

ORIGINAL

MGI

ARMA

MGI PHARMA, INC.
Suite 300 E, Opus Center
9900 Bren Road East
Minnetonka, Minnesota 55343-9667

(Telephone) 612-935-7335
(Facsimile) 612-935-0468

June 9, 1997

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

S-007
SUPPL NEW CORRESP

Via Federal Express

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

RE: NDA #20-237
S-007, Amendment 6

Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment provides a diskette containing the electronic version of the proposed labeling submitted on June 2, 1997 in Amendment 5 to Supplement S-007. The electronic version is in a Wordperfect 6.0/6.1 for Windows format. The document name is S007FDA.wpd.

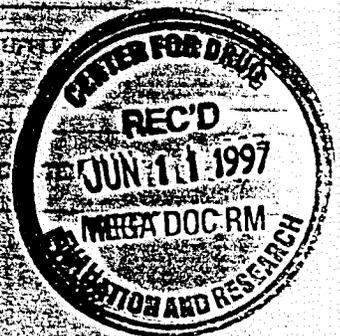
Neither significant new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs

/tj
Enclosures





NEW CORRESP.

CENTRAL

MGI PHARMA, INC.
Suite 300 E. Opus Center
9900 Bren Road East
Minnetonka, Minnesota 55343-9667

(Telephone) 612-935-7335
(Facsimile) 612-935-0462

June 4, 1997

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

RE: NDA #20-237
General Correspondence
May 23, 1997 Meeting: Summary and Next Steps

Dear Dr. Wilkin:

Enclosed please find a copy of MGI PHARMA, Inc.'s "Summary and Next Steps" for our FDA/MGI meeting of May 23, 1997.

Please contact me if you have any questions regarding this submission.

Cordially,


Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs

/tj

enclosure



MGI
P H A R M A

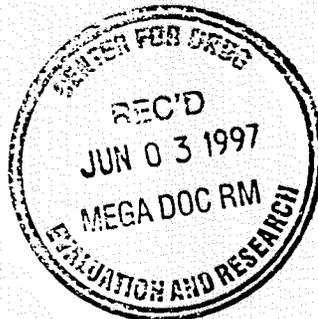
ORIGINAL

MGI PHARMA, INC.
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(Telephone) 612-935-7335
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Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

June 2, 1997



Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

RE: NDA #20-237
S-007, Amendment 5

BL
NDA SUPPL AMENDMENT
S-007

Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment completes MGI PHARMA's response to the "comments for the applicant," which arose from the 45-day meeting on Supplement S-007.

Neither significant new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,

Jo H. Gustafson
Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs

/tj
Enclosures

REVIEWS COMPLETED	
CDO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> IN.A.I.
<input type="checkbox"/> MEMO	
CDO INITIALS	DATE

ORIGINAL



MGI PHARMA, INC.
Suite 300 E, Opus Center
9900 Bren Road East
Minnetonka, Minnesota 55343-9667

(Telephone) 612-935-7335
(Facsimile) 612-935-0468

May 8, 1997

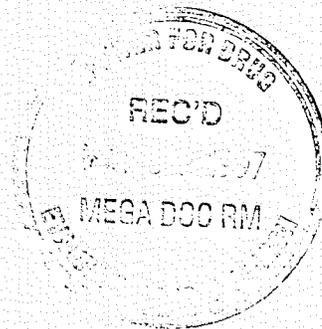
BL
NDA SUPPLEMENT
S-007

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

RE: NDA #20-237
S-007, Amendment 4



Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment is in response to the "comments for the applicant," which arose from the 45-day meeting on Supplement S-007. This meeting was held on or before March 21, 1997. The comments were telefaxed to MGI PHARMA on May 1, 1997.

Neither significant new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,

Jo H. Gustafson
Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs

/tj
Enclosures

REVISIONS COMPLETED



WHICH IS THE ORIGINAL

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Suite 300 E, Opus Center
9900 Bren Road East
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(Telephone) 612-935-7335
(Facsimile) 612-935-0468

May 8, 1997

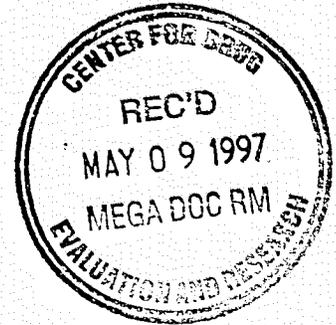
SUPPL NEW CORRESP
SUPPL NEW CORRESP
S-007

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

RE: NDA #20-237
General Correspondence
Background Information for May 23, 1997 Meeting



Dear Dr. Wilkin:

MGI PHARMA has a meeting scheduled with your Division on May 23, 1997, regarding the assignment of review classification to NDA 20-237, Supplement S-007, the supplement to expand the indication for Salagen® Tablets to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome. This general correspondence includes the background information for that meeting. Four desk copies are provided for distribution to Dr. Hyman, Dr. Kelsey, Dr. Chambers, and Dr. Blatt. MGI PHARMA is separately providing copies of this background document to Mr. James Morrison and to Dr. John McCormick.

