CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 21-022

CHEMISTRY REVIEW(S)

SEP 13 1999

DIVISION OF DERMATOLOGIC AND DENTAL DRUG PRODUCTS
HFD-540
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-022 **CHEM.REVIEW #:** 1 **REVIEW DATE:** 10-SEP-1999

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	18-DEC-1998	18-DEC-1998	29-DEC-1998
NEW CORRESP./NC	25-JUN-1999	28-JUN-1999	06-JUL-1999

NAME & ADDRESS OF APPLICANT: Hoechst Marion Roussel, Inc.
10236 Marion Park Drive
Kansas City, MO 64137

L. E. Roebel, Ph.D.,
V.P., N. American Drug Regulatory Affairs

DRUG PRODUCT NAME

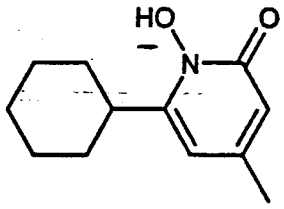
Proprietary:	Loprox Nail Lacquer
Nonproprietary/USAN:	Ciclopirox
Code Names/#'s:	HOE 296b
Chemical Type/	Pyridinone
Therapeutic Class:	Antifungal

ANDA Suitability Petition/DESI/Patent Status: N/A

PHARMACOLOGICAL CATEGORY/INDICATION: For topical treatment of mild to moderate onychomycosis of fingernails and toenails without lunula involvement due to *Trichophyton rubrum*

DOSAGE FORM:	Solution
STRENGTHS:	8.0%
ROUTE OF ADMINISTRATION:	Topical
DISPENSED:	X Rx ____ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL. WT.:
6-Cyclohexyl-1-hydroxy-4-methyl-2-(1*H*)pyridinone
Molecular Formula: $C_{12}H_{17}NO_2$
Molecular Weight: 207.28
CAS Number: [29342-05-0]



SUPPORTING DOCUMENTS:

No. / Type	Subject	Holder	Status	Review Date	Letter Date
DMF — / IV	—			03-FEB-1999	Update request sent: 03-FEB-1999
NDA 18-748	LOPROX Cream, 0.77%		Current		
NDA 19-824	LOPROX Lotion, 0.77%		Current		
NDA 20-519	LOPROX Gel, 0.77%		Current		
IND —	—		Current		

NDA 21-022
TRADENAME® Nail Lacquer (ciclopirox) Topical Solution, 8%
Hoechst Marion Roussel, Inc.

CONSULTS:

The proposed trade name LOPROX Nail Lacquer was sent to the CDER Labeling and Nomenclature Committee on 02-APR-1999. The report, dated 07-JUN-1999, recommended "Nail Lacquer" as part of the trade name, and "Topical Solution" as the standard dosage form.

The proposed trade name ——— Nail Lacquer, submitted as a result of the ——— was sent to the CDER Labeling and Nomenclature Committee on 06-JUL-1999. The report, dated 10-SEP-1999, judged the proposed name unacceptable due to look-alike/sound-alike conflicts with approved drugs BACLOFEN, BACTROBAN, BETAPEN, BETAPACE and BACITRACIN. The previous comments regarding the recognized dosage form are still in force. See Attachments 3-7.

REMARKS/COMMENTS:

During review of this NDA, USP 24/NF 19 was published, effective January 1, 2000. Revision of the established name of the drug substance from "ciclopirox olamine" to "ciclopirox", per earlier recommendation by FDA CMC reviewers, has not yet been made final by USP.

This drug product, if approved, will be the first topical treatment for onychomycosis. An Advisory Committee meeting is being scheduled at the time of this review.

CONCLUSIONS & RECOMMENDATIONS: **APPROVABLE**

Based on the recommendations of the CDER Labeling and Nomenclature Committee, and of the Labeling and Nomenclature Standards Committee, please revise the proprietary name, established name and dosage form to conform to the following format:

TRADENAME® Nail Lacquer (ciclopirox) Topical Solution, 8%

NDA 21-022
TRADENAME® Nail Lacquer (ciclopirox) Topical Solution, 8%
Hoechst Marion Roussel, Inc.

