 580/Chemist/M. Rhee
HFD 805/D. Hussong

Drafted by: D. Hussong, 10/27/2000
R/D initialed by: P. Cooney

Filename, d:\nda\21-225rv1.DOC

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REVIEW FOR HFD-580
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #2 OF NDA

December 1, 2000

A. 1. NDA 21-225/BI amendment

SPONSOR Berlex Laboratories, Inc.
340 Changebridge Road
P.O. Box 1000
Montville, NJ 07045-1000

2. PRODUCT NAMES: Mirena (levonorgestrel-releasing intrauterine system, LNG IUS)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: Intrauterine system

4. METHOD(S) OF STERILIZATION: ETO

5. PHARMACOLOGICAL CATEGORY: contraceptive

6. DRUG PRIORITY CLASSIFICATION: 3S

B. 1. DATE OF INITIAL SUBMISSION: January 31, 2000

2. DATE OF AMENDMENT: November 14, 2000 (subject of this review). See also the FAX communication dated December 1, 2000 that provides a commitment to discontinue the practice of multiplying colony counts by a correction factor to yield an estimated bioburden.

3. RELATED DOCUMENTS: DMF (Leiras Oy, Turku, Finland 12/15/99)

4. ASSIGNED FOR REVIEW: November 30, 2000

C. REMARKS: The product is an intrauterine repository for the slow release of levonorgestrel. The frame of the system resembles a "Tee-shaped" frame of an IUD, but carries a reservoir for the controlled release of the contraceptive drug. The intrauterine system is manfactured by Leiras Oy (Torku, Finland), a subsidiary of Schering AG (Berlin, Germany).

The current amendment is a response to deficiencies from Microbiologist's Review #1.

D. CONCLUSIONS: The submission is recommended for APPROVAL. Technical problems relating to bioburden counts have been resolved by a commitment (see FAX dated December 1, 2000).

/S/

David Hussong, Ph.D.

cc:

Original NDA 21-225
HFD 160/Consult File
HFD 580/Division File
HFD 580/CSO/J. Best
HFD 580/Chemist/M. Rhee
HFD 805/D. Hussong

Drafted by: D. Hussong, 11/30/2000
R/D initialed by: P. Cooney

Filename, d:\nda\21-225rv2.DOC

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