CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-098

CHEMISTRY REVIEW(S)

Summary of Chemistry Review of NDA 21-098 (3rd Review Cycle), Yasmin

A. Drug Substance:

In response to the second approval letter dated July 10, 2000, the sponsor submitted **two** separate **amendments** dated November 6, 2000.

The first amendment indicates a **modified synthetic scheme** for the production of **drospirenone** ———) and the modified synthetic scheme is deemed not to adversely affect the quality of the drug substance.

All facilities involved in the production of the drug substance are **in compliance to cGMP** as of April 4, 2001.

B. Drug Products:

The second amendment dated November 6, 2000 describes a proposal to **delete** the **specification** for **decomposition products** from the specifications of the drug product, and the proposal was **not accepted.** The sponsor **withdrew** the proposal on March 30, 2001.

The amendment also provides a **revised carton label** in accordance with the comments made in the approvable letter, and the subsequent amendment dated November 14, 2000, provides mock-up carton labels. The revised carton labels are **satisfactory.**

The facility for the manufacture of the drug product is **in compliance to cGMP** as of April 4, 2001.

C. CONCLUSION AND RECOMMENDATION:

From the Chemistry point of view, as the primary reviewer recommends, this NDA can be approved.

Moo-Jhong Rhee, Ph.D.
Chemistry Team Leader
For the Division of reproductive and Urologic Drug Products
DNDC II, Office of New Drug Chemistry

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/s/

Moo-Jhong Rhee
4/17/01 03:16:35 PM
CHEMIST

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ON ORIGINAL

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS (HFD-580)

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-098 **DATE REVIEWED:**
CHEMISTRY REVIEW #: 4 **REVIEWER: Suong Tran**

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
AMENDMENT	16-JAN-2001	17-JAN-2001	18-JAN-2001
AMENDMENT	30-MAR-2001	2-APR-2001	6-APR-2001

NAME & ADDRESS OF APPLICANT: Berlex Laboratories, Inc.
340 Changebridge Road
PO Box 1000
Montville, New Jersey 07045-1000

DRUG PRODUCT NAME

Proprietary:	YASMIN™ 28 TABLETS
Established:	drospirenone and ethinyl estradiol
Code Name/#:	ZK 30595, ZK 4944
Chem. Type/Ther. Class:	1S

PHARMACOL. CATEGORY/INDICATION: oral contraceptive

DOSAGE FORM: Tablet

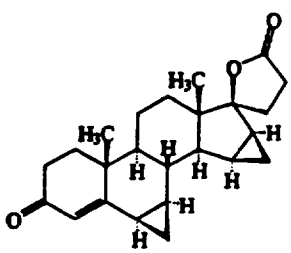
STRENGTHS: 3 mg drospirenone and 0.030 mg ethinyl estradiol per tablet

ROUTE OF ADMINISTRATION: Oral

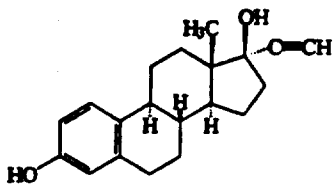
DISPENSED: __X__Rx _____OTC

SPECIAL PRODUCTS: _____Yes __X__No

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:



Drospirenone



Ethinyl estradiol

Drospirenone (USAN name)

1. (6*R*,7*R*,8*R*,9*S*,10*R*,13*S*,14*S*,15*S*,16*S*,17*S*)-1,3′,4′,6,6a,7,8,9,10,11,12,13,14,15,15a,16-hexadecahydro-10,13-dimethylspiro-[17*H*-dicyclopropa[6,7:15,16]cyclopenta[*a*]phenanthrene-17,2′(5*H*)-furan]-3,5′(2*H*)-dione
1. 6β,7β,15 β,16 β-dimethylene-3-oxo-17α-pregn-4-ene-21,17-carbolactone

CAS-67392-87-4
Molecular formula: $C_{24}H_{30}O_3$
Molecular weight: 366.50

Ethinyl estradiol (USAN name)
1. 19-norpregna-1,3,5(10)-trien-20-yne-3,17-diol,(17α)
2. 19-nor-17α-pregna-1,3,5(10)-trien-20-yne-3,17-diol

CAS-57-63-6
Molecular formula: $C_{20}H_{24}O_2$
Molecular weight: 296.41

SUPPORTING DOCUMENTS:

Type/Number	Subject	Holder	Status	Review date	Letter date
[redacted]			Adequate	19-JAN-2001 (by S. Tran)	Not applicable

RELATED DOCUMENTS: none

CONSULTS:
Office of Compliance recommends "Acceptable" for NDA 21-098 on 4-APR-2001.

