CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: **20-966**

ADMINISTRATIVE DOCUMENTS

JANSSEN • PHARMACEUTICA • • RESEARCH FOUNDATION •

SPORANOX® (itraconazole) Injection
NDA 20-966

In accordance with the Generic Drug Enforcement Act of 1992, we certify that Janssen Research Foundation did not and will not use in any capacity the services of any person or firm debarred under subsections (a) or (b) [section 306(a) or (b) of the Federal Food, Drug, and Cosmetic Act] in connection with NDA 20-966 for SPORANOX® (itraconazole) Injection.

We also hereby certify that flawed Intel Pentium computer chips were not used to perform any analyses included in NDA 20-966.

Janssen Research Foundation verifies that all trials conducted in the United States that are used to support NDA 20-966, were conducted in compliance with the Institutional Review Board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR Part 50. Non-US protocols used to support the claims in this application were reviewed by independent Ethics Committees/Review Boards and these trials were performed in accordance with the declaration of Helsinki and its subsequent revisions.

Sandra Kuba for DO
Donna Ohye
Director, Regulatory Affairs

April 27, 1998
Date

JANSSEN AT WASHINGTON CROSSING
1125 TRENTON-HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200

JANSSEN • PHARMACEUTICA • • RESEARCH FOUNDATION •

CERTIFICATION

We certify that a Field copy of the chemistry, manufacturing and controls information submitted in original SPORANOX (itraconazole) injection NDA 20-966 was provided to our home district office.

Jeffrey J. Blumenstein, Ph.D.
Group Director, Technical Regulatory Affairs

4/23/98
Date

g:\tra\itrsonda.496\Mar 23,98\84

JANSSEN AT WASHINGTON CROSSING
1125 TRENTON-HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200

Janssen Research Foundation
SPORANOX® (itraconazole) Injection
NDA 20-966

PATENT AND EXCLUSIVITY INFORMATION

Active Ingredient:	Itraconazole
Strength:	10 mg/mL
Trade Name:	SPORANOX®
Dosage Form:	intravenous solution
Sponsor's Name:	Janssen Research Foundation 1125 Trenton-Harbourton Road P.O. Box 200 Titusville, NJ 08560-0200
NDA Number:	20-966
Approval Date:	pending
Applicable Patent Number:	4,267,179 Expiration date: June 23, 2000
Exclusivity:	Three years from the date of approval as provided by the Drug Price Competition and Patent Term Restoration Act of 1984.

Exclusivity Checklist

NDA:	20966 Sporanox (itraconazole)				
Trade Name:	SPORANOX INJECTION				
Generic Name:	itraconazole				
Applicant Name:	Janssen				
Division:	HFD 590				
Project Manager:	Rene Kirkyes				
Approval Date:					
PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?					
1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.					
a. Is it an original NDA?	Yes	X	No		
b. Is it an effectiveness supplement?	Yes		No	X	
c. If yes, what type? (SE1, SE2, etc.)					
Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")	Yes		No	X	
If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.					
Explanation: Safety data only in order to support bioequivalence claim. for IV formulation.					
If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:					
Explanation:					
d. Did the applicant request exclusivity?	Yes		No	X	
If the answer to (d) is "yes," how many years of exclusivity did the applicant request?					
IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS.					
2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use?	Yes		No	X	
If yes, NDA #					
Drug Name:					
IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS.					
3. Is this drug product or indication a DESI upgrade?	Yes		No	X	
IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS (even if a study was required for the upgrade).					

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES		
(Answer either #1 or #2, as appropriate)		
1. Single active ingredient product.	(Yes)	No
Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.	(Yes)	No
If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s). 20-083, 20-510, 20-654		
Drug Product Sporanox Capsule		
NDA # 20-657		
Drug Product Sporanox Oral Solution		
NDA #		
Drug Product		
NDA #		
2. Combination product.	Yes	(No)
If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)	Yes	No
If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).		
Drug Product		
NDA #		
Drug Product		
NDA #		
Drug Product		
NDA #		
IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS. IF "YES," GO TO PART III.		

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS
To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed

only if the answer to PART II, Question 1 or 2, was "yes."				
1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.	Yes	X	No	
IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS.				
2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application. For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.				
a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?	Yes	X	No	
If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCKS.**				
Basis for conclusion:				
b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?	Yes		No	X
1) If the answer to 2 b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.	Yes		No	
If yes, explain:				
2) If the answer to 2 b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?	Yes		No	X
If yes, explain:				
c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:				

Investigation #1, Study #: ITR-INT-60	
Investigation #2, Study #: ITR-INT-67	
Investigation #3, Study #: ITR-INT-62	

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1	Yes		No	✓
Investigation #2	Yes		No	✓
Investigation #3	Yes		No	✓