Please revise the proposed package insert with respect to the following:

1. All references to the drug product should be revised to incorporate the presentation noted above.

2. In the WARNINGS section, add [redacted] after "intravaginal use".

3. Under the section ADVERSE REACTIONS, it would be acceptable to delete the drug product's strength (8%) from this paragraph to eliminate confusion with the adverse event percentages.

Pending submission of acceptable revised draft container and package insert labeling, and commitment by the applicant to the points noted above and in the draft letter, this application is recommended as "Approvable" for chemistry, manufacturing and controls.

/S/

J. S. Hathaway, Ph.D.
Review Chemist

cc: Orig. NDA 21-022 (with attachments)
HFD-540/Division File (with attachments)
HFD-540/ProjMgr/FHCross
HFD-540/PharmTox/KMainigi
HFD-540/MedOffr/BVaughan
HFD-540/Chem/JSHathaway
HFD-540/ChemTeamLdr/WHDeCamp (with attachments)

/S/ 9/13/99

filename: [redacted]

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DEC 8 1999

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DIVISION OF DERMATOLOGIC AND DENTAL DRUG PRODUCTS
HFD-540
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-022 **CHEM.REVIEW #:** 2 **REVIEW DATE:** 08-DEC-1999

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	18-DEC-1998	18-DEC-1998	Review #1
NEW CORRESP./NC	25-JUN-1999	28-JUN-1999	Review #1
AMENDMENT/BL	27-SEP-1999	28-SEP-1999	06-OCT-1999
AMENDMENT/BL	16-NOV-1999	17-NOV-1999	01-DEC-1999
AMENDMENT/BC	19-NOV-1999	22-NOV-1999	01-DEC-1999

NAME & ADDRESS OF APPLICANT:
Hcechst Marion Roussel, Inc.
1C236 Marion Park Drive
Kansas City, MO 64137

L. E. Roebel, Ph.D.,
V.P., N. American Drug Regulatory Affairs

U.S. Agent
PAREXEL International Corp.
195 West Street
Waltham, MA 02154

Alicia Cabrelli
Regulatory Affairs Associate,
Worldwide Regulatory Affairs

DRUG PRODUCT NAME

Proprietary:	Tradename Nail Lacquer
Nonproprietary/USAN:	Ciclopirox
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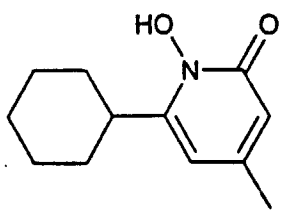

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TRADENAME® Nail Lacquer (ciclopirox) Topical Solution, 8%
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NDA 19-824	LOPROX Lotion, 0.77%		Current		
NDA 20-519	LOPROX Gel, 0.77%		Current		
IND —	—		Current		

CONCLUSIONS & RECOMMENDATIONS: **APPROVAL**

The applicant has adequately addressed all of the issues noted in the Discipline Review letter of 13-SEP-1999. The flammability caution statement should be added at the end of the label (see Review Notes below). Pending the submission of final printed labeling which includes the above statement, this application may be approved.

/S/ 12/8/99

J. S. Hathaway, Ph.D.
Review Chemist

cc: Orig. NDA 21-022
HFD-540/Division File
HFD-540/ProjMgr/FHCross
HFD-540/PharmTox/KMainigi
HFD-540/MedOffr/BVaughan
HFD-540/Chem/JSHathaway
HFD-540/ChemTeamLdr/WHDeCamp /S/ 12/8/99 /S/ 12/8/99

filename:

APPEARS THIS WAY
ON ORIGINAL

2 **Page(s) Redacted**

Draft

Labeling