REMARKS/COMMENTS: refer to the attached Chemist's Review Notes.

CONCLUSION & RECOMMENDATIONS:
All chemistry information in the NDA is satisfactory. NDA 21-098 is recommended for APPROVAL from CMC point of view.

cc:
NDA 21-098:
HFD-580/Division File
HFD-580/JBest/STran/MRhee

Suong T. Tran, Ph.D.
Review Chemist

R/D Init by:
Filename: [redacted]

Moo-Jhong Rhee, Ph.D.
Team Leader

APPEARS THIS WAY
ON ORIGINAL

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

6 pages

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS (HFD-580)

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-098
CHEMISTRY REVIEW #: 3

DATE REVIEWED: 7-DEC-2000
REVIEWER: Suong Tran

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
AMENDMENT	6-NOV-2000	6-NOV-2000	13-NOV-2000
AMENDMENT	14-NOV-2000	16-NOV-2000	5-DEC-2000

NAME & ADDRESS OF APPLICANT: Berlex Laboratories, Inc.
340 Changebridge Road
PO Box 1000
Montville, New Jersey 07045-1000

DRUG PRODUCT NAME

Proprietary:	YASMIN™ 21 TABLETS YASMIN™ 28 TABLETS
Established:	drospirenone and ethinyl estradiol
Code Name/#:	ZK 30595, ZK 4944
Chem. Type/Ther. Class:	1S

PHARMACOL. CATEGORY/INDICATION: oral contraceptive

DOSAGE FORM: Tablet

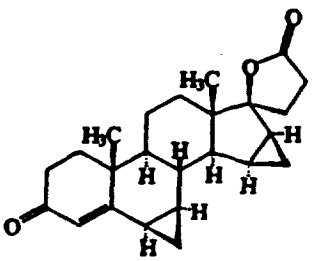
STRENGTHS: 3 mg drospirenone and 0.030 mg ethinyl estradiol per tablet

ROUTE OF ADMINISTRATION: Oral

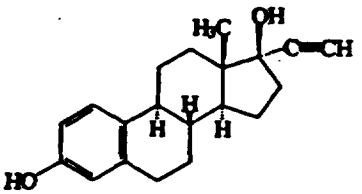
DISPENSED: X Rx _____OTC

SPECIAL PRODUCTS: _____Yes X No

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:



Drospirenone



Ethinyl estradiol

Drospirenone (USAN name)

1. (6*R*,7*R*,8*R*,9*S*,10*R*,13*S*,14*S*,15*S*,16*S*,17*S*)-1,3',4',6,6a,7,8,9,10,11,12,13,14,15,15a,16-hexadecahydro-10,13-dimethylspiro-[17*H*-dicyclopropa[6,7:15,16]cyclopenta[*a*]phenanthrene-17,2'(5*H*)-furan]-3,5'(2*H*)-dione
2. 6β,7β,15 β,16 β-dimethylene-3-oxo-17α-pregn-4-ene-21,17-carbolactone

CAS-67392-87-4
Molecular formula: $C_{24}H_{30}O_3$
Molecular weight: 366.50

Ethinyl estradiol (USAN name)

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2. 19-nor-17α-pregna-1,3,5(10)-trien-20-yne-3,17-diol

CAS-57-63-6
Molecular formula: $C_{20}H_{24}O_2$
Molecular weight: 296.41

SUPPORTING DOCUMENTS:

Type/Number	Subject	Holder	Status	Review date	Letter date
[redacted]			Not adequate	7-DEC-2000 (by S. Tran)	8-DEC-2000

RELATED DOCUMENTS: none

CONSULTS: none

REMARKS/COMMENTS: refer to the attached Chemist's Review Notes.

