CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-026

CHEMISTRY REVIEW(S)

NDA 21-026

VUSION™ Ointment
0.25% Miconazole Nitrate, 15% Zinc Oxide, 81.35% White Petrolatum Ointment

Barrier Therapeutics, Inc.

Joel S. Hathaway, Ph.D.
Office of New Drug Quality Assessment,
Division of Post-Marketing Evaluation,
Branch 8

Table of Contents

Chemistry Review Data Sheet

1. **NDA 21-026**

2. **REVIEW #:** 4

3. **REVIEW DATE:** 13-FEB-2006

4. **REVIEWER:** Joel S. Hathaway, Ph. D.

5. **PREVIOUS DOCUMENTS:**

Document	Document Date
IND 21,542	08 February 1983
IND 21,542 Acknowledgement Letter Transfer from Johnson & Johnson Consumer Companies, Inc. to Barrier Therapeutics, Inc.	05 July 2002
8 August 2003 CMC Telecon Minutes	05 September 2003
IND 21,542/N-046(IC)	04 March 2004
Original Submission NDA 21-026 Johnson & Johnson Consumer Companies, Inc	24 August 1998
Not Approvable (NA) Action Letter	28 June 1999
NDA 21-026/N-000(BC)	08 October 1999
NDA 21-026/N-000(BZ)	30 March 1999
NDA 21-026/N-000(BC)	25 May 1999
Chemistry Review # 1	15 June 1999
NDA 21-026/N-000(AZ)	21 January 2000
NDA 21-026/N-000(BC)	01 February 2000
NDA 21-026/N-000(BL)	17 March 2000
NDA 21-026/N-000(BL)	28 March 2000
Chemistry Review #	13 July 2000
Second NA Action Letter	24 July 2000
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NDA 21-026/N-000/XS Transfer from Johnson & Johnson Consumer Companies, Inc. to Barrier Therapeutics, Inc.	21 June 2002
7 October 2002 End of Phase 2 and Guidance Meeting Minutes (FAX)	22 December 2002
18 December 2003 Teleconference Minutes (FDA Combination Drug Policy: Zinc Oxide and White petrolatum considered active) FAX	29 January 2004
FAX Memorandum	28 October 2004

Chemistry Review Data Sheet
NDA 21-026

Document (continued)	Document Date
NDA 21-026/N-000(AZ) (NDA Resubmission by Barrier Therapeutics, Inc.)	24 November 2004
Information Request (IR) Letter (FAX)	08 December 2004
NDA 21-026/N-000(BC)	13 December 2004
NDA 21-026/N-000(BC)	05 January 2005
Interdisciplinary IR Letter	08 February 2005
NDA 21-026/N-000(BL)	16 February 2005
NDA 21-026/N-000(BC)	10 March 2005
CMC IR Letter # 3 (FAX)	05 April 2005
CMC IR Letter # 4 (FAX)	12 April 2005
CMC T-con with Applicant	19 April 2005
NDA 21-026/N-000(BC)	22 April 2005
CMC IR Letter # 5 (FAX)	25 April 2005
NDA 21-026N-000(BC)	03 May 2005
NDA 21-026/N-000(BC)	05 May 2005
NDA 21-026/N-000(BL) Electronic	17 May 2005
NDA 21-026/N-000(BC) Electronic	20 May 2005
CMC Post-NA IR Letter # 6 (FAX)	24 May 2005

6. SUBMISSION(S) BEING REVIEWED:

Submissions Reviewed	Document Date
NDA 21-026/N-000(AZ)	15-AUG-2005
NDA 21-026/N-000(BL)	25-AUG-2005
NDA 21-026/N-000(BL)	24-OCT-2005
NDA 21-026/N-000(BL)	14-NOV-2005
NDA 21-026/N-000(BL)	30-JAN-2006
NDA 21-026/N-000(BC)	14-FEB-2006

7. NAME & ADDRESS OF APPLICANT:

Name	Barrier Therapeutics, Inc.
Address	600 College Road East, Suite 3200 Princeton, New Jersey 08540
Representative	Isabel Drzewiecki, Global Head, Regulatory Operations
Telephone	(609) 945-1247

8. DRUG PRODUCT NAME/CODE/TYPE:

a) **Proprietary Name:** Trade name VUSION™ was found to be acceptable by ODS; see review dated 30-NOV-2005.

b) **Non-Proprietary Name (USAN):** 0.25% Miconazole Nitrate / 15% Zinc Oxide / 81.35% White Petrolatum

c) **Code Name/#:** ZOOM

d) **Chem. Type/Submission Priority:**

- **Chem. Type:** 3
- **Submission Priority:** S

9. **LEGAL BASIS FOR SUBMISSION:** The original NDA 21-026 was submitted by Johnson & Johnson Consumer Products Companies, Inc., under 505(b)(1). However, by agreement with the Agency, Barrier Pharmaceutics, Inc., the current applicant, was only required to demonstrate the contribution of miconazole nitrate to the efficacy of this drug product. As previously stated, zinc oxide and white petrolatum are listed as active ingredients in the final monograph of Skin Protectant Drug Products for Over-The-Counter Human Use at concentrations of 1 to 25% for zinc oxide, and 30 to 100% for White petrolatum. Both latter drug substances are found in products currently marketed Over-The-Counter for diaper rash (the Applicant's product contains zinc oxide, 15% and white petrolatum, 81.35%). It was the Agency's position that the applicant could rely on evidence already known regarding the contribution of zinc oxide and white petrolatum to efficacy for treatment of diaper rash. Zinc oxide and white petrolatum also serve as part of the delivery vehicle for the applicant's product.

   Thus, the current application (resubmission) is considered to be a 505(b)(2) submission.

