CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-258

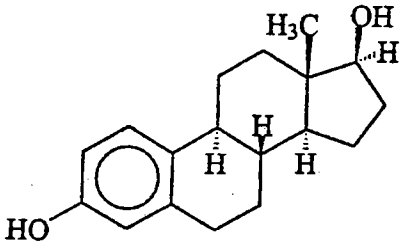
CHEMISTRY REVIEW(S)

NDA 21-258

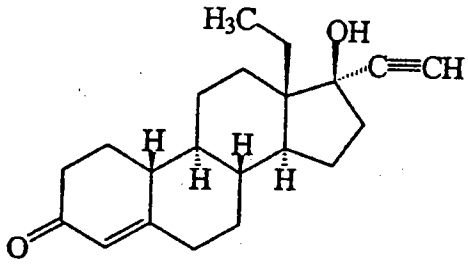
Climara Pro

Berlex Laboratories

Amit K. Mitra, Ph.D
Reproductive and Urologic Drug Products



Estradiol



Levonorgestrel

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-258

2. REVIEW #:3

3. REVIEW DATE: 6-NOV-2003

4. REVIEWER: Amit K. Mitra, Ph.D

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original	29-JUN-2000
Amendment	19-JUL-2000
Amendment	08-AUG-2000
Amendment	05-JUN-2001

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	19-SEP-2003
Amendment	24-OCT-2003

7. NAME & ADDRESS OF APPLICANT:

Name: Berlex Laboratories

Address: 340 Chagebridge Road, P.O. Box 1000, Montville, NJ 07045-1000

Chemistry Review Data Sheet

Representative:	Geoffrey Milligton, Manager, Drug Regulatory Affairs
Telephone:	973-487-2254

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Climara Pro
b) Non-Proprietary Name (USAN): Estradiol/Levonorgestrel transdermal system
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: NA

10. PHARMACOL. CATEGORY: Combination estrogen/progestin, Hormone replacement therapy

11. DOSAGE FORM: Film, Extended Release; Transdermal

12. STRENGTH/POTENCY: ESTRADIOL/LEVONORGESTEREL (4.4 mg/1.39 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.015 mg levonorgestrel per day)

13. ROUTE OF ADMINISTRATION: Transdermal, once a week application

14. Rx/OTC DISPENSED: _x__Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

__x____Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Estradiol- Estra-1,3,5(10)-triene-3, 17-diol (17 β) hemihydrate; Estra-1,3,5(10)-triene-3, 17 β -diol hemihydrate; $C_{18}H_{24}O_2$. ½ H_2O ; Mol wt.: 281.4
Levonorgestrel- (17•)-13-ethyl-17hydroxy-18,19-dinorpregn-4-en-20-yn-3-one; $C_{21}H_{28}O_2$; Mol wt.: 312.45

17. RELATED/SUPPORTING DOCUMENTS: DMF 14923

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
/	II	/	/	1	Adequate	08-MAY-2003	Reviewer: Dr. A. K. Mitra, see Chemistry Review #3 (dated 08-MAY-2003)

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	NA		
EES	Satisfactory	21-DEC-2000/15-OCT-2003	J. D. Ambrogio
Pharm/Tox	NA		
Biopharm	NA		
LNC	NA		
Methods Validation	Will be initiated		
EA	Categorical exclusion granted		
Microbiology	Satisfactory	02-MAY-2003	S. E. Langille

The Chemistry Review for NDA 21-258

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Since all the Chemistry deficiencies were addressed adequately, the application may be approved.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

None

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

(The following information is based on DMF — and it is proprietary. This information should not be released to the sponsor of the NDA).

The drug product is an oval shaped transdermal drug delivery system containing estradiol and levonorgestrel and proposed to be marketed in one strength. The transdermal system contains estradiol and levonorgestrel at 4.4 mg/1.39 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.015 mg levonorgestrel per day.

The drug product is composed of a polyethylene backing film, two drug substances in a — adhesive matrix, and a protective — liner.

