

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-180/S-004**

**CHEMISTRY REVIEW(S)**

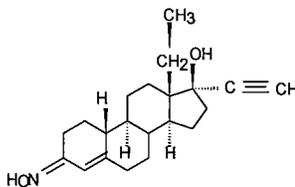
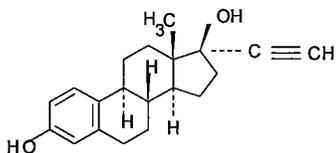
**DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS**  
**REVIEW OF CHEMISTRY MANUFACTURING AND CONTROLS**  
**CHEMIST'S REVIEW #1**

1. NDA NUMBER: 21-180
2. NAME AND ADDRESS OF APPLICANT  
Ortho-McNeil Pharmaceutical, Inc.  
1000 Route 202 South  
P.O. Box 300  
Raritan, NJ 08869-0602
3. SUPPLEMENT NUMBER/DATE/DATE ASSIGNED  
SCM-004/5-15-02/5-16-02
4. NAME OF THE DRUG: ORTHO EVRA
5. NONPROPRIETARY NAME: Norelgestromin/Ethinyl estradiol Transdermal Drug Delivery System
6. SUPPLEMENT PROVIDES FOR: An alternate site for conducting various manufacturing operations such as weighing, storage of drug substance, excipients, packaging components, and drug product, including the QC release and stability testing of the drug substances and drug product.
7. AMENDMENTS/REPORTS/ DATE: None
8. PHARMACOLOGICAL CATEGORY  
Combination estrogen/progestin, prevention of pregnancy.
9. HOW DISPENSED  
Prescription
10. RELATED IND/NDA/DMF/SUPPLEMENT  
None
11. DOSAGE FORM : Transdermal
12. POTENCY  
Norelgestromin/Ethinyl estradiol (6.0 mg/0.75 mg per 20 cm<sup>2</sup>) delivering 150 µg norelgestromin, and 20 µg ethinyl estradiol per day.

### 13. CHEMICAL NAME AND STRUCTURE

Norelgestromin - (17 $\alpha$ )-17-hydroxy- 13-ethyl-18,19-dinorpregn-4-en-20-yn-3-one-3-oxime

Ethinyl estradiol - 19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17 $\alpha$ )



Ethinyl estradiol

Molecular wt: 296.40

Norelgestromin

Molecular weight: 327.47

### 14. COMMENTS

The submission proposes an alternate site for receipt, warehousing, sampling, QC release testing of raw materials, APIs, and packaging components, and dispensing and weighing of batch quantities. Additionally, storage of reserve samples of raw materials and drug product, finished product storage, QC and stability testing, release and shipment to secondary packager are also proposed to be conducted at this site.

An inspection request was submitted and the OC has given an "Acceptable" recommendation for the facility.

### 15. CONCLUSIONS AND RECOMMENDATIONS:

The supplement may be approved with respect to CMC. Please issue an approval letter.

Reviewed By: Amit K. Mitra, Ph.D.

R/D INIT. BY: Moo Jhong Rhee, Ph.D

CC: A. K. MITRA/HFD-580

M.J.RHEE/HFD-580

J. Mercier/HFD-580

NDA 21-180

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/s/

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Moo-Jhong Rhee  
10/2/02 10:22:34 AM

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### CHEMIST'S REVIEW NOTES

The approved facility is Ortho-McNeil Pharmaceutical, Inc., Drug-Delivery Division, 701 Galveston Drive, Redwood City, CA 94063. The proposed alternate site is Ortho-McNeil Pharmaceutical, Inc., Drug Delivery Division, 235 Constitution Drive, Menlo Park, CA 94025. The sponsor proposes to conduct the following activities at the proposed site: receipt, warehousing, sampling, QC release testing of raw materials, APIs, and packaging components, and dispensing and weighing of batch quantities. Additionally, storage of reserve samples of raw materials and drug product, finished product storage, QC and stability testing, release and shipment to secondary packager are also proposed to be conducted at this site.

The OC made an overall recommendation of "Acceptable" (see attached).

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01-OCT-2002

FDA CDER EES  
ESTABLISHMENT EVALUATION REQUEST  
SUMMARY REPORT

Page 1 of 1

Application: NDA 21180/004 Priority: 14S Org Code: 580  
Stamp: 16-MAY-2002 Regulatory Due: 16-SEP-2002 Action Goal: District Goal: 12-AUG-2002  
Applicant: ORTHO MCNEIL PHARM Brand Name: ORTHO  
1000 ROUTE 202 SOUTH EVRA(NORELGESTROMIN/ETHINYL  
RARITAN, NJ 088690602 ESTRAD

Established Name:  
Generic Name: NORELGESTROMIN/ETHINYL  
ESTRADIOL  
Dosage Form: FLM (TRANSDERMAL SYSTEM)  
Strength: NRG/EE (150/20 MCG/DAY)

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

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Overall Recommendation:

**ACCEPTABLE on 12-AUG-2002 by J. D AMBROGIO(HFD-324) 301-827-0062**

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Establishment: 2953118 DMF No:  
ORTHO MCNEIL PHARMACEUTICAL AADA No:  
235 CONSTITUTION DRIVE  
MENLO PARK, CA 94025

Profile: CTL OAI Status: NONE Responsibilities: DRUG SUBSTANCE RELEASE  
Last Milestone: OC RECOMMENDATION TESTER  
Milestone Date: 12-AUG-2002  
Decision: ACCEPTABLE  
Reason: DISTRICT RECOMMENDATION

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31-JUL-2002

FDA CDER EES  
ESTABLISHMENT EVALUATION REQUEST  
DETAIL REPORT

Page 1 of 1

Application: NDA 21180/003  
Stamp: 14-MAY-2002  
Regulatory Due: 14-NOV-2002  
Applicant: ORTHO MCNEIL PHARM  
1000 ROUTE 202 SOUTH  
RARITAN, NJ 088690602  
Priority: 14S  
Org Code: 580

Action Goal:  
District Goal: 10-OCT-2002  
Brand Name: ORTHO  
EVRA (NORELGESTROMIN/ETHINYL  
ESTRAD  
Estab. Name:  
Generic Name: NORELGESTROMIN/ETHINYL  
ESTRADIOL

Dosage Form: (TRANSDERMAL SYSTEM)  
Strength: NRG/EE (150/20 MCG/DAY)

Application Comment:

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

Overall Recommendation: ACCEPTABLE on 22-MAY-2002 by S. FERGUSON (HFD-324) 301-827-0062

Establishment: 2211100

ORTHO PHARMACEUTICAL CORP  
1000 RTE 202  
RARITAN, NJ 08869

DMF No:

AADA:

Responsibilities: DRUG SUBSTANCE OTHER TESTER

Profile: CTL OAI Status: NONE

Estab. Comment: THE SPONSOR WANTS TO INCLUDE WEIGHING BATCH QUANTITIES OF API AT  
THE FACILITY (on 21-MAY-2002 by A. MITRA (HFD-580) 301-827-4238)

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	21-MAY-2002				MITRAA
OC RECOMMENDATION	22-MAY-2002			ACCEPTABLE BASED ON PROFILE	FERGUSONS

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/s/  
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Amit K. Mitra  
10/3/02 07:30:21 AM  
CHEMIST

Moo-Jhong Rhee  
10/3/02 01:48:30 PM  
CHEMIST  
I concur

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