Please contact me if you have any questions regarding this submission.

Cordially,

Jo H. Gustafson
Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs

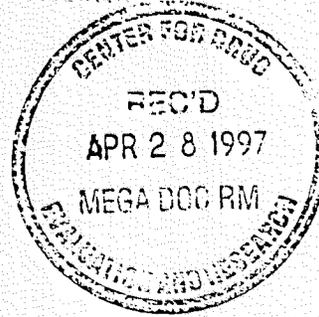
/tj
Enclosures

REVIEWING COMPLETED	
CGO ACTION	
<input type="checkbox"/> LETTER	<input type="checkbox"/> FAX <input type="checkbox"/> OTHER
NO. OF COPIES	DATE



REVIEWS COMPLETED
CSO ACTION:
<input type="checkbox"/> LETTER <input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSO INITIALS _____ DATE _____

ORIGINAL



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 9900 Bren Road East
 Minnetonka, Minnesota 55343-9667
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Jo H. Gustafson, Ph.D.
 Director, Regulatory Affairs
 Direct: 612-939-4665

April 25, 1997

Via Federal Express

Jonathan Wilkin, M.D., Director
 FDA/CDER/ODE V
 Division of Dermatologic and
 Dental Drug Products, HFD-540
 Building 2, Second Floor, Room N203
 9201 Corporate Boulevard
 Rockville, MD 20850

SNC-007
 SUPPL NEW CORRES

RE: Critical Factors in FDA's March, 1997 Determination of a Standard Review for Salagen® Tablets #20-237, Supplement S-007

Dear Dr. Wilkin:

On February 11, 1997, MGI PHARMA submitted a clinical efficacy supplement (S-007) to expand the indication for Salagen® Tablets (pilocarpine hydrochloride) to include treatment of symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome. At the time of submission, MGI PHARMA fully anticipated priority review for this supplement in accordance with CDER's MAPP 6020.3, given that there is currently no effective treatment available for the indication. We were disappointed to learn in March that the Division had determined that a standard review would be conducted which will extend the initial review time from six to 12 months.

To date, our efforts to facilitate the review process include 1) provision on loan of a computer loaded with pivotal study data files in SAS format with SAS programs, as well as copies of all study reports with their corresponding end-of-text tables; 2) rapid response to all questions raised, and 3) rapid provision of all requested desk copies.

We now have a meeting scheduled in May to discuss this issue. We are aware that approximately half of the priority review time period will have elapsed by the time of that meeting. It is important, therefore, that this meeting be as meaningful as possible and that MGI PHARMA is fully prepared to respond to the points on which the Division based its decision. That will permit the Division to reverse its decision if that is appropriate. If, however, MGI is not prepared to address your issues, the meeting may be unproductive and additional time will be lost in determining whether priority review is appropriate.

I have told Sandy Childs that I will provide background information for the meeting two weeks prior to the meeting. It would be extremely helpful to our preparation if the critical

J. Wilkin, M.D.

-2-

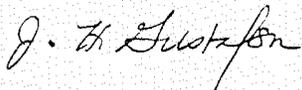
04/25/97

factors in the Division's decision to deny priority review could be communicated to us at least three weeks prior to the meeting so that we can prepare accordingly and make the meeting as meaningful as possible.

We appreciate that there are many demands on your time. However, I strongly believe that clarification of how a Division decision conforms with a CDER MAPP definition is a critical activity for each FDA division. MGI PHARMA continues to believe strongly that its Supplement S-007 does meet the priority review definition in CDER's MAPP 6020.3.

We look forward to learning the bases for the March decision and to our opportunity to discuss the review assignment with your team.

Cordially,



Jo H. Gustafson, Ph.D.

/tj

cc: Peter Vacarri (Office of Orphan Drug Products)
Jim Morrison (CDER Ombudsman)

ORIGINAL



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Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

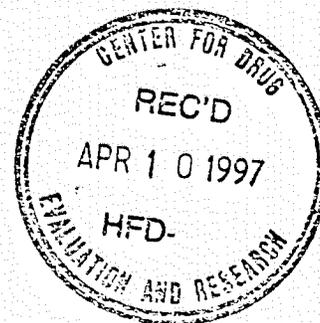
April 8, 1997

S-007
SUPPL NEW CORRESP

Via Federal Express

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

RE: NDA #20-237, General Correspondence
Review Status of S-007



Dear Dr. Wilkin:

Supplement S-007 is a clinical efficacy supplement to expand the indication for Salagen® Tablets (pilocarpine hydrochloride) to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome. On February 28, 1992, this indication received orphan designation by the Office of Orphan Drug Products. In our submission letter of February 11, 1997, MGI requested assignment of priority review for the supplement because there is a significant unmet medical need for treatment of the indication under review in this efficacy supplement.