10. **PHARMACOLOGICAL CATEGORY:** Antifungal

11. **DOSAGE FORM:** Ointment

12. **STRENGTH/POTENCY:** 0.25% Miconazole Nitrate / 15% Zinc Oxide / 81.35% White Petrolatum

13. **ROUTE OF ADMINISTRATION:** Topical

14. **INDICATION:** Treatment of diaper dermatitis complicated by candidiasis

15. **Rx/OTC DISPENSED:** _X_ Rx ___OTC

16. **SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):**

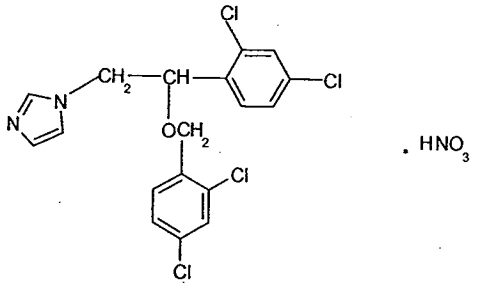
    _____SPOTS product – Form Completed

    ___X___Not a SPOTS product

17. **CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:**

Chemistry Review Data Sheet
NDA 21-026

- 1-(2,4-dichloro-β-[(2,4-dichlorobenzyl)oxy]phenethyl]imidazole mononitrate



- 1-[2(2,4-dichlorophenyl)-2,4-dichlorophenyl)methoxy]ethyl]-1H-imidazole mononitrate

Molecular Formula: $C_{18}H_{14}Cl_4N_2O.HNO_3$
Molecular Weight: 479.15
CAS Number: (Miconazole Nitrate) 22832-87-7
(Miconazole 22916-47-8)

18. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

b(4)

DMF #	TYPE	DMF HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	II			3	Adequate	28-Nov-2003 (Matecka/HFD-590)	
	IV			3	Adequate	19 February 1999 (Timmer/HFD-540)	
	IV						Withdrawn 1991
	III			3	Adequate	19 April 1999 (Timmer/HFD540)	

[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)

Chemistry Review Data Sheet
NDA 21-026

B. Other Documents:

Document Type	Application Number	Holder	Description
IND	21,542	Current Applicant: Barrier Therapeutics, Inc. Former Applicant: Johnson & Johnson Consumer Companies, Inc.	Miconazole Nitrate Ointment
b(4)			
NDA			
NDA	17-450	Advanced Care Products	Monistat-7 Antifungal/Candidiasis
NDA	17-494	Johnson & Johnson Consumer Companies, Inc.	Monistat-Derm Cream, 2% Sclerosing Agents
NDA	18-040	Janssen Pharmaceuticals, Inc.	Monistat Injectable Solution (Systemic Antifungal)
NDA	18-520	Advanced Care Products	Monistat-7 Suppository

19. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
b(4)			
EES* (Drug Substance: Miconazole Nitrate; Manufacturer/Packager/Tester: Janssen Pharmaceutica NV)	Acceptable (Based on review of 2/2005 cGMP inspection, which is based on the investigator's recommendation. No 483 issued).	23-FEB-2005	Shawnte Adams
EES* (Drug Substance: Miconazole Nitrate; Manufacturer/Packager/Tester: Noramco Inc. (Noramc) 1440 Olympic Drive Athens, Georgia	Acceptable (Based on cGMP inspection: EI of 2/22/05- 2/24/05 was NAI. Application was covered. Profile class is acceptable.)	28-FEB-2005	L. Andrews, P. M. Carve Janine D'Ambrogio
EES* (Drug Substance: Zinc Oxide; Manufacturer/ Packager /Tester:	Acceptable (Based on cGMP inspection)	19-MAY-2005	Regina T. Brown, Shirnette Ferguson / Shawnte Adams
EES* (Drug Substance: White Petrolatum Manufacturer/ Packager /Tester:	Acceptable (Based on cGMP profile: Last cGMP Establishment Inspection of 12/18/2002 is classified NAI).	06-APR-2005	K. Campbel Shirnette Ferguson / Janine D'Ambrogio
EES* (Drug product: Miconazole Nitrate Ointment Manufacturer /Packager Tester:	Acceptable (Based on profile: last EI was 7/04).	31-JAN-2005	Janine D'Ambrogio

Chemistry Review Data Sheet
NDA 21-026

DSM Pharmaceuticals, Inc., 5900 Greenville Blvd. NE, Greenville, NC 27348			
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	N/A		
Methods Validation	Deferred		
DMETS: Zimycan	Unacceptable: The appeal by the Applicant for reconsideration, dated 16 February 2005, was denied by DMETS	19-JAN-2005 03-MAY-2005	Denise Toyer Linda Y. Kim-Jung
DMETS:	Unacceptable	06-MAY2005	Tina M. Tezky
DMETS: Vusion	Acceptable	30-NOV-2005	
EA (Categorical Exclusion)	Acceptable	05-MAY-2005	Saleh A. Turujman
Microbiology	N/A		

b(4)

The Chemistry Review for NDA 21-026

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The recommendation for this resubmission remains "Approval" from the standpoint of the CMC (chemistry, manufacturing and controls) information submitted in the application, as amended.

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 and Drug Substances

The combination drug product contains three drug substances and two excipients, . The three APIs are: Miconazole Nitrate (0.25%); Zinc Oxide (15%); White Petrolatum (81.35%). Zinc oxide and white petrolatum are both ingredients in products currently marketed Over-The-Counter for diaper rash. Zinc oxide and white petrolatum also serve as part of the delivery vehicle. b(4)

Miconazole Nitrate

Miconazole nitrate, USP, is an approved antifungal used in several dosage forms approved for marketing, both as a prescription drug and as an OTC drug product. Other imidazole antifungals include ketoconazole, clotrimazole, econazole, and oxiconazole. Imidazole-type antifungal compounds are used worldwide, and are the leading antifungal agents. The marketed concentrations are 2% and 4%. Imidazole compounds are believed to exhibit their antifungal activity mainly by damaging the cell membrane of fungi which have an imidazole group in their chemical structure. Miconazole nitrate, the USAN name of this drug substance, is also the compendial name.

Miconazole nitrate is a chiral molecule with one chiral carbon (and two prochiral carbons). The compendial drug substance, however, is an optically inactive racemate (RS compound). Miconazole nitrate is a fine white to light beige powder, essentially odorless, with a melting range of 178-184°C (decomposition).

Zinc Oxide

Zinc oxide occurs as the mineral zincite. The purified material can occur as white hexagonal crystals or a white, odorless powder commonly known as zinc white. It is practically insoluble in water but soluble in dilute acetic or mineral acids, ammonia, ammonium carbonate, or alkali hydroxide solutions.