B. Description of How the Drug Product is Intended to be Used

Climara Pro is proposed to be marked in one strength: The transdermal system containing estradiol/levonorgestrel at 4.4 mg/1.39 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.015 mg levonorgestrel per day for relief of vasomotor symptoms — in postmenopausal women with intact uterus. The Climara Pro is available in single unit pouch and it is to be applied on the intact skin after removal of the release liner. Only one system should be worn at any one time during one week dosing interval.

The drug product is to be stored under controlled conditions at 25°C (excursions permitted 15-30 °C).

C. Basis for Approvability or Not-Approval Recommendation

The DMF — contains all the CMC information for Climara Pro and it is deemed adequate to support the NDA. All facilities are acceptable according to the Office of Compliance (see attached). The labeling deficiencies were adequately addressed with respect to CMC. Therefore, the application may be approved.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Amit K. Mitra/
Moo-Jhong Rhee/
Kassandra Sherrod/

C. CC Block

2 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

____ § 552(b)(5) Deliberative Process

____ § 552(b)(4) Draft Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Amit K. Mitra
11/19/03 08:17:11 AM
CHEMIST

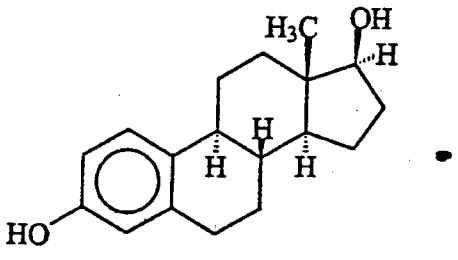
Moo-Jhong Rhee
11/19/03 03:59:53 PM
CHEMIST
I concur

NDA 21-258

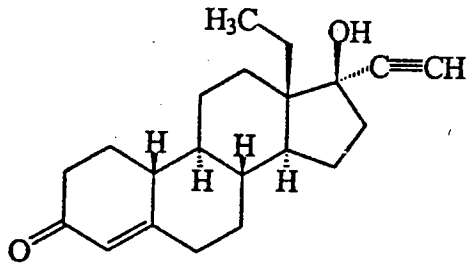
Climara Pro

Berlex Laboratories

Amit K. Mitra, Ph.D
Reproductive and Urologic Drug Products



Estradiol



Levonorgestrel

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-258

2. REVIEW #:2

3. REVIEW DATE: 23-SEP-2002

4. REVIEWER: Amit K. Mitra, Ph.D

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original	29-JUN-2000
Amendment	19-JUL-2000
Amendment	08-AUG-2000

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	05-JUN-2001

7. NAME & ADDRESS OF APPLICANT:

Name: Berlex Laboratories

Address: 340 Chagebridge Road, P.O. Box 1000, Montville, NJ 07045-1000

Chemistry Review Data Sheet

Representative:	Geoffrey Milligton, Manager, Drug Regulatory Affairs
Telephone:	973-487-2254

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Climara Pro
b) Non-Proprietary Name (USAN): None
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: NA

10. PHARMACOL. CATEGORY: Combination estrogen/progestin, Hormone replacement therapy

11. DOSAGE FORM: Transdermal Drug Delivery System

12. STRENGTH/POTENCY: ESTRADIOL/LEVONORGESTEREL (4.4 mg/1.39 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.015 mg levonorgestrel per day ; 4.4 mg/2.75 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.030 mg levonorgestrel per day ; 4.5 mg/3.75 mg per 30 cm^2, delivering 0.045 mg estradiol and 0.040 mg levonorgestrel per day)

13. ROUTE OF ADMINISTRATION: Transdermal, once a week application

14. Rx/OTC DISPENSED: _x__Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM)[Note25]:

_____SPOTS product – Form Completed

_x____Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Estradiol- Estra-1,3,5(10)-triene-3, 17-diol (17 β) hemihydrate; Estra-1,3,5(10)-triene-3, 17 β -diol hemihydrate; $C_{18}H_{24}O_2$. ½ H_2O ; Mol wt.: 281.4
Levonorgestrel- (17α)-13-ethyl-17hydroxy-18,19-dinorpregn-4-en-20-yn-3-one; $C_{21}H_{28}O_2$; Mol wt.: 312.45

