CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-406 / S-017

Trade Name: Prevacid 15 mg and 30 mg Capsules, Oral Suspension and Tablets

Generic Name: lansoprazole

Sponsor: TAP Holdings, Inc.

Approval Date: September 17, 1997

Indications: For an additional manufacturing facility for the drug substance

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-406 / S-017

CONTENTS

Reviews / Information Included in this NDA Review.	
Approval Letter	X
Other Action Letters	
Labeling	
Summary Review	
Officer/Employee List	
Office Director Memo	
Cross Discipline Team Leader Review	
Medical Review(s)	
Chemistry Review(s)	X
Environmental Assessment	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/Biopharmaceutics Review(s)	
Other Reviews	
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Proprietary Name Review(s)	
Administrative/Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-406 / S-017

APPROVAL LETTER

NDA 20-406/S-017

TAP Holdings Inc.
Attention: Judy Decker Wargel
2355 Waukegan Road
Deerfield, IL 60015

SEP 17 1997

Dear Ms. Wargel:

Please refer to your supplemental new drug application dated January 31, 1997, received February 3, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prevacid (lansoprazole) Delayed-Release Capsules.

We acknowledge receipt of your submissions dated July 9 and August 13, 1997.

The supplemental application provides for an additional manufacturing facility for the drug substance.

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, please contact Maria R. Walsh, M.S., Project Manager, at (301) 443-0487.

Sincerely yours,

Eric P. Duffy 9/17/97

Eric P. Duffy, Ph.D.
Chemistry Team Leader
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

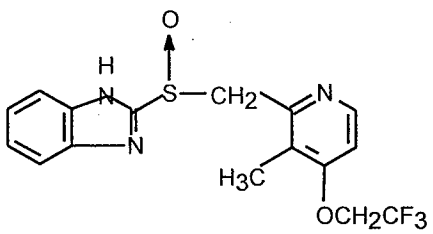
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-406 / S-017

CHEMISTRY REVIEW(S)

58.1

CHEMIST'S REVIEW 1	1. Organization: HFD-180	2. NDA Number: 20-406
3. Name and Address of Applicant (City & State): TAP Holdings, Inc. Bannockburn Lake Plaza 2355 Waukegan Road Deerfield, IL 60015		4. AF Number: APR 30 1997 5. Supplement(s)
6. Name of Drug: Prevacid®	7. Nonproprietary Name: lansoprazole	Numbers: SCM-017 Dates: January 31, 1997
8. Supplement Provides for: qualification of a second Takeda manufacturing facility to produce lansoprazole bulk drug substance.		9. Amendments and Other (Reports, etc.) Dates: Acceptable EER 2/21/97
10. Pharmacological Category: anti-ulcer	11. How Dispensed: RX X OTC __	12. Related IND/NDA/DMF(s):
13. Dosage Form: Delayed-Release Capsules	14. Potency: 15 and 30 mg	
15. Chemical Name and Structure: 2-[[[3-methyl-4-(2,2,-trifluoroethoxy)-2-pyridyl-]methyl]-sulfinyl]benzimidazole 		16. Records and Reports: Current Yes X No ___ Reviewed Yes X No ___

17. Comments: Review notes show table comparing new and old procedures. Stability data for drug product in blister pack is forthcoming. The applicant should be asked to explain some concerns in the manufacturing procedure in an IR letter.

cc: NDA 20-406/SCM-017
HFD-180/Div File
HFD-181/CSO
HFD-180/SFredd
HFD-180/AShaw
R/D init by:EDuffy 2-21-97 EDuffy 4/30/97
ABS/dob **F/T 4-28-97**\WP: c:\wpfiles\chem\S\20406017.1AS

18. Conclusions and Recommendations: The applicant should be sent an Information Request letter. (IR)

19. Reviewer

Name:	Signature	Date Completed:
Arthur B. Shaw, Ph. D.	Arthur B. Shaw 7/28/97	March 6, 1997