White petrolatum

White petrolatum is a purified mixture of semisolid saturated hydrocarbons having the general formula C_nH_{2n+2} and is obtained from petroleum. The hydrocarbons consist mainly of branched and unbranched chains, although some cyclic alkanes and aromatic molecules with paraffin side chains may also be present. This compendial material (since USP 25) may contain a suitable stabilizer, such as butylated hydroxy toluene (BHT). The white petrolatum used in the proposed drug product contains BHT as the stabilizer. Additives, such as microcrystalline wax, may also be used to add body to petrolatum. Petrolatum is practically insoluble in acetone, ethanol, hot or cold ethanol (95%), glycerin, and water; soluble in benzene, carbon disulfide, chloroform, ether, hexane, and most fixed and volatile oils.

Various grades of petrolatum are commercially available, which vary in their physical properties depending upon their source and refining process. White petrolatum obtained from different sources may therefore behave differently in a formulation, a phenomenon which was observed by the previous (original) Applicant of this NDA (J&J). White petrolatum, as a commercial grade, is associated with fewer instances of hypersensitivity reactions and is the preferred petrolatum for use in cosmetics and in pharmaceuticals.

Petrolatum is listed in the CFR as GRAS (Generally Recognized As Safe [as a food additive]).

Drug product, 0.25% Miconazole Nitrate / 15% Zinc Oxide / 81.35% White Petrolatum

The combination drug product, contains the following active ingredients: synthetic antifungal compound, miconazole nitrate (0.25%) zinc oxide and white petrolatum. Each gram of the Ointment contains 2.5 mg of Miconazole Nitrate, USP and 150 mg Zinc Oxide, USP, 813.5 mg White Petrolatum, USP, Trihydroxystearin (hydrogenated castor oil) and of Chemoderm 1001/B (b(4)
). The trihydroxystearin is added to provide physical stability, to optimize spreadability and to sustain the suspension. The drug product is packaged in a 30 g tube for marketing (the initially proposed tube size was withdrawn.

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

The labeled indication for this drug product is for the treatment of diaper dermatitis complicated by a verified concomitant infection by *Candida albicans*. The proposed label directs that the drug product should be applied to the entire affected area at each diaper change after cleansing the skin and "pat" drying. Treatment is recommended to be continued for seven days.

The expiration date, based on the primary stability data provided in the resubmission, is one year (to which the applicant agreed on 14-FEB-2006).

C. Basis for Approvability or Not-Approval Recommendation
N/A

III. Administrative

A. Reviewer's Signature

Joel S. Hathaway, Ph.D.
(see attached electronic signature page)

B. Endorsement Block

Chemist / Date: Joel S. Hathaway, Ph.D./ 14-FEB-2006
Chemistry Branch Chief / Date: Moo-Jhong Rhee, Ph.D./
Project Manager's / Date: Mildred Wright, R.N., M.S.N./

C. CC Block

cc: Original NDA 21-026
OND/DDDDP/Division File
ONDQA/DPE/Chem/JSHathaway
ONDQA/DPA/ChemBranchCh/MJRhee
ONDQA/DPA/ChemPAL/SDing
OND/DDDDP/ProjMgr/MWright
OND/DDDDP/MedOffr/BCarr
OND/DDDDP/MedOffrTL/MLuke
OND/BioPharm/AAdebowale
OND/BioPharmTL/RBaweja
OND/BioPharmTL/DBashaw
OND/Biometrics/SLee

Filename: C:\data\MSWordDocs\NDA Reviews\OrigNDAs\21026\N21026r4.n.000.doc

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_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Chemistry-_____

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/s/

Steve Hathaway
2/14/2006 03:29:59 PM
CHEMIST
AP recommended
For your concurrence

Moo-Jhong Rhee
2/14/2006 04:33:02 PM
CHEMIST
Chief, Branch III

NDA 21-026

Trade Name
0.25% Miconazole Nitrate, 15% Zinc Oxide, 81.35% White Petrolatum Ointment

Barrier Therapeutics, Inc.

Saleh A. Turujman, Ph.D.
Division of Dermatologic and Dental Drug Products
HFD-540

Table of Contents

b(4)

Chemistry Review Data Sheet

1. **NDA 21-026**

2. **REVIEW #:** 3

3. **REVIEW DATE:** May 23, 2005

4. **REVIEWER:** Saleh A. Turujman, Ph. D.

5. **PREVIOUS DOCUMENTS:**

Document	Document Date
IND 21,542	08 February 1983
IND 21,542 Acknowledgement Letter Transfer from Johnson & Johnson Consumer Companies, Inc. to Barrier Therapeutics, Inc.	05 July 2002
8 August 2003 CMC Telecon Minutes	05 September 2003
IND 21,542/N-046(IC)	04 March 2004
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NDA 21-026/N-000(BC)	25 May 1999
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Chemistry Review Data Sheet
NDA 21-026

Document (continued)	Document Date
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NDA 21-026/N-000(BC)	05 January 2005
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6. SUBMISSION(S) BEING REVIEWED:

Submissions Reviewed	Document Date
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NDA 21-026/N-000(BC)	03 May 2005
NDA 21-026/N-000(BC)	05 May 2005
NDA 21-026/N-000(BL) Electronic	17 May 2005
NDA 21-026/N-000(BC) Electronic	20 May 2005

7. NAME & ADDRESS OF APPLICANT:

Name	Barrier Therapeutics, Inc.
Address	600 College Road East, Suite 3200 Princeton, New Jersey 08540
Representative	Isabel Drzewiecki, Global Head, Regulatory Operations
Telephone	(609) 945-1247

8. DRUG PRODUCT NAME/CODE/TYPE:

a) **Proprietary Name:** Trade name to be determined (Zimycan, the trade name proposed by the applicant, was found to be unacceptable by DMETS; the

