CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-632/S002

Trade Name: Meridia Capsules

Generic Name: sibutramine hydrochloride monohydrate

Sponsor: Knoll Pharmaceutical Company

Approval Date: August 7, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 20-632/S002

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Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative/Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-632/S002

APPROVAL LETTER

NDA 20-632/S-002

AUG - 7 1998

Knoll Pharmaceutical Company
Attention: Robert Ashworth, Ph.D.
Director, Regulatory Affairs
199 Cherry Hill Road
Parsippany, NJ 07054

Dear Dr. Ashworth:

Please refer to your supplemental new drug application dated February 9, 1998, received February 10, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Meridia (sibutramine hydrochloride monohydrate) Capsules.

The user fee goal date for this application is August 10, 1998

We note that this supplement was submitted as a "Special Supplement - Changes Being Effected" under 21 CFR 314.70(c). However, as we notified you in our May 22, 1998, letter to this application, the proposed change is not the kind of change permitted by regulation to be put into effect prior to approval of a supplement. Therefore, the supplement was reviewed under 21 CFR 314.70(b).

This supplemental new drug application provides for the use of the Whippany, NJ facility as an alternate packaging facility for Meridia capsules.

We have completed the review of this supplemental application and it is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Maureen Hess, MPH, RD, Project Manager, at (301) 827-6411.

Sincerely,

8/6/98

Duu-Gong Wu, Ph.D.
Chemistry Team Leader II, for the Division of Metabolic and Endocrine Drug Products, (HFD-510)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDA 20-632
HFD-510/Div. Files
HFD-510/M.Hess/MHaber/DWu
HFD-95/DDMS (with labeling)
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: mah/August 5, 1998
final:8.6.98
filename: N20632AP.S02

Concurrences: EGalliers/8.6.98/DWu/8.6.98/MHaber/8.6.98

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-632/S002

CHEMISTRY REVIEW(S)

ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products

Memorandum

Date: August 5, 1998

From: Martin Haber, Ph.D., Review Chemist, HFD-510

Through: Duu-Gong Wu, Ph.D., Team Leader Chemist, HFD-510, DNDCII

Subject: Reversal of recommendation by Division of Manufacturing and Product Quality

To: NDA 20-632/S-002

Knoll Pharmaceuticals submitted two supplements to NDA 20-632 providing for a facility in Whippany, NJ as a new testing (S-001) and packaging (S-002) site. The EES report of 7/16/98 recommended to withhold approval for both supplements based on the inspection results. The chemistry review dated 7/16/98 therefore recommended a not approvable letter. However, as per a e-mail dated August 5, 1998 from Randall Woods , DMPQ, the Investigations and Preapproval Compliance Branch (HFD-324) now recommends approval for NDA 20-632/S-002. After review of the inspection report, DMPQ concludes that the observations do not reach the threshold required to withhold approval, see attachments. Therefore, issue an approval letter for S-002.

Martin Haber, Ph.D.
Review Chemist

R/D Init by: Dr. Duu-Gong Wu, Team Leader Chemist 8/6/98

Orig. NDA 20-632
cc: HFD-510/Division file/M.Haber/D-G.Wu/M.Hess

CDER Establishment Evaluation Report
for August 05, 1998

Application: **NDA 20632/002**
Priority: **1S**
Org Code: **510**
Stamp: **10-FEB-1998** Regulatory Due: **10-AUG-1998**
Action Goal:
District Goal: **05-JUN-1998**
Applicant: **KNOLL PHARM**
199 CHERRY HILL RD
PARSIPPANY, NJ 07054
Brand Name: **MERIDIA (SIBUTRAMINE HCL MONOHYDRATE)**
Established Name:
Generic Name: **SIBUTRAMINE HCL MONOHYDRATE**
Dosage Form: **CAP (CAPSULE)**
Strength: **5,10, 15, 20 MG**

FDA Contacts:

M. HESS	**(HFD-510)**	**301-827-6411**	**, Project Manager**
M. HABER	**(HFD-510)**	**301-827-6430**	**, Review Chemist**
D. WU	**(HFD-510)**	**301-827-6430**	**, Team Leader**

Overall Recommendation:

ACCEPTABLE on 05-AUG-1998 by R. WOODS (HFD-324) 301-827-0062

Establishment: **2211084**
KNOLL PHARMACEUTICALS
30 NORTH JEFFERSON RD
WHIPPANY, NJ 07981
DMF No:
AADA No:

Profile: **CHG** OAI Status: **NONE**
Responsibilities: **FINISHED DOSAGE PACKAGER**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **05-AUG-1998**
Decision: **ACCEPTABLE**
Reason: **OBSER. NOT SIGNIFICANT ENOUG**

CDER Establishment Evaluation Report
for July 15, 1998

Application: **NDA 20632/002**
Priority: **1S**
Org Code: **510**
Stamp: **10-FEB-1998** Regulatory Due: **10-AUG-1998**
Action Goal:
District Goal: **05-JUN-1998**
Applicant: **KNOLL PHARM**
199 CHERRY HILL RD
PARSIPPANY, NJ 07054
Brand Name: **MERIDIA (SIBUTRAMINE HCL MONOHYDRATE)**
Established Name:
Generic Name: **SIBUTRAMINE HCL MONOHYDRATE**
Dosage Form: **CAP (CAPSULE)**
Strength: **5,10, 15, 20 MG**

FDA Contacts:			
	M. HESS	**(HFD-510)**	**301-827-6411 , Project Manager**
	M. HABER	**(HFD-510)**	**301-827-6430 , Review Chemist**
	D. WU	**(HFD-510)**	**301-827-6430 , Team Leader**

Overall Recommendation:

Establishment: **2211084**
KNOLL PHARMACEUTICALS
30 NORTH JEFFERSON RD
WHIPPANY, NJ 07981
DMF No:
AADA No:

Profile: **CHG** OAI Status: **NONE**
Responsibilities: **FINISHED DOSAGE PACKAGER**
Last Milestone: **DO RECOMMENDATION**
Milestone Date **15-MAY-1998**
Decision: **WITHHOLD**
Reason: **PACKAGING/LABELING CONTRO**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-632/S002

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

cc: NDA Arch
HFD-510/Div. File
HFD-510/DWu/Mhaber/MHess
HFD-820/JGibbs
HFD-357
HFD-358
DISTRICT OFFICE

Concurrences: EGalliers/5.19.98/

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-632/S-002

KNOLL PHARMACEUTICAL, COMPANY
199 Cherry Hill Road
Parsippany, New Jersey 07054

FEB 25 1998

Attention: Robert W. Ashworth, Ph.D., Director, Regulatory Affairs

Dear Dr. R. W. Ashworth:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: MERIDIA (sibutramine hydrochloride monohydrate) Capsules

NDA Number: 20-632

Supplement Number: S-002

Date of Supplement: February 9, 1998

Date of Receipt: February 10, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on April 11, 1998, in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Attention: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

Enid Galliers
Chief, Project Management Staff
Division of Metabolic and Endocrine
Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 20-632/S-002
HFD-510/Div. Files
HFD-510/CSO/M. Hess

filename:

SUPPLEMENT ACKNOWLEDGEMENT

Knoll Pharmaceutical Company NDA NO. 20632 REF. NO. 002
NDA SUPPL FOR SCM

ORIGINAL

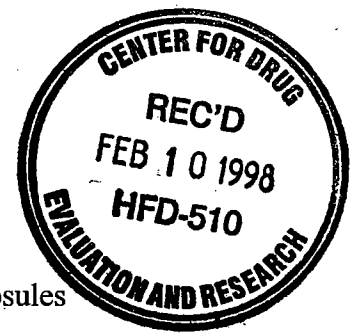
knoll® NDA SUPPLEMENT

VIA FEDERAL EXPRESS

February 9, 1998

BASF Pharma

Solomon Sobel, M.D.
Director
Division of Metabolism and Endocrine Drug Products
HFD-510, Document Control Room 14B-04
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857



RE: MERIDIA® (sibutramine hydrochloride monohydrate) Capsules
NDA 20-632/S-002
SUPAC-IR Supplemental Application
Special Supplement - Changes Being Effected (CBE)

Dear Dr. Sobel:

Reference is made to the Agency's February 18, 1997 letter to industry that clarifies the mode of submission for a stand-alone packaging site change under SUPAC IR guidance. This letter permits the filing of a stand-alone packaging site change as a "Changes Being Effected" Supplement provided that certain criteria have been satisfied.