Form FDH 2266 (7/75) ALT R

4 Page(s) Withheld

√ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
FOOD AND DRUG ADMINISTRATION

58.1

ESTABLISHMENT EVALUATION REQUEST

REQUEST TYPE *(Check One)*: ☒ Original ☐ Follow-Up ☐ FUR	DATE: **February 10, 1997**	PHONE NO.: (301) 443-0487	EER ID #
REQUESTER NAME: Arthur Shaw	DIVISION: Gastrointestinal and Coagulation Drug Products		MAIL CODE: **HFD-180**
APPLICATION AND SUPPLEMENT NUMBER: NDA 20-406/S-017			
BRAND NAME: Prevacid	ESTABLISHED NAME: lansoprazole		
DOSAGE STRENGTH: 15 and 30 mg Delayed-Release Capsules			STERILE: ☐ Yes ☒ No
PROFILE CLASS: CTR	PRIORITY CLASSIFICATION (See SMG CDER-4820.3): Type 1S		
APPLICANT'S NAME: TAP Holdings, Inc.			
ADDRESS: Bannockburn Lake Office Plaza 2355 Waukegan Road Deerfield, IL 60015			
COMMENTS : This supplement provides for an additional manufacturing facility for the drug substance. This facility is a new building located at the current facility, Takeda's Hikari plant in Hikari, Japan.			

FACILITIES TO BE EVALUATED

(Name and Complete Address)	RESPONSIBILITY	DMF NUMBER/ PROFILE CODE	FKEY/ CIRTIS ID		HFD-324 USE ONLY
1. Takeda Chemical Industries, Ltd. Hikari Plant, Buliding G-27 4720 Takeda Mitsui Hikari Yamaguchi 743, Japan	Manufacturing of bulk drug	CSN			
2.					
3.					
4.					
5.					

FOR HFD-324 USE ONLY:	CSO	DATE RECEIVED
	CGMP COMPLIANCE STATUS	DATE

Of 3274 (8/92) Distribution: Original and Yellow Copy: HFD-324.
:: al NDA 20-406/S-017 HFD-180/Div. File, HFD-180/CSO/M.Walsh, HFD-180/Arthur Shaw HFD-180/Katie Johnson

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-406 / S-017

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

58.1

NDA 20-406/S-017

JUN 18 1997

TAP Holdings Inc.
Attention: Judy Decker Wargel
2355 Waukegan Road
Deerfield, IL 60015

Dear Ms. Wargel:

Please refer to your pending January 31, 1997 supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prevacid(R) (lansoprazole) Delayed-Release Capsules.

To complete our review of your submission, we request the following:

1. Please explain why the [redacted]

2. [redacted] b(4)

We would appreciate your prompt written response so we can continue our evaluation of your supplemental application.

If you have any questions, please contact Maria R. Walsh, M.S., Project Manager, at (301) 443-0487.

Sincerely yours,

Eric P. Duffy 6/17/97

Eric P. Duffy, Ph.D.
Chemistry Team Leader
Division of Gastrointestinal and Coagulation
Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:

Original NDA 20-406/S-017
HFD-180/Div. Files
HFD-180/CSO/M.Walsh
HFD-180/A.Shaw
E.Duffy
HFD-820/ONDC Division Director (only for CMC related issues)

Drafted by: M.Walsh 5/5/97
Initialed by: A.Shaw 5/5/97
E.Duffy 6/16/97
final: M.Walsh 6/17/97
filename: 20406S17.ir

INFORMATION REQUEST (IR)

TAP HOLDINGS INC.
parent of TAP Pharmaceuticals Inc.

Bannockburn Lake Office Plaza
2355 Waukegan Rd.
Deerfield, IL 60015

February 13, 1997

Division of Gastrointestinal and Coagulation Drug Produ HFD-180
Document Control Room 6B-24
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

ORIGINAL

Attn: Stephen B. Fredd, M.D.