Applicant's appeal of the decision was denied; the alternate name proposed , the secondary distributor of the drug product (to hospitals), was also found to be unacceptable by DMETS) b(4)

b) **Non-Proprietary Name (USAN):** 0.25% Miconazole Nitrate / 15% Zinc Oxide / 81.35% White Petrolatum

c) **Code Name/#:** ZOOM

d) **Chem. Type/Submission Priority:**

- **Chem. Type:** 3
- **Submission Priority:** S

9. **LEGAL BASIS FOR SUBMISSION:** The original NDA 21-026 was submitted by Johnson & Johnson Consumer Products Companies, Inc., under 505(b)(1). However, by agreement with the Agency, Barrier Pharmaceutics, Inc., the current applicant, was only required to demonstrate the contribution of miconazole nitrate to the efficacy of this drug product. As previously stated, zinc oxide and white petrolatum are listed as active ingredients in the final monograph of Skin Protectant Drug Products for Over-The-Counter Human Use at concentrations of 1 to 25% for zinc oxide, and 30 to 100% for White petrolatum. Both latter drug substances are found in products currently marketed Over-The-Counter for diaper rash (the Applicant's product contains zinc oxide, 15% and white petrolatum, 81.35%). It was the Agency's position that the applicant could rely on evidence already known regarding the contribution of zinc oxide and white petrolatum to efficacy for treatment of diaper rash. Zinc oxide and white petrolatum also serve as part of the delivery vehicle for the applicant's product.

   Thus, the current application (resubmission) is considered to be a 505(b)(2) submission.

10. **PHARMACOLOGICAL CATEGORY:** Antifungal

11. **DOSAGE FORM:** Ointment

12. **STRENGTH/POTENCY:** 0.25% Miconazole Nitrate / 15% Zinc Oxide / 81.35% White Petrolatum

13. **ROUTE OF ADMINISTRATION:** Topical

14. **INDICATION:** Treatment of diaper dermatitis complicated by candidiasis

15. **Rx/OTC DISPENSED:** _X_Rx ___OTC

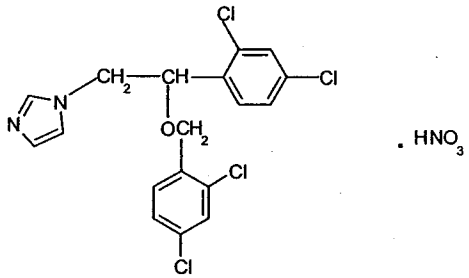
16. **SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):**

_____SPOTS product – Form Completed

___X___Not a SPOTS product

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

♦ 1-(2,4-dichloro-β-[(2,4-dichlorobenzyl)oxy]phenethyl]imidazole mononitrate



♦ 1-[2(2,4-dichlorophenyl)-2,4-dichlorophenyl)methoxy]ethyl]-1H-imidazole mononitrate

Molecular Formula: $C_{18}H_{14}Cl_4N_2O.HNO_3$
Molecular Weight: 479.15
CAS Number: (Miconazole Nitrate) 22832-87-7
(Miconazole 22916-47-8)

18. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	DMF HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
b(4)	II			3	Adequate	28-Nov-2003 (Matecka/HFD-590)	b(4)
	IV			3	Adequate	19 February 1999 (Timmer/HFD540)	
	IV						Withdrawn 1991
	III			3	Adequate	19 April 1999 (Timmer/HFD540)	

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
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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:

Document Type	Application Number	Holder	Description
IND	21,542	Current Applicant: Barrier Therapeutics, Inc. Former Applicant: Johnson & Johnson Consumer Companies, Inc.	Miconazole Nitrate Ointment
b(4) IND			
NDA			
NDA	17-450	Advanced Care Products	Monistat-7 Antifungal/Candidiasis
NDA	17-494	Johnson & Johnson Consumer Companies, Inc.	Monistat-Derm Cream, 2% Sclerosing Agents
NDA	18-040	Janssen Pharmaceuticals, Inc.	Monistat Injectable Solution (Systemic Antifungal)
NDA	18-520	Advanced Care Products	Monistat-7 Suppository

19. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES* (Drug Substance: Miconazole Nitrate; Manufacturer/Packager/Tester: Janssen Pharmaceutica NV)	Acceptable (Based on review of 2/2005 cGMP inspection, which is based on the investigator's recommendation. No 483 issued).	23 February 2005	Shawnte Adams
b(4) EES* (Drug Substance: Miconazole Nitrate; Manufacturer/Packager/Tester: Noramco Inc. (Noramc) 1440 Olympic Drive Athens, Georgia	Acceptable (Based on cGMP inspection: EI of 2/22/05- 2/24/05 was NAI. Application was covered. Profile class is acceptable.)	28 February 2005	L. Andrews, P. M. Carve Janine D'Ambrogio
EES* (Drug Substance: Zinc Oxide; Manufacturer/ Packager /Tester:	Acceptable (Based on cGMP inspection)	19 May 2005	Regina T. Brown, Shirnette Ferguson / Shawnte Adams
EES* (Drug Substance: White Petrolatum Manufacturer/ Packager /Tester:	Acceptable (Based on cGMP profile: Last cGMP Establishment Inspection of 12/18/2002 is classified NAI).	6 April 2005	K. Campbel Shirnette Ferguson / Janine D'Ambrogio

Chemistry Review Data Sheet
NDA 21-026

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES* (Drug product: Miconazole Nitrate Ointment Manufacturer /Packager Tester: DSM Pharmaceuticals, Inc., 5900 Greenville Blvd. NE, Greenville, NC 27348	Acceptable (Based on profile: last EI was 7/04).	31 January 2005	Janine D'Ambrogio
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	N/A		
Methods Validation	Deferred		
DMETS: Zimycan	Unacceptable: The appeal by the Applicant for reconsideration, dated 16 February 2005, was denied by DMETS	19 January 2005 3 May 2005	Denise Toyer Linda Y. Kim-Jung
DMETS:	Unacceptable	6 May 2005	Tina M. Tezky
EA (Categorical Exclusion)	Acceptable	5 May 2005	Saleh A. Turujman
Microbiology	N/A		

* See Appendix 1 for EES report

Appears This Way
On Original

The Chemistry Review for NDA 21-026

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The recommendation for this resubmission is "Approval" from a CMC standpoint

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

Barrier Therapeutics, Inc., commits to determine the particle size distribution for five batches of zinc oxide to evaluate any potential effect of particle size on the *in vitro* release rate and to implement any appropriate control measures in the drug product specification. In support of the transition of manufacturing the drug product from Janssen N.V., in Belgium, to DSM, in the USA, Barrier Therapeutics, also commits to determining the *in-vitro* release profile using the SUPAC-SS test methodology on the first five DSM production batches the drug product, 0.25% Miconazole Nitrate / 15% Zinc Oxide / 81.35% White Petrolatum, Ointment.