CONCLUSION & RECOMMENDATIONS:
The 14-NOV-2000 amendment (revised carton labeling per FDA's request) is acceptable. The 6-NOV-2000 amendment to the original submission of NDA 21-098 currently has incomplete information. Please issue an Information Request letter (refer to the attached Draft Letter).

cc:
NDA 21-098:
HFD-580/Division File
HFD-580/JBest/STran/MRhee
HFD-820/JGibbs/SKoepke

Suong T. Tran, Ph.D.
Review Chemist

R/D Init by:
Filename: [redacted]

Moo-Jhong Rhee, Ph.D.
Team Leader

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

6 pages

Memorandum

Date July 6, 2000

JUL 06 2000

From Steven R. Koepke,
Deputy Director, Division of New Drug Chemistry II,
Office of New Drug Chemistry

Subject NDA 21-098
Yasmin 28 Tablets
(drospirenone/ethinyl estradiol)
Berlex Laboratories, Inc.

Yasmin is an oral contraceptive drug product containing both drospirenone (3.0 mg) and ethinyl estradiol (0.03mg) in 21 of the 28 provided tablets. Both drug substances are purchased from other firms and the corresponding DMFs have been found to be adequate for this product (see below). The specifications for each of these drug substances are in the corresponding DMFs but are provided to the Applicant as a part of the Certificate of Analysis (COA). This is adequate, but not ideal. The Applicant should be encouraged to submit both the numerical specifications and regulatory methods directly to the NDA.

Overall recommendation from CMC: This application is recommended for approval from CMC as of CMC review #2 (2/24/00). The Division concurs with this recommendation with comment (on labeling, nomenclature and administrative handling of specifications of drug substance).

EER: Compliance overall recommendation was acceptable 10/1/99

DMFs: Drug Substances adequate 2/10/00 and 12/6/99). Packaging DMFs were adequate 10/5/99 and 9/19/97 respectively.

EA: Firm requested categorical exclusion in original submission.

Nomenclature: OPDRA consult indicates that trade name Yasmin is acceptable 6/6/00. The trade name appears to be Yasmin 28 Tablets as indicated in the labeling. (Was the entire trade name submitted to OPDRA?).

Labeling: The strength of the drug is not listed on the cartons. The established name is listed as drospirenone and ethinyl estradiol. The established name should be drospirenone and ethinyl estradiol tablets. The established name must include the dosage form. The prominence of the established name appears to be less than half of that of the trade name YASMIN. The established name must be at least one half the prominence of the trade name.

Package Insert: The regulations require that the established name be associated with the trade name at least once on every page of the package insert, no matter how many times the trade name occurs on a page. Since the copy of the package insert submitted for review was on 8.5 x 11 paper, it is difficult to determine that the established name is associated with the trade name at least once on every page. The Applicant should be reminded of this requirement since it appears that the established name may not appear in this frequency.

JUL 0 7 2000

Addendum to Revised Summary of Chemistry Review of NDA21-098

To: Chemistry Review #2 of NDA 21-098

CC: Division File/STran/JBest/MRhee

From: Moo-Jhong Rhee, Ph.D. Chemistry Team Leader /S/

Date: 07/07/00

Re: Labeling

In Dr. Steve Koepke's tertiary review, several comments were made concerning the labeling of this NDA.

1) He suggested to include "tablets" in the established name, i.e., (drospirenone and ethinyl estradiol tablets). This is one way of describing the dosage form, however, when the dosage form "tablets" is already specified in the label usually right after the tradename, this has been deemed acceptable.

2) He indicated that the strengths of the drug are not specified in the carton label.

   One panel of the carton label describes that "This blister contains one blister of 21 tablets; 21 yellow tablets containing 3mg of drospirenone and 0.03mg of ethinyl estardiol;" At least, it meets the requirement, but it could be specified as (3mg/0.03mg) right under the establsihed name to make them more prominent.

3) He also indicated that the size of established name is not as big as what the regulation requires. Although it looks like they are less than 50% of the size of the tradename, however, when measured, their height is 50% of that of the tradename, which barely meet the requirement.

We could suggest sponsor:

1) To put the dosage strength in the front panel of carton label underneath the established name

2) To remove the line between the tradename and established name in the labels.

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[redacted]

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

1 page

JUL 07 2000

Addendum #2

To: Chemistry Review #2 of NDA 21-098

CC: Division File/STran/JBest/MRhee

From: Moo-Jhong Rhee, Ph.D. Chemistry Team Leader /S/

Date: July 6, 2000

Re: Specifications for drospirenone and ethinyl estradiol

In the NDA, specifications for drug substances were not provided, but the information was referenced to [redacted] for drospirenone and ethinyl estradiol, respectively.