RE: PREVACID® (Lansoprazole) Delayed-Release Capsules
NDA: 20-406
General Correspondence **SNDA 017**

Dear Dr. Fredd:

Our original submission of this SNDA on January 31, 1997, contained several errors due to glitches in spell-checking of the document. These occurred on pages 008, 009, 022, and 023 (NDA pagination, lower right corner). I spoke to Ms. Walsh about this on February 11, 1997. She suggested I send the replacement pages as correspondence to the SNDA.

Enclosed are three sets of replacement pages (archival, chemistry and field copy). Also included are the original pages with the errors highlighted. As you can see, the scientific integrity of the report was not affected.

Should you have any questions or need further clarification, please do not hesitate to contact me.

Sincerely,

Judy Decker Wargel

Judy Decker Wargel
Associate Director, Regulatory Affairs
Phone: (847) 317-5781
Fax: (847) 317-5795

JDW/pjp

cc: Raymond Mlecko

2/24/97

cc:
Original NDA 20-406/S-017
HFD-180/Div. Files
HFD-180/CSO/M.Walsh
HFD-180/A.Shaw
E.Duffy
HFD-820/ONDC Division Director
HFD-92/DDM-DIAB
DISTRICT OFFICE

Drafted by: M.Walsh 9/10/97
Initialed by: E.Duffy
final: M.Walsh
filename: 20406S17.AP

APPROVAL (AP)

58.1

NDA 20-406/S-017

TAP Holdings Inc.
Attention: Judy Decker Wargel
2355 Waukegan Road
Deerfield, IL 60015

FEB - 7 1997

Dear Ms. Wargel:

We acknowledge receipt of your supplemental application for the following:

Name of Drug Product: Prevacid (lansoprazole) Delayed-Release Capsules

NDA Number: NDA 20-406

Supplement Number: S-017

Therapeutic Classification: Standard

Date of Supplement: January 31, 1997

Date of Receipt: February 3, 1997

This supplement provides for an additional manufacturing facility for the drug substance.

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on April 4, 1997 in accordance with 21 CFR 314.101(a).

All communications concerning this supplemental application should be addressed as follows:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Gastrointestinal and Coagulation Drug Products, HFD-180
Attention: DOCUMENT CONTROL ROOM
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, please contact me at (301) 443-0487.

Sincerely yours,

Maria R. Walsh, M.S.
Project Manager
Division of Gastrointestinal and
Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Original NDA 20-406/S-017
HFD-180/Div. Files
HFD-180/CSO/M.Walsh
HFD-180/A.Shaw
E.Duffy
DISTRICT OFFICE

MRW 2/6/97

Final: M.Walsh/2/6/97

SUPPLEMENT ACKNOWLEDGEMENT (AC)

TAP HOLDINGS INC.
parent of TAP Pharmaceuticals Inc.

Bannockburn Lake Office Plaza
2355 Waukegan Rd.
Deerfield, IL 60015

ORIGINAL

January 31, 1997

Division of Gastrointestinal and Coagulation Drug Products, HFD-180
Document Control Room 6B-24
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

NDA 20406 SER. NO. 017
NDA SUPPL FOR SCM

CENTER FOR DRUG EVALUATION AND RESEARCH
FEB 03 1997
HFD-180

Attn: Stephen B. Fredd, M.D.

RE: PREVACID® (Lansoprazole) Delayed-Release Capsules
NDA: 20-406
Supplemental Application for Manufacturing Change SNDA 017
New Facility

Dear Dr. Fredd:

The sponsor, TAP Holdings Inc., submits this Supplemental Application under the provisions of Section 505 (i) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.70 (b) (3).

The purpose of this supplement is to qualify a second Takeda manufacturing facility to produce lansoprazole bulk drug for formulation into lansoprazole drug product for export to the United States. This second facility is located next to the current facility at Takeda's Hikari plant in Hikari, Japan.