The post marketing stability commitment will be revised to indicate that the Applicant will conduct stability studies on the first three commercial batches of any size included within the range bracketed by the primary stability studies. Those first three batches will be tested according to the protocol of the primary stability studies. The Applicant will also revise the commitment for each subsequent year to indicate that they will conduct stability studies for one batch of each tube size that is manufactured during that year. Those subsequent studies will be tested according to the post-approval stability protocol.

II. Summary of Chemistry Assessments

A. Description of the Drug Product and Drug Substances

The combination drug product contains three drug substances and two excipients, one of which is a fragrance. The three APIs are: Miconazole Nitrate (0.25%); Zinc Oxide (15%); White Petrolatum (81.35%). Zinc oxide and white petrolatum are both ingredients in products currently marketed Over-The-Counter for diaper rash. Zinc oxide and white petrolatum also serve as part of the delivery vehicle.

Miconazole Nitrate

Miconazole nitrate, USP, is an approved antifungal used in several dosage forms approved for marketing, both as a prescription drug and as an OTC drug product. Other imidazole antifungals include ketoconazole, clotrimazole, econazole, and oxiconazole. Imidazole-type antifungal compounds are used worldwide, and are the leading antifungal agents. The marketed concentrations are 2% and 4%. Imidazole compounds are believed to exhibit their antifungal activity mainly by damaging the cell membrane of fungi which have an imidazole group in their chemical structure. Miconazole nitrate,

in the amendment dated May 3, 2005, submitted in response to the IR letters dated February 8, 2005, and April 12, 2005, and the Telecon with the Applicant on April 16, 2005.

A retest date [redacted] is assigned to the zinc oxide used in the drug product.

White petrolatum b(4)

Synonyms: *Merkur*; mineral jelly; petroleum jelly; *Silkolene*; *Snow White* [redacted] *Perfecta* [redacted]; Soft white; yellow petrolatum; yellow petroleum jelly (proprietary names are italicized).

White petrolatum is a purified mixture of semisolid saturated hydrocarbons having the general formula C_nH_{2n+2} and is obtained from petroleum. The hydrocarbons consist mainly of branched and unbranched chains although some cyclic alkanes and aromatic molecules with paraffin side chains may also be present. The compendial material (since USP 25) may contain a suitable stabilizer, such as butylated hydroxy toluene (BHT). The white petrolatum used in the proposed drug product does contain butylated hydroxytoluene (BHT) as stabilizer.

Various grades of petrolatum are commercially available, which vary in their physical properties depending upon their source and refining process. White petrolatum obtained from different sources may therefore behave differently in a formulation, which is what the previous (original) Applicant (J&J) of this NDA discovered.

Care is required in heating petrolatum because of its large coefficient of thermal expansion. It has been shown by both rheological and spectrophotometric methods that petrolatum undergoes phase transition at temperatures between 30-40°C.

Additives, such as microcrystalline wax, may also be used to add body to petrolatum.

Petrolatum is listed in the CFR as GRAS (generally recognized as safe [as a food additive]). White petrolatum, as a commercial grade, is associated with fewer instances of hypersensitivity reactions and is the preferred petrolatum for use in cosmetics and in pharmaceuticals.

Petrolatum is a pale yellow to yellow-colored, translucent, soft unctuous mass, which is odorless and tasteless. Its rheological properties are determined by the ratio of the unbranched chains to the branched chains and cyclic components of the mixture. Petrolatum contains relatively high amounts of branched and cyclic hydrocarbons, in contrast to paraffin, which accounts for its softer character and makes it an ideal ointment base.

Petrolatum is practically insoluble in acetone, ethanol, hot or cold ethanol (95%), glycerin, and water; soluble in benzene, carbon disulfide, chloroform, ether, hexane, and most fixed and volatile oils.

The specification for white petrolatum used in the manufacture of 0.25% Miconazole Nitrate / 15% Zinc Oxide / 81.35% White Petrolatum Ointment is the same as the current USP specification, except that the range for consistency is narrower than the range in the USP monograph (100 - 300 for the compendial grade), and there is an additional test for butylated hydroxytoluene (BHT). The Applicant chose white petrolatum with consistency for the manufacture of the drug product based on the results of several *in-vitro* studies to determine the effect of different grades of petrolatum equivalence of the drug product prepared from the different grades. b(4)

It is noted that the white petrolatum used in the PK study (Formulation F100) is the grade, which has a consistency of . The white petrolatum used in the clinical studies (Formulation F114) and in the to-be-marketed product is the with a consistency . As indicated in the review, the *in-vitro* release results of these two formulations, using the CDER SUPAC-SS Guidance, were found to be different. There are no PK studies using the to-be-marketed product. b(4)

The initial CMC information on the white petrolatum drug substance was deficient in the original resubmission dated November 24, 2004. Acceptable CMC data were provided in the amendment dated May 3, 2005, submitted in response to the IR letters dated February 8, 2005, and April 12, 2005, and the Telecon with the Applicant on April 16, 2005.

