CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-105

ADMINISTRATIVE DOCUMENTS

ORIGINAL DECLARATION

U.S. Patent Application Serial No.: 08/803,903
A MEDICINAL PACKAGE FOR DISPENSING AN ENTIRE MEDICINAL COURSE OF TREATMENT

Filed: February 21, 1997

The undersigned declares that U.S.Patent Application Serial No.: 08/803,903 covers the packaging of Zotrim™ *UTI* Therapy. This product is the subject of this application for which approval is sought.

Peter J. Mione
Vice President, Clinical and
Regulatory Affairs - DynaGen, Inc.

2/14/99
Date

ORIGINAL DECLARATION

U.S. Patent Application Serial No.: 08/803,894
A MEDICINAL PACKAGE FOR DISPENSING AN ENTIRE MEDICINAL COURSE OF TREATMENT FOR URINARY TRACT INFECTIONS

Filed: February 21, 1997

The undersigned declares that U.S.Patent Application Serial No.: 08/803,894 covers the packaging of Zotrim™ *UTI* Therapy. This product is the subject of this application for which approval is sought.

Peter J. Mione
Vice President, Clinical and
Regulatory Affairs - DynaGen, Inc.

2/18/99
Date

ABLE
LABORATORIES
INC. Subsidiary of DynaGen, Inc.

NEW DRUG APPLICATION
Zotrim™ *UTI* Therapy
NDA # 21-105

SECTION XIX GENERIC DRUG ENFORCEMENT ACT OF 1992 CERTIFICATION

Section 306 (k) (1) Requirement

In accordance with section 306 (a) or (b) of the Generic Drug Enforcement Act of 1992, ABLE LABORATORIES, INC. did not knowingly and will not knowingly use in any capacity the services of any person debarred under subsections 306 (a) or (b), in connection with such application.

Section 306 (k) (2) Requirement

ABLE LABORATORIES, INC. has no relevant convictions to report under 306 (a) and (b) for any persons (including contracted affiliations) responsible for the development of data or other information used to support this application.

ABLE LABORATORIES, INC.

Mr. Shashikant Shah, R.Ph.
V.P. Quality/Regulatory

9/5/00
Date

6 Hollywood Court ◢ South Plainfield ◢ New Jersey 07080
Telephone: 908-754-2253 ◢ Fax: 908-754-2476

PATENT CERTIFICATION

PARAGRAPH II CERTIFICATION

I hereby certify that under 21 CFR Part 314.50 (i)(1)(i)(A) and in the opinion of and to the best of their knowledge, DynaGen, Inc. and its subsidiary ABLE LABORATORIES, INC. claim that all relevant patents for the drugs (Trimethoprim-Sulfamethoxazole DS and Phenazopyridine hydrochloride) referred to in this application have expired.

Peter J. Mione

Peter J. Mione
Vice President, Clinical and
Regulatory Affairs - DynaGen, Inc.

2/18/99
Date

Zotrim™ *UTI* Therapy is a pharmaceutical therapy for urinary tract infections. It consists of two well-known drugs, Trimethoprim-Sulfamethoxazole DS (160 mg trimethoprim:800 mg sulfamethoxazole) and Phenazopyridine Hydrochloride (200 mg). Trimethoprim-Sulfamethoxazole DS is an antibacterial for the treatment of urinary tract infections due to susceptible organisms. Phenazopyridine hydrochloride is a urinary tract analgesic employed for the symptomatic relief of pain, urgency, burning, frequency, and other discomforts arising from irritation of the lower urinary tract.

Zotrim™ *UTI* Therapy is a combination of both products (Trimethoprim-Sulfamethoxazole DS and Phenazopyridine Hydrochloride tablets) packaged on a single blister card package for the complete treatment of urinary tract infection.

The applicant of this new drug application, Able Laboratories, Inc., (subsidiary of DynaGen, Inc.) will manufacture the phenazopyridine hydrochloride component of Zotrim™ *UTI* Therapy [redacted] will provide the trimethoprim-sulfamethoxazole DS component. Both components will be packaged as a single drug product (Zotrim™ *UTI* Therapy) by [redacted]

To the best of our knowledge, all relevant patents regarding trimethoprim-sulfamethoxazole and phenazopyridine hydrochloride have expired.

DynaGen has filed two patent applications regarding the packaging for Zotrim™ *UTI* Therapy.