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

Investigation #1 -- NDA Number	
Investigation #2 -- NDA Number	
Investigation #3 -- NDA Number	

b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1	Yes		No	✓
Investigation #2	Yes		No	✓
Investigation #3	Yes		No	✓

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

Investigation #1 -- NDA Number	
Investigation #2 -- NDA Number	
Investigation #3 -- NDA Number	

If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #1 ITR-INT-60	
Investigation #2 ITR-INT-61	
Investigation #3 ITR-INT-62	

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a. For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 no 1571 – submitted with NDA	Yes		No	
IND#:				
Explain:				
Investigation #2 " " "	Yes		No	
IND#:				
Explain:				
Investigation #3 " " "	Yes		No	
IND#:				
Explain:				

b. For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	Yes		No	
IND#:				
Explain:				
Investigation #2	Yes		No	
IND#:				
Explain:				
Investigation #3	Yes		No	
IND#:				
Explain:				

c. Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)	Yes		No	
If yes, explain:				

BACK TO TOP

Signature of PM/CSO /S/
Date: 3/24/99

Signature of Division Director /S/
Date: 3/30/99

cc:
Original NDA
Division File
HFD-93 Mary Ann Holovac

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

PLA/PMA # 20-966 Supplement # _____ Circle one: SE1 SE2 SE3 SE4 SE5 SE6

HFD-590____ Trade and generic names/dosage form:Sporanox (itraconazole) injection10 mg/mL Action: AP

Applicant Janssen Research Foundation Therapeutic Class Antifungal

Indication(s) previously approved None for IV formulation

Pediatric information in labeling of approved indication(s) is adequate ___ inadequate ___
Proposed indication in this application _____

FOR SUPPLEMENTS, ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION.

IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS? ___Yes (Continue with questions) ___No (Sign and return the form)
WHAT PEDIATRIC AGE GROUPS IS THE DRUG NEEDED? (Check all that apply)
__Neonates (Birth-1month) __Infants (1month-2yrs) __Children (2-12yrs) __Adolecents(12-16yrs)

___ 1. **PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.

___ 2. **PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.

3. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.
   ___ a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.
   ___ b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.
   ___ c. The applicant has committed to doing such studies as will be required.
      ___ (1) Studies are ongoing.
      ___ (2) Protocols were submitted and approved.
      ___ (3) Protocols were submitted and are under review.
      ___ (4) If no protocol has been submitted, attach memo describing status of discussions.
   ___ d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

___ 4. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed.

___ 5. **PEDIATRIC LABELING MAY NOT BE ADEQUATE.**
   ___ a. Pediatric studies are needed.
   ___ b. Pediatric studies may not be needed but a pediatric supplement is needed.

___ 6. **If none of the above apply, attach an explanation, as necessary. Safety and effectiveness in pediatric patients have not been established.**

ARE THERE ANY PEDIATRIC PHASE IV COMMITMENTS IN THE ACTION LETTER? ___ Yes _X__ No
ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

Rene Kimzey, Regulatory Project Manager /S/ 3/24/99
Signature of Preparer and Title Date

cc: Orig NDA/PLA/PMA # 20966
HFD-590 /Div File
NDA/PLA Action Package
HFD-006/ KRoberts

(revised 9/15/97)

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Application: NDA 20966/000
Stamp: 27-APR-1998 Regulatory Due: 27-APR-1999
Applicant: JANSSEN
1125 TRENTON HARBOURTON RD
TITUSVILLE, NJ 08560

Priority: 3S Org Code: 590
Action Goal: District Goal: 26-DEC-1998
Brand Name: SPORANOX (ITRACONAZOLE) 10MG/ML INJ
Established Name:
Generic Name: ITRACONAZOLE
Dosage Form: INJ (INJECTION)
Strength: 10 MG/ML

FDA Contacts: R Kinzay
~~E. FRANK~~ (HFD-590) 301-827-2127 , Project Manager
G. HOLBERT (HFD-590) 301-827-2399 , Review Chemist
N. SCHMUFF (HFD-590) 301-827-2425 , Team Leader

Overall Recommendation:

ACCEPTABLE on 01-DEC-1998 by J. D AMBROGIO (HFD-324) 301-827-0062
ACCEPTABLE on 26-OCT-1998 by J. D AMBROGIO (HFD-324) 301-827-0062
WITHHOLD on 01-OCT-1998 by J. SINGER (HFD-324) 301-827-0066

Establishment:

DMF No:
AADA No:

Profile: SVS OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date 26-OCT-1998
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: FINISHED DOSAGE LABELER
FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER

Establishment: 2242843
JANSSEN PHARMACEUTICA INC
1125 TRENTON HARBOURTON RD
TITUSVILLE, NJ 08560

DMF No:
AADA No:

Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date 04-MAY-1998
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities: FINISHED DOSAGE OTHER TESTER
FINISHED DOSAGE RELEASE TESTER