A retest period is assigned to the white petrolatum used in the drug product. b(4)

Drug product, 0.25% Miconazole Nitrate / 15% Zinc Oxide / 81.35% White Petrolatum

The combination drug product, contains the following active ingredients: synthetic antifungal compound, miconazole nitrate (0.25%) zinc oxide and white petrolatum. Each gram of the Ointment contains 2.5 mg of Miconazole Nitrate, USP and 150 mg Zinc Oxide, USP, 813.5 mg White Petrolatum, USP, Trihydroxystearin (hydrogenated castor oil) and of Chemoderm 1001/B . The trihydroxystearin is added to provide physical stability, to optimize spreadability, and to sustain the suspension. The drug product is packaged in a 30 g tube size for marketing (the initially proposed tube size was withdrawn by the Applicant). The Applicant's plan to distribute 5 g and 30 g professional sample tubes for free distribution was deemed unacceptable by the Clinical Division, and by Dr. Frederic Marsik, the Microbiology Reviewer (but the Applicant was to be notified of the decision when labeling was finalized). The drug product is to be applied to the diaper area at every diaper change, and the treatment duration is seven days. b(4)

Miconazole is an imidazole antifungal agent. This class of fungal agents acts to inhibit sterol biosynthesis, specifically the synthesis of ergosterol, a component of the fungal

While the difference of *in-vitro* results is consistent with the difference in the age of the tested products (the Janssen sample tested was 11 months older than the DSM sample), it could not be confirmed since the manufacture of the drug product had been discontinued at the Janssen site. The difference could be also ascribed to the differences in zinc oxide particle size. The latter interpretation was the basis for the Applicant's commitment in the original submission to monitor the particle size distribution of the first five commercial batches. In the Telecon with the Agency, the Applicant nonetheless asserted that the difference is not due to differences of zinc oxide particle size distribution, but rather due to the difference in the age of the tested samples. However, see next paragraph.

Barrier Therapeutics, Inc., commits to determine the particle size distribution for five batches of zinc oxide to evaluate any potential effect on the *in-vitro* release rate and to implement any appropriate control measures in the drug product specification. In support of the Janssen to DSM transition, Barrier Therapeutics, also commits to determining the *in-vitro* release profile using the SUPAC-SS test methodology on the first five DSM production batches the drug product, 0.25% Miconazole Nitrate / 15% Zinc Oxide / 81.35% White petrolatum. These commitments should be included in the action letter.

Barrier Therapeutics, Inc., commits to remove "with possible slight separation" from the Appearance of the drug product in the drug product specification.

After evaluation for GMP compliance, the manufacturing, packaging and testing facilities of the drug product were found to be acceptable. The manufacturing, packaging and testing facilities for the three drug substances (miconazole nitrate, white petrolatum and zinc oxide), were found to be acceptable.

The Applicant does not identify critical points or critical steps in the manufacturing process, other than a visual agglomeration test at the end of the process. The applicant was requested to include a microscopic test to assure that no agglomerates are present, or to propose an alternate test for homogeneity i.e. to provide substantiation of the adequacy (efficacy) of the mixing processes. The Applicant states that there have been no changes made to the manufacturing processes of the drug product manufactured at DSM, the current manufacturing site from those at Janssen, the original manufacturing site. Although the identification and control of critical points or critical steps in the manufacturing process is a quality control parameter, this information was provided in the original NDA submission by (J&J) for the manufacture of the drug product at the Janssen plant, and was approved by Dr. William C. Timmer, the Chemistry reviewer (but note next paragraph). In response to the Agency letter, the Applicant proposes to use a gauge as the in-process control for the presence of agglomerates during the manufacturing process. A gauge is a precision instrument that is used according to the test methodology of b(4)

Differences were found in the *in vitro* release rates between the drug product manufactured by Janssen, the original manufacturing site, and the drug product manufactured by DSM, the current manufacturing site. These differences may be attributed to the 11 month difference in the age of the drug product materials being compared, but it could also be attributed to the difference in particle size distribution of the zinc oxide. The Applicant states that the data on the particle size distribution of zinc oxide are currently not available. However, the Applicant did not include a particle size acceptance criterion in the specification of zinc oxide. The Applicant was requested to include a particle size acceptance criterion (with the appropriate method) in the specification of zinc oxide, and to have the analytical method validated.

The Applicant provides a Certificate of Analysis of miconazole nitrate manufactured at the Janssen, but does not provides a Certificate of Analysis of miconazole nitrate manufactured at Noramco (the USA facility). The Applicant was requested to provide a Certificate of Analysis (COA) of miconazole nitrate manufactured at the Noramco site in the U.S.A. The applicant was also requested to provide a chromatographic comparison (impurity profile) for a batch of miconazole nitrate manufactured at each site. A satisfactory COA for the Noramco site, and a tabular comparison of the profile of the drug substance from the two sites was provided.

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

The proposed label directs that the drug product should be applied to the entire affected area at each diaper change after cleansing the skin and "pat" drying. Treatment is recommended to be continued for seven days.

In phase 3 trials, the reported average use was 38.69 g of ointment in one week (approximately 96.73 mg of miconazole, *i.e.* approximately 13.8 mg miconazole per day). It was noted however, that the only commercial size will contain only 30 g aluminum tubes, *i.e.*, the 30 g tube will not be sufficient for a full weeks treatment, and a second 30 g tube will be needed to complete the treatment, as indicated. However, this would lead to about —of unused antifungal drug product (with concerns about use without the physician's directive, and the concomitant development of miconazole nitrate resistant *Candida albicans* long term or preventative use of an anti-microbial may result in the development of drug resistance. The issue was conveyed to the Medical Officer and to the Microbiology Reviewer. Ensuing discussions led to, among other outcomes, the denial of the Applicant's proposal to offer two free professional sample sizes: 5 g and 30 g. b(4)

The indication for this drug product in the original NDA 21-026 submission was for the treatment of severe diaper dermatitis where *Candida albicans* may be a factor.

The expiration date, based on the primary stability data provided in the resubmission, is one year.

C. Basis for Approvability or Not-Approval Recommendation
N/A

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Chemist's Name / Date: Saleh A. Turujman, Ph.D./ May 23, 2005
Chemistry Team Leader Name / Date: Ramesh K. Sood, Ph.D./
Project Manager's Name / Date: Mildred Wright, R.N., M.S.N./

C. CC Block

Cc: Original NDA 21-026
HFD-540/Division File
HFD-540/Chem/SATurujman
HFD-540/ChemTL/RKSood
HFD-540/ProjMgr/MWright
HFD-540/MedOff/BCarr
HFD-540/MedOffTL/MLuke
HFD-540/BioPharm/AAdebowale
HFD-540/BioPharmTL/RBaweja
HFD-540/BioPharmTL/DBashaw
HFD-540/Biometrics/SLee

C:\Data\My Documents\turujman\reviews\NDA\2005\21-026 RS Tradename Ointment\21-026 CMC Rev#3.doc

137 Page(s) Withheld

6 Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Chemistry-_____

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

/s/

Saleh Turujman
5/23/05 10:16:38 PM
CHEMIST

For your concurrence

Ramesh Sood
5/24/05 10:36:04 AM
CHEMIST
The post-approval CMC commitment in sec. 1B of executive summary refers to applicant's commitment when the application is eventually approved. The applicant has also agreed to three point post-approval stability commitment consistent with ICH guidlines.