On March 21, 1997, Dr. Hal Blatt left a voice mail message for me that FDA had accepted that supplement for filing. However, he also left a message that there would be a standard 12-month review. On March 21st, I returned Dr. Blatt's call, was unable to reach him directly, and left a voice mail message that we would like to address the decision with respect to priority and standard review. I requested the bases for assignment of a standard review, acknowledging that it could be included in the telefax he told me he would be sending with the additional information requests that came out of the 45 day meeting.

Since then, I have not been able to learn the basis of the assignment of a standard review. However, time is critical. I have reviewed CDER's Manual of Policies and Procedures with respect to "Priority Review Policy" (MAPP 6020.3).

MAPP 6020.3's purpose is stated as, "This MAPP describes the review priority classification of New Drug Applications (NDA's) and effectiveness supplements."

REVIEWS COMPLETED
CORRECTION:
<input type="checkbox"/> LETTER <input type="checkbox"/> MAIL <input type="checkbox"/> MEMO

April 8, 1997

Within this MAPP, CDER defines priority review as:

"The drug product, if approved, would be a significant improvement compared to marketed products [approved (if such is required), including non-"drug" product/therapies] in the treatment, diagnosis, or prevention of a disease. Improvement can be demonstrated by, for example: (1) evidence of increased effectiveness in treatment, prevention or diagnosis of disease; (2) elimination or substantial reduction of a treatment-limiting drug reaction; (3) documented enhancement of patient compliance; or (4) evidence of safety and effectiveness of (SIC) a new subpopulation."

pp 1-2, MAPP 6020.3, 4/22/96

Clearly, items 1 and 4 are applicable to Salagen® Tablets. It must be noted that Salagen® Tablets were given a priority review for the first indication of treatment of symptoms of radiation-induced xerostomia. The current supplement provides evidence of safety and effectiveness in a second (new) subpopulation of patients with xerostomia.

Salagen® Tablets received orphan designation for this drug product because there is an unmet medical need. Therefore, there are no marketed products, including non-"drug" product/therapies for the treatment of dry eyes and dry mouth within the Sjögren's syndrome disease state.

MGI PHARMA strongly believes that S-007 to NDA #20-237 meets CDER's standards for priority review, and requests a meeting to discuss review assignment for this supplement.

Cordially,



Jo H. Gustafson, Ph.D.

/tj

cc: Marlene E. Haffner, M.D., M.P.H.
Director, Office of Orphan Products Development



ORIGINAL

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Suite 300 E. Opus Center
9900 Bren Road East
Minnetonka, Minnesota 55343-9667

(Telephone) 612-935-7335
(Facsimile) 612-935-0468

April 8, 1997

SNC -007
SUPPL NEW CORRESP

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express



**RE: NDA #20-237
S-007, Amendment 3**

Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment provides on loan a computer to be used by Dr. Farr in reviewing S-007. All information has been placed on the hard drive. There are no separate floppy disks in this submission.

This amendment also includes a guidebook for use of this laptop, with the SAS data sets and the SAS programs. A desk copy of this guidebook is provided for Dr. Farr, in addition to the two copies for the official supplement filings.

Neither new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

As Dr. Farr reviews the information on this computer, MGI PHARMA is most willing and prepared to visit with her for a one-on-one introduction to the computer, its programs and its data. In that regard, I will contact your office within the week to see if she would like a meeting scheduled.

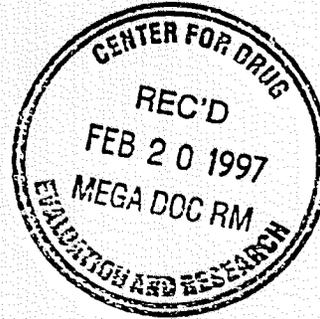
Please contact me if you have any questions regarding this submission.

Cordially,

Jo H. Gustafson
Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs

/tj
Enclosures

REVIEWS COMPLETED
CSO ACTION:
<input type="checkbox"/> LETTER <input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSO INITIALS
DATE



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Suite 300 E, Opus Center
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Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: (612) 939-4665

February 19, 1997

MC
NEW CORRESP

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

RE: NDA 20-237
Salagen® Tablets
Amendment to February 11, 1997 Clinical Efficacy Supplement

Includes Desk Copies

Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is submitting an amendment to the February 11, 1997 labeling supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment provides: 1) a hard copy of the certification statement previously telefaxed to Hal Blatt; 2) a volume containing the master table of contents, along with the individual tables of contents for each of the 132 volumes in the February 11, 1997 supplement; and 3) a compilation of the summary components of the February 11, 1997 supplement. This compilation includes portions of Volumes 1, 5, and 132 of that supplement. The page numbers in that compilation are the page numbers used in the original supplement.