Establishment: 9610028
JANSSEN PHARMACEUTICA NV
TURNHOUTSEBAAN 30, B-2340
BEERSE, , BE

DMF No:
AADA No:

Profile: CTL OAI Status: NONE

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Last Milestone: **OC RECOMMENDATION**
Milestone Date **24-AUG-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON FILE REVIEW**

Responsibilities: **FINISHED DOSAGE OTHER TESTER**
FINISHED DOSAGE RELEASE TESTER

Establishment: **9610034**
JANSSEN PHARMACEUTICA NV
JANSSEN PHARMACEUTICA LAAN 3
GEEL, , BE

DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **01-DEC-1998**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

Establishment:

DMF No:
AADA No:

Profile: **SVS** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **04-MAY-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **FINISHED DOSAGE LABELER**
FINISHED DOSAGE PACKAGER

REQUEST FOR PROPRIETARY/ESTABLISHED NAME REVIEW

To: CDER Labeling and Nomenclature Committee
Attention: Dan Boring, R.Ph., Ph.D., Chair
HFD-530
9201 Corporate Blvd, Room N461

From: Gene W. Holbert, DSPIDP (HFD-590) GWH

Date: October 16, 1998

Application Status (IND/NDA/ANDA): NDA 20-966

Proposed Proprietary Name: Sporanox® (itraconazole) Injection

Trademark registration status/Countries registered (if known):

Company trade name: Sporanox

Other proprietary names by same firm for companion products:
Sporanox ® Oral Solution, Sporanox® Capsules

United States Adopted Name, dosage form, strength and dosing schedule:
Itraconazole, 10 mg/mL 200 mg b.i.d. (two one-hour infusions) for 2 days followed by 200 mg q.d. (one one-hour infusion).

Indication for use: Treatment of blastomycosis, histoplasmosis and aspergillosis.

Comments from submitter (concerns, observations, etc.): This drug is formulated with HYDROXYPROPYL-β-CYCLODEXTRIN.

Meetings of the Committee are scheduled for the 4th Tuesday of each month. Please submit this form at least one week before the meeting. Responses will be as timely as possible.
Rev. 2/97

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on last page

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Janssen Research Foundation	March 24, 1999
TELEPHONE NO. (*Include Area Code*)	FACSIMILE (FAX) Number (*Include Area Code*)
(609) 730-3486	(609) 730-3122

APPLICANT ADDRESS (*Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued*):
1125 Trenton –Harbourton Road
P.O. Box 200
Titusville, NJ 08560-0200

AUTHORIZED U.S. AGENT NAME & ADDRESS (*Number, Street, City, State, ZIP Code, telephone & FAX number*) IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 20-966

ESTABLISHED NAME (*e.g., Proper name, USP/USAN name*)	PROPRIETARY NAME (*trade name*) IF ANY
Itraconazole	SPORANOX® Injection

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (*if any*)
(±)-1-[(RS)-sec-butyl]-4-[p-[4-[p-[[2R,4S)-2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]phenyl]-Δ^2-1,2,4-triazolin-5-one

CODE NAME (*if any*)
R051211

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Injection	10 mg/mL	Intravenous infusion

(PROPOSED) INDICATION(S) FOR USE: Treatment of blastomycosis, histoplasmosis and aspergillosis in immunocompromised and non-immunocompromised patients

APPLICATION INFORMATION

APPLICATION TYPE

(check one) ☒ NEW DRUG APPLICATION (21 CFR 314.50) ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)

BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b) (1) 505 (b) (2) 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

Name of Drug Holder of Approved Application

TYPE OF SUBMISSION

(check one) ☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION RESUBMISSION

PRESUBMISSION ANNUAL REPORT ESTABLISHMENT DESCRIPTION SUPPLEMENT SUPAC SUPPLEMENT

EFFICACY SUPPLEMENT LABELING SUPPLEMENT CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT OTHER

REASON FOR SUBMISSION
Phase IV Commitments

PROPOSED MARKETING STATUS (check one) ☒ PRESCRIPTION PRODUCT (Rx) OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED	THIS APPLICATION IS
1	☒ PAPER PAPER AND ELECTRONIC ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application) NDA 20-083, 20-657, 20-510

This application contains the following items: (*Check all that apply*)	
	1. Index
	2. Labeling (check one) ☒ Draft Labeling Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case reports forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	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. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.5 (k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
X	19. OTHER (Specify): Phase IV commitments

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I will comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. 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.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
[signature]	Edward G. Brann, Asst. Dir., Regulatory Affairs	March 24, 1999

ADDRESS (*Street, City, State, and ZIP Code*)	Telephone Number
1125 Trenton-Harbourton Road, P.O. Box 200, Titusville, NJ 08560-0200	(609) 730-3486

Please DO NOT RETURN this form to this address.