U.S. FOOD & DRUG ADMINISTRATION **OFFICE OF NEW DRUG CHEMISTRY**

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

NDA #: 21-026 **CHEM.REVIEW #:** 2 **REVIEW DATE:** July 11, 2000

JUL 13 2000

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
AZ	21-JAN-00	24-JAN-00	24-JAN-00
BC	01-FEB-00	02-FEB-00	03-FEB-00
BL	17-MAR-00	20-MAR-00	21-MAR-00
BC	28-MAR-00	29-MAR-00	29-MAR-00

NAME & ADDRESS OF APPLICANT:

Johnson & Johnson, Inc.
Consumer Companies
199 Grandview Road
Skillman, NJ 08558-9418

Paul F. Manley
Director, Drug Regulatory Affairs
(908) 874-1700

DRUG PRODUCT NAME:

Proprietary: Pedistat, Micatin7, Monistat7, Daktozin7, Daktarin7
Nonproprietary/USAN: Miconazole Nitrate, RINN (1969), USAN (1970)
Code Names/#'s: R14,889; RO14889
Chemical Type: 3-S
Therapeutic Class: antifungal

PATENT STATUS: U.S. Patent No. 4,911,932

PHARMACOLOGICAL INDICATION: Severe diaper dermatitis where *Candida albicans* may be a factor.

DOSAGE FORM: ointment
STRENGTHS: 0.25%
RTE OF ADMIN: topical
DISPENSED: _X_ Rx ___ OTC

CHEMICAL NAME, MOLECULAR FORMULA, MOLECULAR WEIGHT:

1H-Imidazole,1-[2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl)-methoxy]ethyl]-,mononitrate;

1-[2,4-Dichloro-b-[2,4-dichlorobenzyl)oxy]phenethyl]imidazole mononitrate

Molc. Formula: $C_{18}H_{14}Cl_4N_2O \cdot HNO_3$ Molc. Wt.: 479.15 g/mol CAS Number: 22832-87-7

SUPPORTING DOCUMENTS:

b(4)

IND 21,542* Miconazole nitrate; Johnson & Johnson, Skillman, NJ.

Type IV DMF;

Type I DMF;

b(4)

Type II DMF;

Type III DMF;

NDA 17-450* Monistat-7 vaginal cream. Advanced Care Products, Raritan, NJ.

NDA 17-494* Monistat dermal cream, 2%. Johnson & Johnson, Skillman, NJ.

NDA 18-040* Monistat indictable solution. Janssen Pharmaceutica, Titusville, NJ.

NDA 18-520* Monistat 7 vaginal suppositories. Advanced Care Products, Raritan, NJ.

b(4)

*Note: All references from these INDs/NDAs are included in the submission, therefore authorization letters are not needed.

REMARKS/COMMENTS: None

CONCLUSIONS & RECOMMENDATIONS:

The application is recommended for APPROVAL under section 505 of the FFD&C Act.

William C. Timmer, Ph.D.

cc: Orig. NDA 21-026
HFD-540/Division File
HFD-540/WTimmer/July 11, 2000
HFD-540/ChemTmLdr/WHDeCamp for WHD by JSH 7/13/2000
HFD-540/MO/HSKo
HFD-540/Pharm/ANostrandt
HFD-540/Biopharm/VTandon
HFD-540/PM/Mwright 7/16/00

filename: c:\my documents\regulatory reviews\nda\n21026_2nd.doc

9 Page(s) Withheld

8 Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Chemistry-_____

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Date: June 25, 1999

JUN 2 5 1999

To: NDA 21-026 file

From: Wilson H. DeCamp, Ph.D.
Chemistry Team Leader, HFD-540

Subject: Team Leader Addendum to Chemist's Review #1, June 15, 1999

Through: Jonathan K. Wilkin, M.D.
Director, HFD-540

In the "Summary of Information Requests" in Chemist's review #1, the following changes should be made:

item #1 is neither an NA issue nor an information request;

item #3 is correctly considered to be an NA issue, i.e., one which must be addressed in a complete response.

Wilson H. DeCamp, Ph.D.

cc: Orig. NDA 21-026
HFD-540/Division File
HFD-540/CH/Timmer
HFD-540/MO/Ko
HFD-540/Pharm/Nostrandt
HFD-540/Biopharm/Tandon
HFD-540/PM/Wright

Summary of Information Requests

Note to PM: I will place all the information requests on the N drive after the Chem TL has signed-off on the review.

The following represent **NOT APPROVABLE** issues for **NDA 21-026**:

1. The drug product manufacturer must complete a successful GMP inspection.

2. The release testing program is **UNACCEPTABLE** in that:

    a) degradation testing must be included in the release testing program,
    b) the Appearance, Odor, and Weight tests, as well as the ZnO ID and assay tests, must should be part of the release testing program,
    c) the ID test for miconazole nitrate should be changed to USP <197> or <201>, and,
    d) the batch sampling plan is unacceptable. Every batch lot must meet its analytical specifications via testing (*c.f.*, 21 CFR 211.165).

b(4) The following represent **CMC issues** (*i.e.*, information requests) for this NDA: b(4)

1. A range should be specified for the individual excipients in the batch formula..

2. The procedure to determine the free fatty acids in trihydroxystearin lacks detail. Please submit the exact test method or SOP to measure free fatty acids. Alternately, the compendial method may be used.