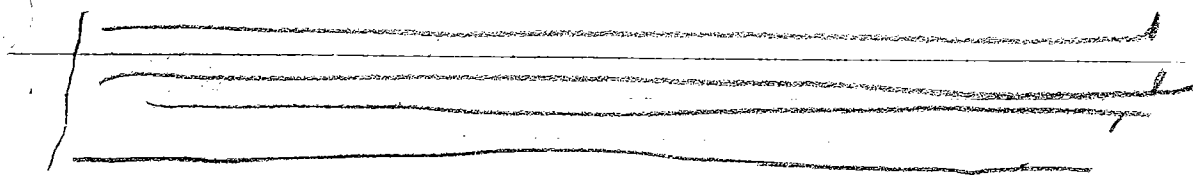
Accordingly, Knoll Pharmaceutical Company, hereby submits this supplemental CBE application to provide for the use of an additional packaging facility for MERIDIA Capsules. Currently, the manufacturing and packaging of MERIDIA Capsules is performed at BASF Corporation (formerly Knoll Pharmaceutical Company), Shreveport, Louisiana facility. This supplement provides for Knoll Pharmaceutical Company, Whippany, New Jersey, as the alternate packaging facility. The additional packaging site is needed to accommodate the increasing workload at our Shreveport facility.

The address of the facilities are listed below:

Current Manufacturing, Packaging and Analytical Site

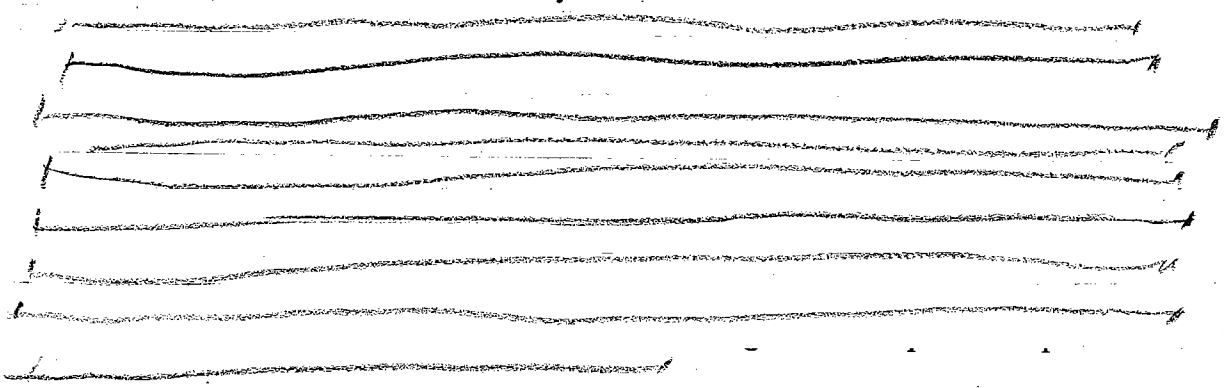
BASF Corporation
8800 Line Avenue
Shreveport, Louisiana 71106

As stated above, the facility in Whippany, New Jersey is designated as an alternate packaging and labeling facility. Whippany, New Jersey for packaging and labeling in the marketed packages. The MERIDIA Capsules



The marketed packages to be utilized in Whippany are identical to the container/closure system provided in the original NDA (Volume 1.4, pages 0169 and 0177). Please note that there will be no revisions required to the current labeling since our parent corporation for both the Shreveport and Whippany sites is the same. are included in Attachment 2.

Stability data is provided in Attachment 3. The for the attached stability studies



We certify that the packaging facility at our Whippany plant operates in compliance with cGMP's and commit to place the first of each strength packaged in Whippany in our stability program. The stability program will be conducted according to the protocol submitted in the original NDA. The stability results will be submitted to the Agency in an annual report.

It is our intention to implement the packaging site change on April 1, 1998.

In accordance with 21 CFR § 314.71(b), a field copy of this supplement will be concurrently submitted to the New Jersey District Office of the Food and Drug Administration.

If you have any questions regarding this submission, please call me at (973) 331-7570.

Sincerely,

Kimberly A Davis for

Robert W. Ashworth, Ph.D.
Director, Regulatory Affairs

Enclosures