17. RELATED/SUPPORTING DOCUMENTS: DMF 14923

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	II	✓	✓	1	Inadequate	23-SEP-2002	Reviewer: Dr. A. K. Mitra, see Chemistry Review #1 (dated 5-7-01) and Chemistry Review #2 (dated 9-23-01)

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	NA		
EES	Satisfactory	21-DEC-2000	J. D. Ambrogio
Pharm/Tox	NA		
Biopharm	NA		
LNC	NA		
Methods Validation	Will be initiated		
OPDRA	Trademark Climara Pro Acceptable	21-Aug-2001	A. R. Mahmud
EA	Categorical exclusion granted		
Microbiology	Approvable, Pending revision of DMF	06-SEP-2002	S. E. Langille

The Chemistry Review for NDA 21-258

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is approvable pending resolution of all the deficiencies in the Chemistry Review #2 and Microbiology Review #2 DMF —

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Since the drug product is non-approvable for clinical reasons, the Phase IV commitments were not sought.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

(The following information is based on DMF — and it is proprietary. This information should not be released to the sponsor of the NDA).

The drug product is an oval shaped transdermal drug delivery system containing estradiol and levonorgestrel and proposed to be marketed — The transdermal systems contain estradiol and levonorgestrel at 4.4 mg/1.39 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.015 mg levonorgestrel per day; 4.4 mg/2.75 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.030 mg levonorgestrel per day ; 4.5 mg/3.75 mg per 30 cm^2, delivering 0.045 mg estradiol and 0.040 mg levonorgestrel per day.

The drug product is composed of a polyethylene backing film, two drug substances in a adhesive matrix, and a protective — liner. The sponsor was requested to manufacture the drug product using estradiol from — and provide at least — accelerated stability data to the Agency prior to releasing the finished drug product. The sponsor agreed to commit to this activity as a post approval commitment that is satisfactory. The specification for — were provided and those are satisfactory.

The sponsor should clarify the specific analytical testing conducted during in-process control. The analytical testing during in-process control should assure that —

The sponsor is also asked to provide the details of the pouching operation. The specification for the adhesive laminate includes a specification for — ft

includes — The acceptance criterion set for vinyl acetate (could be a maximum of — is too high based on toxicologist's recommendation. The sponsor is asked to adopt a specific acceptance criteria for vinyl acetate since it is a possible carcinogen (according to the toxicologist).

All these deficiencies have been recorded in the Chemistry Review #2 for DMF — dated 23-SEP-2002. The DMF is deficient.

B. Description of How the Drug Product is Intended to be Used

Climara Pro is proposed to be marked — . The transdermal systems containing estradiol and levonorgestrel at 4.4 mg/1.39 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.015 mg levonorgestrel per day; transdermal system containing 4.4 mg/2.75 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.030 mg levonorgestrel per day ; transdermal system containing 4.5 mg/3.75 mg per 30 cm^2, delivering 0.045 mg estradiol and 0.040 mg levonorgestrel per day for relief of vasomotor symptoms — — in postmenopausal women with intact uterus. The Climara Pro is available in single unit pouch and it is to be applied on the intact skin after removal of the release liner. Only one system should be worn at any one time during one week dosing interval.

The drug product is to be stored under controlled conditions at 25°C (excursions permitted 15-30 °C).

C. Basis for Approvability or Not-Approval Recommendation

The DMF — contains all the CMC information for Climara Pro and it is deemed deficient. The reviewer recommends to send a separate Information Request letter to the DMF holder and the NDA holder should receive a response that the DMF is still deficient.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Amit K. Mitra/9-23-02: Same date as draft review
Moo-Jhong Rhee/
Dornette Spell-lesane/Date

C. CC Block

3 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

____ § 552(b)(5) Deliberative Process

____ § 552(b)(4) Draft Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Amit K. Mitra
9/26/02 01:47:11 PM
CHEMIST

Moo-Jhong Rhee
9/26/02 02:12:10 PM
CHEMIST
I concur

Summary of Chemistry Review of NDA 21-258 (Climarapro)

A. Drug Substances:

Estradiol is a synthetic estrogen, which has been widely used in the hormone replacement therapy. It is manufactured and supplied by [redacted] are in general adequate for supporting this NDA, however, since the [redacted] **estradiol** has not been used in the stability studies with the new adhesive matrix, it is necessary for the sponsor to provide **stability data from at least two batches** of drug product using estradiol from [redacted]

Schering AG and Diosynth BV are **in compliance with cGMP**.

