

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**50-763**

**Correspondence**



DUPLICATE

NEW CORRESP

NC

March 26, 2002

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448



**Sub: NDA 50-763  
MITOExtra™ (Mitomycin for Injection)  
Major Amendment**

**“USER FEE COVER SHEET”**

Dear Dr. Pazdur:

Reference is made to NDA 50-763 for MITOExtra™ (mitomycin for injection) and the “Major Amendment” submitted on March 20, 2002. Reference is also made to the telephone conversation on March 25, 2002 between Dr. Sam Boddapati, SuperGen, Inc., and Ms. Brenda Atkins, Project Manager, Division of Oncology Drug Products, regarding the submission of “User Fee Cover Sheet” to the above-mentioned amendment.

As requested, we are herewith submitting the “User Fee Cover Sheet” to NDA 50-763, “Major Amendment” submitted on March 1, 2002.

Should you require additional information, please contact the undersigned at 925-560-0100.

Sincerely,

**Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs**

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT SuperGen, Inc.	DATE OF SUBMISSION March 26, 2002
TELEPHONE NO. (Include Area Code) 925-560-0100	FACSIMILE (FAX) Number (Include Area Code) 925-551-6472
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 4140 Dublin Blvd., Suite 200 Dublin, CA 94568	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) NDA 50-763		
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) mitomycin for injection	PROPRIETARY NAME (trade name) IF ANY MITOExtra(TM)	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 7-amino-9a-methoxymitosane		CODE NAME (If any)
DOSAGE FORM: vial	STRENGTHS: .5 mg/vial	ROUTE OF ADMINISTRATION: Intravenous

(PROPOSED) INDICATION(S) FOR USE:  
see attachment

APPLICATION INFORMATION

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input checked="" type="checkbox"/> 505 (b)(2)
IF AN ANDA, OR 505 (B)(2), 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) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO A PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION _____
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> PRIOR APPROVAL (PA)
REASON FOR SUBMISSION User fee cover sheet

PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)  
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)

This application contains the following items: (Check all that apply)

<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling (check one) <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d)(1), 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g. 21 CFR 314.50 (e)(2)(i), 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d)(2), 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d)(3), 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g. 21 CFR 314.50 (d)(5), 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g. 21 CFR 314.50 (d)(6), 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g. 21 CFR 314.50 (f)(1), 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g. 21 CFR 314.50 (f)(2), 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input checked="" type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input type="checkbox"/>	20. OTHER (Specify)

**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 Parts 210 and 211, or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 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 Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 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 <i>Sam Boddapati</i> for Sam Boddapati, PhD		TYPED NAME AND TITLE Sam Boddapati, PhD Senior Director, Regulatory Affairs	DATE March 26, 2002
ADDRESS (Street, City, State, and ZIP Code) 4140 Dublin Blvd., Suite 200 Dublin, CA 94568		Telephone Number ( 925 ) 560-0100	
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:			
Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448		Food and Drug Administration CDER, HFD-94 12420 Parklawn Dr., Room 3048 Rockville, MD 20852	
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.			

**INDICATION FOR USE:**

Mitozytrex™ is not recommended as single-agent, primary therapy. It has been shown to be useful in the therapy of disseminated adenocarcinoma of the stomach or pancreas in proven combinations with other approved chemotherapeutic agents and as palliative treatment when other modalities have failed. Mitozytrex is not recommended to replace appropriate surgery and/or radiotherapy.

**DRUG SUBSTANCE:****Manufacturer**

Phone:  
Fax:

— manufacturing and testing information was submitted to the Agency

**Supplier and US Agent**

Contact Name:  
Phone:  
Fax:

**Testing Laboratories for Drug Substance**

testing of Mitomycin is carried out at this testing facility

**DRUG PRODUCT**

**Manufacturer**

/

**Testing Laboratories for Drug Product**

1)

— testing of drug product, including microbiological tests, are carried out at —

2)

/

— testing of HPBCD is carried out at this facility.

4 pages redacted from this section of  
the approval package consisted of draft labeling

**ATTACHMENT 1**

**(PROPOSED) INDICATION(S) FOR USE**

MITOExtra™ is not recommended as single-agent, primary therapy. It has been shown to be useful in the therapy of disseminated adenocarcinoma of the stomach or pancreas in proven combinations with other approved chemotherapeutic agents and as palliative treatment when other modalities have failed. MITOExtra is not recommended to replace appropriate surgery and/or radiotherapy.

**APPEARS THIS WAY  
ON ORIGINAL**



November 12, 2002

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

**Sub: NDA 50-763**  
**Mitozytrex™ (Mitomycin for Injection)**  
**(New proposed name, formerly MitoExtra™)**  
**AMENDMENT**  
**Request for Update on Patent Certification and Debarred**  
**Persons**  
**Certification**

Dear Dr. Pazdur:

Reference is made to NDA 50-763 for **Mitozytrex™** (new proposed trade name, formerly MitoExtra™) submitted December 10, 1997. Reference is also made to the telephone request dated November 11, 2002 by Ms. Brenda Atkins regarding the updated information on Debarred Persons Certification and Patent Certification.

We are providing the requested information on the following pages.

Should you require any additional information, please contact the undersigned at 925-560-0100.

Sincerely,

Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs



October 21, 2002

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

**Sub: NDA 50-763**  
**Mitozytrex™ (Mitomycin for Injection)**  
**(New proposed name, formerly MitoExtra™)**  
**AMENDMENT—Chemistry/Labeling Deficiencies**

Dear Dr. Pazdur:

Reference is made to NDA 50-763 for **Mitozytrex™** (new proposed trade name, formerly MitoExtra™) submitted December 10, 1997 and amendment submitted March 20, 2002. Reference is also made to the fax communication dated August 30, 2002 from Ms. Brenda Atkins requesting additional information on chemistry and labeling deficiencies.