1. U.S. Patent Application entitled: **A MEDICINAL PACKAGE FOR DISPENSING AN ENTIRE MEDICINAL COURSE OF TREATMENT FOR URINARY TRACT INFECTIONS**

Filed:	February 21, 1997
Serial No.:	08/803,894
Owner:	DynaGen, Inc. Riverside Technology Center 840 Memorial Drive Cambridge, MA 02139
Patent Type:	Drug Product Packaging

2. U.S. Patent Application entitled: **A MEDICINAL PACKAGE FOR DISPENSING AN ENTIRE MEDICINAL COURSE OF TREATMENT**

Filed:	February 21, 1997
Serial No.:	08/803,903
Owner:	DynaGen, Inc. Riverside Technology Center 840 Memorial Drive Cambridge, MA 02139
Patent Type:	Drug Product Packaging

Appropriate certifications/declarations are included in the following pages. The stated claims for the above-mentioned patent applications are included in Patent Information Appendices 1 and 2.

EXCLUSIVITY SUMMARY for NDA # 21-105 **SUPPL #** _____

Trade Name none **Generic Name** Sulfamethoxazole and Trimethoprim Tablets USP and Phenazopyridine Hydrochloride Tablets, USP

Applicant Name Able Laboratories **HFD-** 520

Approval Date June 26, 2001

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 /✓/ NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO /✓/

      If yes, what type(SE1, SE2, etc.)? _____

   c) 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 /___/

      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.

      _____

      _____

      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:

      _____

      _____

d) Did the applicant request exclusivity?

YES /___/ NO /✓/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

_____

_____

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /✓/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

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? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /✓/ NO /___/

If yes, NDA # 17-377 Drug Name Bactrim

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /✓/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (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.

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).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

2. Combination product.

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).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: <u>THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS</u>

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 /___/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

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 /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

_____

_____

(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 /___/

(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 /___/

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 # _____

Investigation #2, Study # _____

Investigation #3, Study # _____

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:

NDA # _____ Study # _____
NDA # _____ Study # _____
NDA # _____ Study # _____

(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:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

(c) 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 #__, Study # _____

Investigation #__, Study # _____

Investigation #__, Study # _____

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

IND # _____ YES /___/ NO /___/ Explain: _____

_____

_____

Investigation #2

IND # _____ YES /___/ NO /___/ 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 /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

Investigation #2

YES /___/ Explain _____ NO /___/ 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: _____

_____

_____

/S/

Signature of Preparer
Title: Project Manager

6/7/01
Date

/S/

Signature of Office or Division Director

6/28/01
Date

cc:
Archival NDA
HFD-520/Division File
HFD-520/RPM/B. Duvall-Miller
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA Number: N 021105
Trade Name: none
Generic Name: TMP/SMZ/160/800MG/PHENAZOPYRIDINE 200MG
Supplement Number. 000 **Supplement Type:** N
Dosage Form:
Regulatory Action: UN **Action Date:** 2/24/99
COMIS Indication: TREATMENT OF URINARY TRACT INFECTION

Indication #1: Treatment of urinary tract infections and the symptomatic relief of pain, burning, urgency, frequency, and other discomforts arising from irritation of the lower urinary tract mucosa caused by infection
Label Adequacy: Other - see comments
Formulation Needed: Other
Comments (if any) Contraindicated in pediatric patients

Lower Range	Upper Range	Status	Date
0 years	Adult	Waived	7/8/01

Comments: Contraindicated in pediatric patients

This page was last edited on 6/7/01

Signature /S/ Date 6/7/01

PEDIATRIC PAGE
(Complete for all original applications and all efficacy supplements)

(NDA)/PLA/PMA # 21-105 Supplement # _____ Circle one: SE1 SE2 SE3 SE4 SE5 SE6

HFD-520 Trade and generic names/dosage form: _____ Action: (AP) AE NA

Applicant Able Laboratories Therapeutic Class 45

Indication(s) previously approved _____
Pediatric information in labeling of approved indication(s) is adequate ___ inadequate ___

Indication in this application treatment of urinary tract infections (For supplemen answer the following questions in relation to the proposed indication.)

___ 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 tc 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. Contraindicated in pediatric patients.