The _____scheme for producing lansoprazole remains unchanged. There are, however, some changes in equipment and processes as well as an increase in scale. These changes are thoroughly described in the overview as well in Takeda Report No. A-29-2270. b(4)

Takeda has produced three scale-up lots (H702, H703 and H704) in this new facility and placed them on stability. Interim results are presented in Takeda Report No. A-29-2264. One of these lots, H702, was run through the entire manufacturing procedure. Both 15 mg and 30 mg capsules produced from this lot of bulk drug were sent to the United States and packaged by Abbott Laboratories in HDPE bottles of 100 count and placed on stability. This plan was presented to the Agency on June 10, 1996 (IND Amendment No. 294) and their concurrence received by letter dated July 22, 1996. Results showed no difference in the stability profile from capsules produced from bulk drug from the new facility as compared to capsules utilizing bulk drug produced in the current facility. A comparison of results in tabular form is included as well as the stability reports.

2/6/97

Stability data will also be generated in the blister pack and submitted as an amendment to this SNDA per an agreement with the Agency (teleconference with Ms. Walsh on January 7, 1997).

Finally, this new bulk facility has been validated and is ready for an FDA preapproval inspection if the Agency wishes to request one.

If you have any questions, please direct them to my attention.

Sincerely,

Judy Decker Wargel

Judy Decker Wargel
Associate Director, Regulatory Affairs
Phone: (847) 317-5781
Fax: (847) 317-5795

JDW/pjp

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. *0910-0297*
Expiration Date: *November 30, 1996.*

USER FEE COVER SHEET

See Instructions on Reverse Before Completing This Form.

1. APPLICANT'S NAME AND ADDRESS
TAP Holdings Inc.
2355 Waukegan Road
Deerfield, IL 60015

2. USER FEE BILLING NAME, ADDRESS, AND CONTACT
TAP Holdings Inc.
2355 Waukegan Road
Deerfield, IL 60015

Contact: Judy Decker Wargel
Associate Director,
Regulatory Affairs

3. TELEPHONE NUMBER *(Include Area Code)*
(847) 317-5781

4. PRODUCT NAME
PREVACID® (lansoprazole) Delayed-Release Capsules

5. DOES THIS APPLICATION CONTAIN CLINICAL DATA? ☐ YES ☒ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

6. USER FEE I.D. NUMBER

7. LICENSE NUMBER/NDA NUMBER

8. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED BEFORE 9/1/92

☐ AN INSULIN PRODUCT SUBMITTED UNDER 506

☐ THE APPLICATION IS SUBMITTED UNDER 505(b)(2) *(See reverse before checking box.)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/52

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGIC PRODUCT LICENSED UNDER 351 OF THE PHS ACT

9. a. HAS THIS APPLICATION QUALIFIED FOR A SMALL BUSINESS EXCEPTION? ☐ YES ☐ NO *(See reverse if answered YES)*

b. HAS A WAIVER OF APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☐ NO *(See reverse if answered YES)*

This completed form must be signed and accompany each new drug or biologic product, original or supplement.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Judy Decker Wargel	Associate Director, Regulatory Affairs	January 31, 1997

FORM FDA 3397 (12/93)

581

MEMORANDUM OF TELECON

DATE: January 7, 1997

APPLICATION NUMBER: NDA 20-406/SCM-017; Prevacid (lansoprazole) Delayed-Release Capsules

BETWEEN:

Name: Judy Decker Wargel
Phone: (847) 317-5781
Representing: TAP Holdings, Inc.

AND

Name: Maria R. Walsh, Project Manager
Division of Gastrointestinal and Coagulation Drug Products, HFD-180

SUBJECT: Stability Data for Future Supplement for New Bulk Drug Facility

TODAY'S CALL: Ms. Wargel called me about the Agency's letter of July 22, 1996 regarding the sponsor's proposal for a future supplement providing for a new bulk drug facility. Point #2 of that letter requested that the sponsor compare the accelerated stability data of the drug product manufactured with the bulk drug from the new facility with that of the drug product manufactured with the bulk drug from the current facility in both bottles and blisters. Ms. Wargel stated that the request for data in blisters was inadvertantly overlooked when stabiltiy studies were initiated. The sponsor intends to put the blisters on stability as soon as possible. Ms. Wargel asked me if the sponsor can submit the supplement as planned at the end of January and amend the application with the stability data in blisters.