Since certificate of analyses of these two drug substances were submitted in the amendment dated January 28, 2000, and they list all the tests specified in the DMFs together with numerical ranges and actual results, these are deemed satisfactory for having specifications of drug substances listed in the NDA.

APPEARS THIS WAY
ON ORIGINAL

[redacted]

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

6 pages

JUN 2 2 2000

Addendum

To: Chemistry Review #2 of NDA 21-098

CC: Division File/STran/JBest/MRhee

From: Moo-Jhong Rhee, Ph.D. Chemistry Team Leader /S/

Date: 06/22/00

Re: Amendments Dated 29-FEB-2000, 9-May-2000, and 21-June-2000

The amendment dated February 29, 2000, and received on March 1, 2000, contained mock-up labels for immediate container and cartons. They are deemed acceptable except for omission of Lot # and expiry date in the carton labels. This was conveyed to the sponsor on June 16, 2000, and revised labels indicating the locations of lot # and expiry date were faxed on June 21, 2000, which are satisfactory.

The amendment dated May 9, 2000 contains the final revised package insert which has the same chemistry information as revised previously.

From Chemistry point of view, all the information in labeling are now considered satisfactory.

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FEB 24 2000

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS (HFD-580)

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-098
CHEMISTRY REVIEW #: 2

DATE REVIEWED: 23-FEB-2000
REVIEWER: Suong Tran

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
AMENDMENT	7-JAN-2000	10-JAN-2000	12-JAN-2000
AMENDMENT	28-JAN-2000	31-JAN-2000	2-FEB-2000
AMENDMENT	18-FEB-2000	18-FEB-2000	18-FEB-2000
AMENDMENT	23-FEB-2000	23-FEB-2000	23-FEB-2000

NAME & ADDRESS OF APPLICANT: Berlex Laboratories, Inc.
340 Changebridge Road
PO Box 1000
Montville, New Jersey 07045-1000

DRUG PRODUCT NAME

Proprietary:	YASMIN™ 21 TABLETS YASMIN™ 28 TABLETS
Established:	drospirenone and ethinyl estradiol
Code Name/#:	ZK 30595, ZK 4944
Chem. Type/Ther. Class:	1S

PHARMACOL. CATEGORY/INDICATION: oral contraceptive

DOSAGE FORM: Tablet

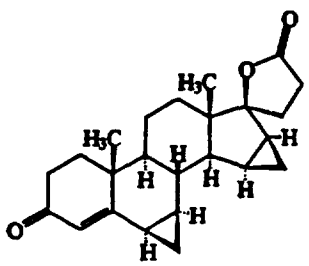
STRENGTHS: 3 mg drospirenone and 0.030 mg ethinyl estradiol per tablet

ROUTE OF ADMINISTRATION: Oral

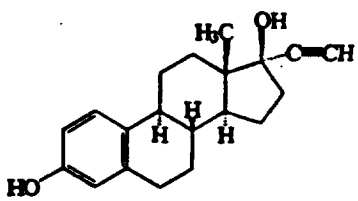
DISPENSED: X Rx _____OTC

SPECIAL PRODUCTS: _____Yes X No

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:



Drospirenone



Ethinyl estradiol

Drospirenone (USAN name)

1. (6*R*,7*R*,8*R*,9*S*,10*R*,13*S*,14*S*,15*S*,16*S*,17*S*)-1,3',4',6,6a,7,8,9,10,11,12,13,14,15,15a,16-hexadecahydro-10,13-dimethylspiro-[17*H*-dicyclopropa[6,7:15,16]cyclopenta[*a*]phenanthrene-17,2'(5*H*)-furan]-3,5'(2*H*)-dione
2. 6β,7β,15 β,16 β-dimethylene-3-oxo-17α-pregn-4-ene-21,17-carbolactone

CAS-67392-87-4
Molecular formula: $C_{24}H_{30}O_3$
Molecular weight: 366.50

Ethinyl estradiol (USAN name)

1. 19-norpregna-1,3,5(10)-trien-20-yne-3,17-diol,(17α)
2. 19-nor-17α-pregna-1,3,5(10)-trien-20-yne-3,17-diol

CAS-57-63-6
Molecular formula: $C_{20}H_{24}O_2$
Molecular weight: 296.41

SUPPORTING DOCUMENTS:

Type/Number	Subject	Holder	Status	Review date	Letter date
			Active	Not applicable	Not applicable
			Adequate	6-DEC-1999 (by S. Tran)	Not applicable
			Adequate	5-OCT-1999 (by S. Tran)	Not applicable
			Adequate	19-SEP-1997 (by D. Lin)	Not applicable
			Adequate	22-FEB-2000 (by S. Tran)	Not applicable

RELATED DOCUMENTS:

- Chemistry Review #1 dated 10-DEC-1999.
- IR letter dated 16-DEC-1999.
- Chemistry Review #1 dated 7-DEC-1999.
- Deficiency letter dated ... Chemistry Review #1.
- 11-FEB-2000 and 23-FEB-2000 teleconference meeting minutes.