___ 5. **If none of the above apply,** attach an explanation, as necessary.

ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

/S/ Project Manager 9/1/00
Signature of Preparer and Title Date

cc: Orig (NDA)/PLA/PMA # 21-105
HFD-520 /Div File
(NDA)/PLA Action Package
HFD-006/ SOImstead (plus, for CDER/CBER APs and AEs, copy of action letter and labeling)

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. (revised)

REQUEST FOR TRADEMARK REVIEW

To: Office of Post-Marketing Drug Risk Assessment (OPDRA)
Attention: Jerry Phillips

From: Division of Anti-Infective Drug Products	**HFD-520**
Attention: Beth Duvall-Miller	**Phone:** (301) 827-2125
Date: July 17, 2000 (previously submitted Zotrim UTI Therapy on November 30, 1999 and UroPAK, Phenoxin, and PyriTrim on May 26, 2000)	
Subject: Request for Assessment of a Trademark for a Proposed New Drug Product	
Proposed Trademarks: ZoTRAC (1), BacTRAC (2)	**NDA/ANDA#** 21-105
Established name, including dosage form: Six phenazopyridine HCl (200 mg) tablets and twenty sulfamethoxazole/trimethoprim DS (800 mg/160 mg) tablets in a blister package	
Other trademarks by the same firm for companion products: none	
Indications for Use (may be a summary if proposed statement is lengthy): urinary tract infections	
Initial Comments from the submitter (concerns, observations, etc.): ▸ "Zotrim UTI Therapy" previously rejected (see OPDRA consult # 99-098 reviewed by Lauren Lee, Pharm.D.); ▸ "UroPAK", "Phenoxin", and "PyriTrim" also rejected (see attached email from Sammie Beam dated 6/7/00); ▸ Request **EXPEDITED** review of these names. Extended PDUFA due date is September 7, 2000.	

cc:
Original NDA 21-105
HFD-520/Division file
HFD-520/PM/B. Duvall-Miller
HFD-520/Chem/B.V. Shetty

/S/ 7/17/00

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

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

See OMB Statement on page 2

FOR FDA USE ONLY

APPLICATION NUMBER

RECEIVED FEB 22 1999 FOR DRUG EVALUATION AND RESEARCH

FEB 19 1999

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Able Laboratories, Inc.	2/18/99
TELEPHONE NO. (Include Area Code) (908) 754-2253	**FACSIMILE (FAX) Number (Include Area Code)** (908) 754-2476
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code/Mail Code, and U.S. License number if previously issued) 6 Hollywood Court South Plainfield, NJ 07080 U.S.A.	**AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE** N/A

PRODUCT DESCRIPTION

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

ESTABLISHED NAME (e.g., Proper name, USP/USAN name)	PROPRIETARY NAME (Trade name) IF ANY
Phenazopyridine HCl Tablets and Sulfamethoxazole-Trimethoprim DS Tablets	Zotrim™ UTI Therapy

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any): See Attached

CODE NAME (If any)

DOSAGE FORM	STRENGTHS	ROUTE OF ADMINISTRATION
Tablets	TMP-SMZ: 160 mg-800 mg Phenazopyridine HCl: 200 mg	Oral

(PROPOSED) INDICATION(S) FOR USE: Urinary Tract Infection

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: N/A 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: Original New Drug Application for marketing approval of Zotrim UTI therapy compliance package

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

NUMBER OF VOLUMES SUBMITTED _____ THIS APPLICATION IS ☒ 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.

See Attached

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

See Attached

X	1. Index
X	2. Labeling (check one) ☒ Draft Labeling ☐ Final Printed Labeling
X	3. Summary (21 CFR 314.50 (c))
X	4. Chemistry section
X	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)
X	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
X	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
X	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
X	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
X	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 report forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
X	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
X	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))
X	17. Field copy certification (21 CFR 314.50 (k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
X	19. OTHER (Specify) Copy of Field Copy Certification, Copy of Financial Arrangement Certification

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 agree to 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 review 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
Peter J. Mione	Peter J. Mione VP, Clinical & Regulatory Affairs- DynaGen, Inc.	2/18/99

ADDRESS (Street City, State, and ZIP Code)	Telephone Number
840 Memorial Drive, Cambridge, MA 02139	(617)491-2527;fax(617)354-3902

Public reporting burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0338)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please DO NOT RETURN this form to this address

FORM FDA 356h (7/97)