3. The sponsor should be asked to verify that no reprocessing of the drug product will occur under any circumstances.

b(4)

JUN 15 1999

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

NDA #: 21-026 **CHEM.REVIEW #:** 1 **REVIEW DATE:** June 15, 1999

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	24-AUG-98	25-AUG-98	25-AUG-98
BC	06-OCT-98	07-OCT-98	07-OCT-98

NAME & ADDRESS OF APPLICANT:

Johnson & Johnson, Inc.
Consumer Companies
199 Grandview Road
Skillman, NJ 08558-9418

Paul F. Manley
Director, Drug Regulatory Affairs
(908) 874-1700

DRUG PRODUCT NAME

Proprietary:	Pedistat™, Micatin®, Monistat®, Daktozin®, Daktarin®
Nonproprietary/USAN:	Miconazole Nitrate, RINN (1969), USAN (1970)
Code Names/#'s:	R14,889; RO14889
Chemical Type:	3
Therapeutic Class:	S

PATENT STATUS: U.S. Patent No. 4,911,932

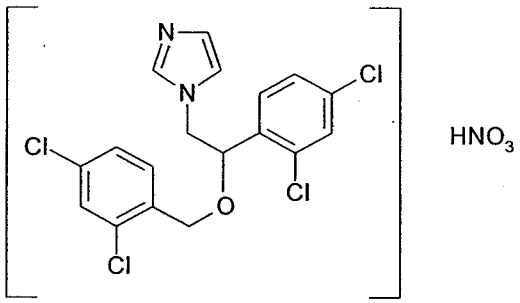
Issue date:	27 March 1990
Expiration date:	27 March 2007
Patent Owner:	Johnson & Johnson
Type of Patent:	Drug product composition
Claims:	The formulation, composition, and/or method of use of 0.25% miconazole nitrate ointment.

PHARMACOLOGICAL CATEGORY/INDICATION: Severe diaper dermatitis where *Candida albicans* may be a factor.

DOSAGE FORM:	ointment
STRENGTHS:	0.25%
ROUTE OF ADMINISTRATION:	topical
DISPENSED:	X R_x _____ OTC

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

- 1H-Imidazole,1-[2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl)-methoxy]ethyl]-,mononitrate;



- 1-[2,4-Dichloro-β-[2,4-dichlorobenzyl)oxy]phenethyl]imidazole mononitrate

Molecular Formula: $C_{18}H_{14}Cl_4N_2O \cdot HNO_3$

Molecular Weight: 479.15 g/mol

CAS Number: 22832-87-7

SUPPORTING DOCUMENTS:

b(4)

IND 21,542* Miconazole nitrate; Johnson & Johnson, Skillman, NJ.

Type IV DMF;

Type I DMF;

Type II DMF;

Type III DMF;

NDA 17-450*	Monistat-7 vaginal cream. Advanced Care Products, Raritan, NJ.
NDA 17-494*	Monistat derm cream, 2%. Johnson & Johnson, Skillman, NJ.
NDA 18-040*	Monistat injectable solution. Janssen Pharmaceutica, Titusville, NJ.
NDA 18-520*	Monistat 7 vaginal suppositories. Advanced Care Products, Raritan, NJ.

b(4)

*Note: All references from these INDs/NDAs are included in the submission, therefore authorization letters are not needed.

RELATED DOCUMENTS: None

CONSULTS: Labeling and Nomenclature Committee

REMARKS/COMMENTS: None

CONCLUSIONS & RECOMMENDATIONS:

The application is recommended as NOT APPROVABLE under section 505 of the FFD&C Act.

Attached (last page) are the NOT APPROVABLE issues as well as several information requests.

William C. Timmer, Ph.D.

cc: Orig. NDA 21-026
HFD-540/Division File
HFD-540/WTimmer/June 15, 1999
HFD-540/ChemTmLdr/WHDeCamp WD 6/15/99
HFD-540/MO/HSKo
HFD-540/Pharm/ANostrandt
HFD-540/Biopharm/VTandon
HFD-540/PM/MWright 6/23/99

filename: c:\wpwin61\wpdocs\cder\nda\nda21026\n21026.org

38 Page(s) Withheld

8 Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Chemistry-_____

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Date: June 23, 1999

JUN 2 3 1999

To: NDA 21-026 file

From: Wilson H. DeCamp, Ph.D.
Chemistry Team Leader, HFD-540

Subject: Team Leader Addendum to Chemist's Review #1, June 15, 1999

Through: Jonathan K. Wilkin, M.D.
Director, HFD-540

Item G of Chemist's Review #1 noted that the establishment inspections were incomplete as of the date of the review.

The establishment evaluation has now been completed, and recommends withholding approval (EER attached). This does not alter the recommended action in the review. However, this does complete the chemistry review process, and a letter may be issued.

Wilson H. DeCamp, Ph.D.

cc: Orig. NDA 21-026
HFD-540/Division File
HFD-540/CH/Timmer
HFD-540/MO/Ko
HFD-540/Pharm/Nostrandt
HFD-540/Biopharm/Tandon
HFD-540/PM/Wright

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 21026/000**
Priority: **3S**
Org Code: **540**
Stamp: **24-AUG-1998** Regulatory Due: **24-AUG-1999**
Action Goal:
District Goal: **25-APR-1999**
Applicant: **JOHNSON AND JOHNSON**
Brand Name: **PEDIASTAT (MICONAZOLE NITRATE)OINT 0.25%**
Established Name:
Generic Name: **MICONAZOLE NITRATE**
Dosage Form: **ONT (OINTMENT)**
Strength: **0.25%**

FDA Contacts:			
	M. WRIGHT	**(HFD-540)**	**301-827-2084 , Project Manager**
	W. TIMMER	**(HFD-540)**	**301-827-2048 , Review Chemist**
	W. DECAMP II	**(HFD-540)**	**301-827-2041 , Team Leader**

Overall Recommendation:

WITHHOLD on 23-JUN-1999 by M. EGAS (HFD-322) 301-594-0095

Establishment: **9610028**
JANSSEN PHARMACEUTICA NV
TURNHOUTSEBAAN 30, B-2340
BEERSE, , BE
DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **22-SEP-1998**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Profile: **OIN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **23-JUN-1999**
Decision: **WITHHOLD**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **DRUG SUBSTANCE MANUFACTURER**
FINISHED DOSAGE MANUFACTURER

Establishment: **2243656**
JOHNSON AND JOHNSON
GRANDVIEW RD
SKILLMAN, NJ 08558
DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **05-OCT-1998**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE OTHER TESTER**