Levonorgestrel is a synthetic progestin, which has been widely used in previously approved contraceptives. It is manufactured by [redacted] **in compliance with cGMP** and [redacted] is still **adequate** for supporting this NDA.

B. Drug Product:

(The following information is based on DMF [redacted], and it is proprietary information not to be released to this NDA sponsor)

The drug product is a transdermal drug delivery system with two different sizes of patches with three different strengths (4.4mg (E_2)/1.39mg(LNG)/22cm^2, 4.4mg(E_2)/2.75mg(LNG)/22cm^2, 4,5mg(E_2)/3.75mg(LNG)/30cm^2). This is a new combination-product-version of the previously approved Climara with levonogestrel.

It is composed of [redacted] film backing [redacted] adhesive matrix [redacted] containing the estradiol, levonorgestrel, and [redacted] and protective polyester liner [redacted] When the liner is removed from the patch and applied to the patients, the drug substances in the adhesive matrix are to be continuously released to the skin for seven days.

During manufacturing process, [redacted] proposes to use a polyester film coated with silicone as an alternate interim release however, no specifications are provided for the controls of **polyester film, silicone** [redacted] should **establish** these **specifications** since these are critical for [redacted] during the manufacturing process.

Process controls for critical steps in the manufacture of transdermal systems are not provided. Since these controls are crucial for producing products with uniform quality, the DMF holder **should provide** this information, unless justified.

The quality of the transdermal system is controlled by specifications such as [redacted] But the following issues should be clarified before approval.

nas **not** been clarified satisfactorily from microbiologist's point of view.

The DMF holder has not provided **method validation** for analyzing drug product **impurities** and this **should be submitted**, unless justified.

The patches are to be packaged into pouches and sponsor proposed two types of pouches (Pouch 1 and Pouch 2) and each pouch is consists of — respectively. All the components involved are deemed satisfactory for serving the purpose.

The proposed — expiry date is not acceptable, but based on real time data — **of expiry date** can be granted.

The tradename, **Climarapro**, was **not accepted** by OPDRA. The sponsor needs to propose a new tradename.

C. Conclusion and Recommendation:

From chemistry, manufacturing, and controls point of view, this NDA may not be approved until those issues noted in the DMF — are satisfactorily resolved.

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Moo-Jhong Rhee
6/15/01 08:49:07 AM
CHEMIST

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS (HFD-580)
REVIEW OF CHEMISTRY AND MANUFACTURING CONTROLS

NDA # 21-258 Chemistry Review # 1 Review Date: 5-7-01

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Original	6-29-00	6-29-00	7-6-00
Amendment	7-19-00	7-21-00	7-21-00
Amendment	8-8-00	8-14-00	8-14-00

NAME AND ADDRESS OF APPLICANT
Berlex Laboratories
340 Changebridge Road
Montville, New Jersey 07450-1000

DRUG PRODUCT NAME
Proprietary: CLIMARAPRO
Non-proprietary/USAN: Estradiol/Levonorgestrel Transdermal Drug Delivery System (E2/LNG Transdermal Drug Delivery System)
Compendium: does not apply
Code name/number: None
Chem. Type/Ther. Class: 4 S

ANDA SUITABILITY PETITION/DESI/PATENT STATUS: N/A

PHARMACOL. CATEGORY/INDICATION: Combination estrogen/progestin, Hormone replacement in postmenopausal women.