CONSULTS:

- EER was sent to Compliance by chemist A. Mitra. An "Acceptable" recommendation was issued on 1-OCT-1999 (S Ferguson; see the attached reports in Chem. Review # 1).
- The Biopharmaceutics consult review (by V. Jarugula) finds the dissolution specifications of Q = for ethinyl estradiol, to be acceptable. (These specifications are proposed in the 18-FEB-2000 amendment.)

- The proposed propriety name was sent to the Nomenclature and Labeling Committee on 5-OCT-1999. The OPDRA review is currently ongoing.

REMARKS/COMMENTS:

- Amendment dated 7-JAN-2000: 12-month stability data as agreed during the pre-NDA meeting on 12-FEB-1997 between Berlex and FDA and as requested in the Information Request Letter dated 16-DEC-1999. In addition, per Dr. Moo-Jhong Rhee's request for information on 30-NOV-1999 regarding the USAN approval of the name "drospirenone", this amendment includes a letter from USAN stating that this name has been adopted by USAN although it did not appear in the 1998 USAN publication.
- Amendment dated 28-JAN-2000: response to the Information Request Letter dated 16-DEC-1999, including an updated 18-month stability report.
- Amendment dated 18-FEB-2000: response to FDA's request for further information as discussed in the teleconference on 11-FEB-2000 (issues: dissolution specifications and release testing for impurities).
- Amendment dated 23-FEB-2000: response to FDA's request for further information as discussed in the teleconference on 23-FEB-2000 (issue: expiration dating period of the drug product). FDA and the applicant agree on an expiry of 24 months at room temperature for the drug product. Refer to the Chemist's Review Notes for details.

CONCLUSION & RECOMMENDATIONS:

All information provided to the Chemistry, Manufacturing, and Controls section of NDA 21-098 is satisfactory. NDA 21-098 is recommended for approval.

cc:
NDA 21-098:
HFD-580/Division File
HFD-580/JBest/STran/MRhee
HFD-820/JGibbs/SKoepke

/S/

Suong T. Tran, Ph.D.
Review Chemist

/S/

Moo-Jhong Rhee, Ph.D.
Team Leader

R/D Init by:
Filename:

APPEARS THIS WAY
ON ORIGINAL

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

11 pages

DEC 10 1999 /S/

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS (HFD-580)

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-098 **REVIEW #: 1** **REVIEW DATE: 1-NOV-1999**
CHEMIST: Suong Tran (REVISED 7-DEC-1999)

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	14-MAY-1999	17-MAY-1999	17-SEP-1999

NAME & ADDRESS OF APPLICANT: Berlex Laboratories, Inc.
340 Changebridge Road
PO Box 1000
Montville, New Jersey 07045-1000

DRUG PRODUCT NAME

Proprietary:	YASMIN™ 21 TABLETS YASMIN™ 28 TABLETS
Nonproprietary:	drospirenone and ethinyl estradiol tablets
Code Name/#:	ZK 30595, ZK 4944
Chem. Type/Ther. Class:	1S

PHARMACOL. CATEGORY/INDICATION: oral contraceptive

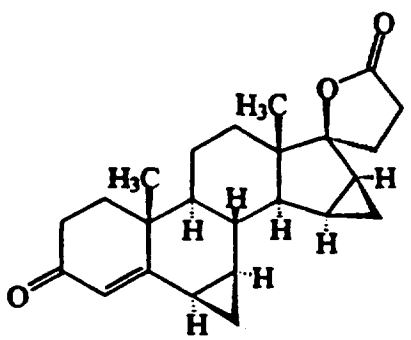
DOSAGE FORM: Tablet

STRENGTHS: 3 mg drospirenone and 0.030 mg ethinyl estradiol per tablet

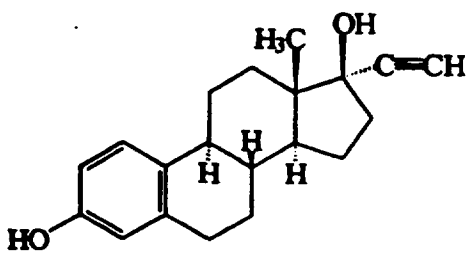
ROUTE OF ADMINISTRATION: Oral

DISPENSED: __X__ Rx _____ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:



Drospirenone



Ethinyl estradiol

Drospirenone (USAN name)

1. (6*R*,7*R*,8*R*,9*S*,10*R*,13*S*,14*S*,15*S*,16*S*,17*S*)-1,3',4',6,6a,7,8,9,10,11,12,13,14,15,15a,16-hexadecahydro-10,13-dimethylspiro-[17*H*-dicyclopropa[6,7:15,16]cyclopenta[*a*]phenanthrene-17,2'(5*H*)-furan]-3,5'(2*H*)-dione
2. 6β,7β,15 β,16 β-dimethylene-3-oxo-17α-pregn-4-ene-21,17-carbolactone

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CAS-57-63-6
Molecular formula: $C_{20}H_{24}O_2$
Molecular weight: 296.41

SUPPORTING DOCUMENTS:

Type/Number	Subject	Holder	Status	Review date	Letter date
[redacted]			Active	Not applicable	Not applicable
[redacted]			Adequate	6-DEC-1999 (by S. Tran)	Not applicable
[redacted]			Adequate	5-OCT-1999 (by S. Tran)	Not applicable
[redacted]			Adequate	19-SEP-1997 (by D. Lin)	Not applicable
[redacted]			Deficient	6-DEC-1999 (by S. Tran)	10-DEC-1999

RELATED DOCUMENTS:
None

CONSULTS:

- EER was sent to Compliance by chemist A. Mitra. An "Acceptable" recommendation was issued on 1-OCT-1999 (S Ferguson; see the attached reports).
- The proposed propriety name was sent to the Nomenclature and Labeling Committee on 5-OCT-1999.
- A Biopharmaceutics consult review of the drug product dissolution test and specifications is currently ongoing.

REMARKS/COMMENTS:
NDA 21-098 is for an oral contraceptive in tablet form. YASMIN™ consists of two drug substances, 3 mg drospirenone and 0.030 mg ethinyl estradiol. Drospirenone is a new molecular entity. The inactive

ingredients in the drug product are Lactose monohydrate, NF, Corn starch, NF, Modified starch, NF, Povidone 25000, USP, Magnesium stearate, NF, Hydroxypropylmethylcellulose, USP, Macrogol 6000, NF, Talc, USP, Titanium dioxide, USP, and Ferric oxide yellow, NF. YASMIN™ 21 TABLETS is a blister pack containing 21 active drug tablets. YASMIN™ 28 TABLETS is a blister pack containing 7 placebo tablets and 21 active drug tablets. The primary packaging of the drug product is a blister pack composed of a water-resistant PVC film and an aluminum sheet with a heat-sealable side. The blister pack is inserted into the aluminum pouch. The pouch is packaged in a box with two patient insert documents and a day label. The shelf life of the drug product will be proposed in an amendment to this original submission of the NDA.

CONCLUSION &RECOMMENDATIONS:
The NDA currently has incomplete information. Please issue an Information Request letter (attached Draft Letter).

cc:
Orig. NDA # 21-098
HFD-580/Division File
HFD-580/JBest/STran/MRhee
HFD-820/JGibbs/SKoepke

/S/
Suong T. Tran, Ph.D.
Review Chemist

R/D Init by:

/S/
Moo-Jhong Rhee, Ph.D.
Team Leader

Filename

APPEARS THIS WAY
ON ORIGINAL

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

18 pages

NDA 21-098
Yasmin® 28 Tablets (drospirenone/ethinyl estradiol)
Berlex Laboratories, Inc.

Statistical Review of Stability Protocol is NA for this drug product.