After conferring with Dr. Arthur Shaw, Chemistry Reviewer, I informed Ms. Wargel that this was acceptable. The call was then concluded.

Maria R. Walsh 2/10/97

Maria R. Walsh
Project Manager

cc: Original NDA 20-406/S-017
HFD-180/Div. File
HFD-180/M.Walsh
HFD-180/A.Shaw
E.Duffy

TELECON

gg. SU 12-1-12-39

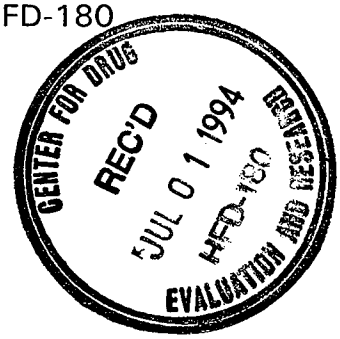
TAP PHARMACEUTICALS INC.

ORIGINAL

June 30, 1994

Bannockburn Lake Office Plaza
2355 Waukegan Road
Deerfield, Illinois 60015

Division of Gastrointestinal and Coagulation Drug Products, HFD-180
Document Control Room 6B-24
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857



Attn: Stephen B. Fredd, M.D.

RE: Lansoprazole (Prevacid®) **NDA 20-406**
Amendment No. 017

Dear Dr. Fredd:

In accordance with section 505(b) of the Food, Drug and Cosmetic Act and 21 CFR 314.60, TAP Pharmaceuticals Inc., submits this amendment to the pending NDA for lansoprazole.

Appended is the complete safety update for lansoprazole as requested by Dr. Hugo Gallo-Torres. The update includes the following items:

Volume 20.1: Submission Contents, Updated Marketing Status, Membership and Consensus Statement from Eye Safety Subcommittee, Eye Findings from Clinical Studies and an Overview of Retinal Atrophy and Results from Mechanistic Studies. In addition to the archival copy of this volume, four review copies (pharmacology, pharmacokinetics, clinical and statistical) are being submitted.

Volume 20.2: Preclinical study reports and references cited in the overview not included in the NDA. Two copies, archival and review (pharmacology), of this volume are included.

Volumes 20.3 - 20.11: Reports for pharmacokinetic studies which have become available since filing the NDA. Two copies of this volume are included, one archival, the other review (pharmacokinetics).

Volumes 20.12 - 20.25: Clinical study reports which have become available since filing the NDA are being submitted as additional evidence of the safety of lansoprazole. A review (clinical) copy is included as well as the archival copy.

lanso/june3

7/7/94 gg

Volumes 20.26 - 20.30: Updated Integrated Summary of Safety for the clinical reviewer. Two copies are included, one archival, the other review (clinical).

Volumes 20.31 - 20.35: Updated Integrated Summary of Safety for the statistical reviewer. Two copies are included, one archival, the other review (statistical).

Volumes 20.36 - 20.39: Case Report Forms for patients who died during a clinical study or discontinued due to an adverse event. Two copies are included, one archival, the other review (clinical).

Should you have any questions about the contents of this submission, please do not hesitate to call me.

Sincerely,

Judy Decker Wargel

Judy Decker Wargel
Regulatory Products Manager
Phone: (708) 317-5781
Fax: (708) 317-5795

JDW/pjp

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001
Expiration Date: December 31, 1992
See OMB Statement on Page 3.