DOSAGE FORM: Transdermal Delivery System

STRENGTHS: ESTRADIOL/LEVONORGESTEREL (4.4 mg/1.39 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.015 mg levonorgestrel per day; 4.4 mg/2.75 mg per 22 cm^2, delivering 0.045 mg estradiol and 0.030 mg levonorgestrel per day ; 4.5 mg/3.75 mg per 30 cm^2, delivering 0.045 mg estradiol and 0.040 mg levonorgestrel per day)

ROUTE OF ADMINISTRATION: Transdermal, once a week application

Dispensed: By prescription

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT.:
Estradiol- Estra-1,3,5(10)-triene-3, 17-diol (17 β); Estra-1,3,5(10)-triene-3, 17 β -diol;
Levonorgestrel- (17α)-13-ethyl-17hydroxy-18,19-dinorpregn-4-en-20-yn-3-one

SUPPORTING DOCUMENTS
DMF

RELATED DOCUMENTS
None

CONSULTS
1. The EER for the manufacturing facilities were submitted. The inspection results are satisfactory.
2. The trademark "Climarpro" is not acceptable to OPDRA. The division decision is still pending

REMARKS
The chemistry, manufacturing and control information for the drug substances, and the drug product was provided in the type II DMF — The labeling information was submitted in the NDA 21-258 and the labeling information is reviewed here. The amendment dated 7-19-00 states that — submitted a desk copy of the CMC section. The amendment dated 8-8-00 provides clarifications on the manufacturing facilities for the drug substances, estradiol and levonorgestrel. The DMF — s not adequate to support the NDA 21-258. An Information Request letter is being sent to the sponsor of the DMF —

CONCLUSION AND RECOMMENDATION
From chemistry, manufacturing, and controls point of view, this NDA is not approvable until all the deficiencies noted in the DMF — as well as in this NDA are satisfactorily clarified.

cc: NDA 21-258
HFD-580/A. K. Mitra, Ph.D
HFD-580/M.J. Rhee, Ph.D
HFD-580/D. Moore
R/D. Init. By-

Amit K. Mitra, Ph.D

2 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

___ § 552(b)(5) Deliberative Process

___ § 552(b)(4) Draft Labeling

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21258/000
Stamp: 29-JUN-2000 Regulatory Due: 29-APR-2001
Applicant: BERLEX LABS
340 CHANGEBRIDGE RD
MONTVILLE, NJ 070451000

Priority: 4S Org Code: 580
Action Goal: District Goal: 28-FEB-2001
Brand Name: CLIMARA PRO
(ESTRADIOL/LEVONORGESTREL TR
Established Name:
Generic Name: ESTRADIOL/LEVONORGESTREL TRANSDERMAL SYS
Dosage Form: TDP (TRANSDERMAL PATCH)
Strength: 4.40/1.39 MG AND OTHERS

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

Overall Recommendation:

ACCEPTABLE on 21-DEC-2000 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment:

DMF No:
AADA No:

Profile: TDP OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date 21-DEC-2000
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities:

Establishment:

DMF No:
AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date 01-AUG-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities:

Establishment:

DMF No:
AADA No:

Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date 05-SEP-2000
Decision: ACCEPTABLE

Responsibilities:

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Reason: **DISTRICT RECOMMENDATION**

Establishment: /

/

DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE** Responsibilities: /
Last Milestone: **OC RECOMMENDATION**
Milestone Date **09-AUG-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: /

/

DMF No:
AADA No:

Profile: **CRU** OAI Status: **NONE** Responsibilities: /
Last Milestone: **OC RECOMMENDATION**
Milestone Date **11-AUG-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Amit K. Mitra
5/7/01 05:04:03 PM
CHEMIST

Moo-Jhong Rhee
5/8/01 10:13:28 AM
CHEMIST
I concur

NDA 21-258
Climarapro™ (estradiol transdermal system) estradiol/levonorgestrel 0.045/0.015, 0.045/0.030 and 0.045/0.040 mg per day
Berlex laboratories, Inc.

Environmental Assessment

A categorical exclusion is claimed for this NDA in accordance with 21 CFR part 25.31 (b), as amended in the 29-Jul-1997 Federal Register. This was found to be satisfactory (see Chemistry DMF Review # — dated May 7, 2001).

Diane Moore 6/11/01

81 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

____ § 552(b)(5) Deliberative Process

____ § 552(b)(4) Draft Labeling