/S/ 4/18/01

APPEARS THIS WAY
ON ORIGINAL

THIS SECTION
WAS
DETERMINED
NOT
TO BE
RELEASABLE

43 pages

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Application: **NDA 21098/000**
Priority: **14S** Org Code: **580**
Stamp: **17-MAY-1999** Regulatory Due: **13-MAY-2001**
Action Goal: District Goal: **14-MAR-2001**
Applicant: **BERLEX LABS**
340 CHANGEBRIDGE RD
MONTVILLE, NJ 070451000
Brand Name: **YASMIN(DROSPIRENONE 3MG/ETHINYL ESTRADIO**
Established Name:
Generic Name: **DROSPIRENONE 3MG/ETHINYL ESTRADIOL .30MG**
Dosage Form: **TAB (TABLET)**
Strength: **3.0 MG DROS/0.030 MG EE**

FDA Contacts: **A. MITRA (HFD-580) 301-827-4238 , Review Chemist**

Overall Recommendation:

ACCEPTABLE on 04-APR-2001 by M. GARCIA (HFD-322) 301-594-0095
ACCEPTABLE on 01-OCT-1999 by S. FERGUSON (HFD-324) 301-827-0062

Establishment: **9610131**
SCHERING AG
D-13353
BERLIN, , GM
AADA No: **021098**

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **17-JAN-2001**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**
Responsibilities: **DRUG SUBSTANCE OTHER TESTER**
DRUG SUBSTANCE PACKAGER

Establishment: **9611626**
SCHERING AG
D-59179
BERGKAMEN, , GM
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **17-JAN-2001**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**
Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

Establishment: **9611633**
SCHERING AG
MAX DORN STRABE 8-10
CHARLOTTENBURG, BERLIN, GM D
DMF No:
AADA No:

Profile: **CRU** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **17-JAN-2001**
Responsibilities: **DRUG SUBSTANCE MICRONIZER**

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: **9614946**
SCHERING GMBH UND CO PRODUK'
99427
WEIMAR, , GM

DMF No:
AADA No:

Profile: **TCM** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **04-APR-2001**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE MANUFACTURER**

APPEARS THIS WAY
ON ORIGINAL

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Application: NDA 21098/000
Priority: S
Org Code: 580
Stamp: 17-MAY-1999 Regulatory Due: 17-MAR-2000
Action Goal:
District Goal: 17-JAN-2000
Applicant: BERLEX LABS
340 CHANGEBRIDGE RD
MONTVILLE, NJ 070451000
Brand Name: YASMIN(DROSPIRENONE 3MG/ETHINYL ESTRADIO
Established Name:
Generic Name: DROSPIRENONE 3MG/ETHINYL ESTRADIOL .030M
Dosage Form: TAB (TABLET)
Strength: 3.0 MG DROS/0.030 MG EE

FDA Contacts: A. MITRA (HFD-580) 301-827-4238 , Review Chemist

Overall Recommendation:

ACCEPTABLE on 01-OCT-1999 by S. FERGUSON (HFD-324) 301-827-0062

Establishment: 9610131
SCHERING AG
MUELLER STRASSE 178, D-13353
BERLIN, , GM
DMF No:
AADA No: 021098

Profile: CTL
OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 01-OCT-1999
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION
Responsibilities: DRUG SUBSTANCE OTHER TESTER
DRUG SUBSTANCE PACKAGER

Establishment: 9611626
SCHERING AG
ERNST-SCHERING STRABE 14
BERGKAMEN, , GM D-59179
DMF No:
AADA No:

Profile: CRU
OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 01-JUL-1999
Decision: ACCEPTABLE
Reason: BASED ON FILE REVIEW
Responsibilities: DRUG SUBSTANCE MANUFACTURER

Establishment: 9611633
SCHERING AG
MAX DOHRM STRASSE 8-10, D-1000
BERLIN-CHARLOTTENBERG, , GM
DMF No:
AADA No:

Profile: CRU
OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 01-JUL-1999
Decision: ACCEPTABLE
Responsibilities: DRUG SUBSTANCE MICRONIZER

ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Reason: **DISTRICT RECOMMENDATION**

Establishment: **9614946**
SCHERING GMBH UND CO PRODUK'
DOBEREINERSTRASSE 20
WEIMAR, , GM 99427

DMF No:
AADA No:

Profile: **TCM** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **01-OCT-1999**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE MANUFACTURER**

APPEARS THIS WAY
ON ORIGINAL

NDA 21-098
Yasmin® 28 Tablets (drospirenone/ethinyl estradiol)
Berlex Laboratories, Inc.

The Methods Validation is pending for this drug product.

/S/

4/18/01

APPEARS THIS WAY
ON ORIGINAL