FOR FDA USE ONLY	
DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO ASS

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314).*

NAME OF APPLICANT	DATE OF SUBMISSION
TAP Pharmaceuticals Inc.	June 30, 1994
ADDRESS *(Number, Street, City, State and Zip Code)* 2355 Waukegan Road Deerfield, IL 60015	TELEPHONE NO. *(Include Area Code)* (708) 317-5781
	NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (If previously issued) 20-406

DRUG PRODUCT

ESTABLISHED NAME *(e.g., USP/USAN)*	PROPRIETARY NAME *(If any)*
Lansoprazole	Prevacid®

CODE NAME *(If any)*	CHEMICAL NAME
AG-1749, A-65006	2[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]benzimidazole

DOSAGE FORM	ROUTE OF ADMINISTRATION	STRENGTH(S)
Capsules	Oral	15 mg 30 mg

PROPOSED INDICATIONS FOR USE

Reflux esophagitis
Reflux esophagitis: maintenance of healing
Duodenal ulcer
Gastric ulcer
Pathological hypersecretory conditions including Zollinger-Ellison syndrome

LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS *(21 CFR Part 312)*, NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, AND DRUG MASTER FILES *(21CFR 314.420)* REFERRED TO IN THIS APPLICATION:

INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

☐ THIS SUBMISSION IS A FULL APPLICATION *(21 CFR 314.50)* ☐ THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) (21 CFR 314 55)

IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG	HOLDER OF APPROVED APPLICATION

TYPE SUBMISSION *(Check one)*

☐ PRESUBMISSION ☒ AN AMENDMENT TO A PENDING APPLICATION ☐ SUPPLEMENTAL APPLICATION
☐ ORIGINAL APPLICATION ☐ RESUBMISSION

SPECIFIC REGULATION(S) TO SUPPORT CHANGE OF APPLICATION *(e.g., Part 314.70(b)(2)(iv))* _____

PROPOSED MARKETING STATUS *(Check one)*

☒ APPLICATION FOR A PRESCRIPTION DRUG PRODUCT *(Rx)* ☐ APPLICATION FOR AN OVER - THE - COUNTER PRODUCT *(OTC)*

CONTENTS OF APPLICATION	
This application contains the following items: *(Check all that apply)*	
	1. Index
	2. Summary (21 CFR 314.50 (c))
	3. Chemistry, manufacturing, and control section (21 CFR 314.50 (d) (1))
	4. a. Samples (21 CFR 314.50 (e) (1)) (Submit only upon FDA's request)
	b. Methods Validation Package (21 CFR 314.50 (e) (2) (i))
	c. Labeling (21 CFR 314.50 (e) (2) (ii))
	i. draft labeling *(4 copies)*
	ii. final printed labeling (12 copies)
X	5. Nonclinical pharmacology and toxicology section (21 CFR 314.50 (d) (2))
X	6. Human pharmacokinetics and bioavailability section (21 CFR 314.50 (d) (3))
	7. Microbiology section (21 CFR 314.50 (d) (4))
X	8. Clinical data section (21 CFR 314.50 (d) (5))
X	9. Safety update report (21 CFR 314.50 (d) (5) (vi) (b))
X	10. Statistical section (21 CFR 314.50 (d) (6))
	11. Case report tabulations (21 CFR 314.50 (f) (1))
X	12. Case reports forms (21 CFR 314.50 (f) (1))
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
	15. OTHER *(Specify)*

I agree to update this application with new safety information about the drug that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling I agree to submit these safety update reports as follows: (1) 4 months after the initial submission, (2) following receipt of an approvable letter and (3) at other times as requested by FDA. If this application is approved, I agree to comply with all laws and regulations that apply to approved applications, including the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211.
2. Labeling regulations in 21 CFR 201
3. In the case of a prescription drug product, prescription drug advertising regulations in 21 CFR 202.
4. Regulations on making changes in application in 21 CFR 314.70, 314.71, and 314.72.
5. Regulations on reports in 21 CFR 314.80 and 314.81.
6. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the controlled substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

NAME OF RESPONSIBLE OFFICIAL OR AGENT	SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	DATE
Judy Decker Wargel Regulatory Products Manager	Judy Decker Wargel	June 30, 1994
ADDRESS *(Street, City, State, Zip Code)* 2355 Waukegan Road Deerfield, IL 60015		**TELEPHONE NO.** *(Include Area Code)* (708) 317-5781

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec.1001.)