Neither new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,

Jo H. Gustafson, Ph.D.

/tj
Enclosures

REVIEWS COMPLETED	
CSD ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSD INITIALS	DATE

MGI

PHARMA

NDA NO. 20137 REF. NO. 56007

NDA SUPPL FOR SE7

February 11, 1997

MGI PHARMA, INC.
Suite 300 E, Opus Center
9900 Bren Road East
Minnetonka, Minnesota 55343-9666

(Telephone) 612-935-7333
(Facsimile) 612-935-0466

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: (612) 939-4661

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

RE: NDA 20-237
Salagen® Tablets
Clinical Efficacy Supplement

Dear Dr. Wilkin:

In accordance with 21 CFR 314.70(b)(3), MGI PHARMA, INC. is submitting a labeling supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

On February 28, 1992, the Office of Orphan Products Development determined that pilocarpine hydrochloride "qualifies for orphan designation for the treatment of xerostomia and keratoconjunctivitis sicca in Sjögren's syndrome patients." This reflects a determination that there is a significant unmet medical need for treatment of this indication.

Therefore, by this letter and with this submission, MGI PHARMA, INC. is requesting assignment of priority review for this supplement.

Please contact me if you have any questions regarding this submission.

Cordially,



Jo H. Gustafson, Ph.D.

/tj

Enclosure



DUPLICATE

**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: June 30, 1991
See OMB Statement on Page 3.

FOR FDA USE ONLY

DATE RECEIVED	DATED 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
MGI PHARMA, INC.

DATE OF SUBMISSION
August 14, 1997

ADDRESS (Number, Street, City, State and Zip Code)

Suite 300E, Opus Center
9900 Brea Road East
Minnetonka, MN 55343

TELEPHONE NO. (Include Area Code)
612-935-7335

NEW DRUG OR ANTIBIOTIC APPLICATION
NUMBER (If previously issued)
20-237

ESTABLISHED NAME (e.g. USP/USAN) DRUG PRODUCT

pilocarpine hydrochloride

PROPRIETARY NAME (If any)

Salagen® Tablets

CODE NAME (If any)

CHEMICAL NAME

2(3H)-Furanone, 3-ethylidihydro-4-((1-methyl-1H-imidazol-5-yl)methyl)-
-monohydrochloride, (3S-cis)

DOSAGE FORM

tablets

ROUTE OF ADMINISTRATION

oral

STRENGTH(S)

5 mg

PROPOSED INDICATIONS FOR USE

For treatment of symptoms of dry mouth and dry eyes in patients with Sjögren's 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 (21 CFR 314.420) REFERRED TO IN THIS APPLICATION:

IND #
DMF
DMF
DMF
DMF
DMF

DMF
DMF

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)

NAME OF DRUG

IF AN ANDA IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
HOLDER OF APPROVED APPLICATION

PRESUBMISSION

STATUS OF APPLICATION (Check one)

ORIGINAL APPLICATION

AN AMENDMENT TO A PENDING APPLICATION

SUPPLEMENTAL APPLICATION

RESUBMISSION

General Correspondence

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)

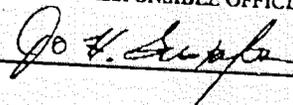
- 1. Index
- 2. Summary (21 CFR 314.50(c))
- 3. Chemistry, manufacturing, and control section (21 CFR 314.50(d)(1))
- 4. a. Samples (21 CFR 314.50(e)(1)) (Submit only upon FDA's request)
- b. Methods Validation Package (21 CFR 314.50(e)(2)(i))
- c. Labeling (21 CFR 314.50(e)(2)(ii))
 - i. draft labeling (4 copies)
 - ii. final printed labeling (12 copies)
- 5. Nonclinical pharmacology and toxicology section (21 CFR 314.50(d)(2))
- 6. Human pharmacokinetics and bioavailability section (21 CFR 314.50(d)(3))
- 7. Microbiology section (21 CFR 314.50(d)(4))
- 8. Clinical data section (21 CFR 314.50(d)(5))
- 9. Safety update report (21 CFR 314.50(d)(5)(vi)(b))
- 10. Statistical section (21 CFR 314.50(d)(6))
- 11. Case report tabulations (21 CFR 314.50(f)(1))
- 12. Case report 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))
- X 15. OTHER (Specify) General Correspondence

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 approvable letter and (3) at other times as requested by the 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
 Jo H. Gustafson, Ph.D.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT


DATE
 August 14, 1997

ADDRESS (Street, City, State, Zip Code)
 Suite 300E, Opus Center, 9900 Brea Road East
 Minnetonka, MN 55343

TELEPHONE NO. (Include Area Code)
 612-935-7335

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)
 FORM FDA 356a (12/90)