We are providing responses to the deficiencies identified in the fax communication:

- 1) peak eluted at —
- 2) statistical analysis supporting the proposed expiration dating
- 3) stability of HPβCD
- 4) extractables from IV bags
- 5) utility time for admixtures in sodium lactate and
- 6) revised carton, vial, and package insert labeling.

Should you require any additional information, please contact the undersigned at 925-560-0100.

Sincerely,

Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs

**SuperGen<sup>®</sup>, Inc.**  
**NDA: 50-763 Mitozytrex<sup>™</sup> (Mitomycin for Injection)**

**Chemistry Deficiencies**

Item B:

**The following comments pertain to the markup of vial and carton label and package insert provided in the amendment dated 21-May-02:**

**1. Carton and Vial Labeling:**

- a) It is recommended that you revise the expression of established name so that the letters are at least half as large as the letters comprising the proprietary name with a prominence commensurate with which the proprietary name appears. Please refer to 21 CFR 201.10(g)(2) for guidance.

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**Response:**

Our revised labeling pieces have had their font size revised so that the letters of our established name are at least half as large as the letters of our new proposed proprietary name in accordance with 21 CFR 201.10(g)(2).

The following pages contain our revised carton and vial labeling. Please note, our proposed trade name has been changed from MITOExtra to Mitozytrex.

Please note, our storage conditions statement has been revised to reflect the type of language we were asked to adopt in the package insert (see item B: 2. (a)).

**APPEARS THIS WAY  
ON ORIGINAL**

3 pages redacted from this section of  
the approval package consisted of draft labeling



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 50-763

SuperGen, Inc.  
Attention: Sam Boddapati, Ph.D.  
4140 Dublin Boulevard, Suite 200  
Dublin, CA 94568

Dear Dr. Boddapati:

We acknowledge receipt on March 21, 2002 of your March 20, 2002 resubmission to your new drug application (NDA) for MITOExtra (mitomycin) Injection. On May 14, 2002, we received your May 13, 2002 amendment to your NDA for MITOExtra (mitomycin) Injection. This is a major amendment that will extend the review time by 180 days.

We consider these submissions a complete, class 2 response to our December 11, 1998 action letter. Therefore, the user fee goal date is November 14, 2002.

If you have any questions, call Brenda Atkins, Regulatory Project Manager, at (301) 594-5767.

Sincerely,

{See appended *electronic signature page*}

**/s/**  
Dotti Pease  
Chief, Project Management Staff  
Division of Oncology Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

-----  
**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
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/s/

-----  
Brenda Atkins  
5/20/02 09:55:46 AM  
Signing for CPMS, Dotti Pease



DUBLIN BOULEVARD, SUITE 200

May 13, 2002

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

*BFA*  
*AZ*  
*Major amendment changes*  
*UF goal date 6 months*  
*from 5-14-02 to*  
*which is 11-14-02*

**Sub: NDA 50-763**  
**MITOExtra™ (Mitomycin for Injection)**  
**AMENDMENT-Request for Missing Information**

Dear Dr. Pazdur:

Reference is made to the above NDA for **MITOExtra™** (Mitomycin for Injection) submitted on December 10, 1997, amendment submitted on March 20, 2002 and fax communication dated May 7, 2002 requesting additional information.

We are herewith providing responses to items 2 and 3 in the above mentioned fax communication. We are herewith submitting the requested case report forms and electronic copies of the proposed MITOExtra package insert.

Response to item 1 (financial disclosure information) was sent separately on May 10, 2002.

Should you require any additional information, please contact the undersigned at 925-560-0100.

Sincerely,

**Sam Boddapati, Ph.D.**  
**Senior Director, Regulatory Affairs**

**SuperGen, Inc.**  
**NDA 50-763 MITOExtra™ (mitomycin for injection)**

Our preliminary review of your application indicated that the following items were Missing.

- 1) Please submit FDA forms 3454 and 3455 for study ME2 in accordance with 21 CFR 54-FINANCIAL DISCLOSURE BY CLINICAL INVESTIGATORS.

Please respond to the above comment as soon as possible on or before May 17, 2002. Omission of forms 3454 and 3455 is grounds to refuse to file your application (refer to 21 CFR 54.4(c)).

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FDA form 3454 for study ME2 was sent under separate cover May 10, 2002. As no investigators do not have any financial interests with SuperGen, Form 3455 was unnecessary.

APPEARS THIS WAY  
ON ORIGINAL

## **ATTACHMENT 1**

### **(PROPOSED) INDICATION(S) FOR USE**

MITOExtra™ is not recommended as single-agent, primary therapy. It has been shown to be useful in the therapy of disseminated adenocarcinoma of the stomach or pancreas in proven combinations with other approved chemotherapeutic agents and as palliative treatment when other modalities have failed. MITOExtra is not recommended to replace appropriate surgery and/or radiotherapy.

**APPEARS THIS WAY  
ON ORIGINAL**

pperGen, Inc.  
DA 50-763 MITOExtra™ (mitomycin for injection)

In accordance with 21 CFR 314.50, which states that the archival copy of the application is required to contain individual case report forms for each patient who died during a clinical study or who did not complete the study because of an adverse event, whether believed to be drug related or not, including patients receiving reference drugs or placebo, please submit the applicable case report forms (CRFs) from Study ME2.

We are herewith providing copies of individual case report forms for each patient who died during a clinical study or who did not complete the study because of an adverse event, including for those patients receiving reference drugs or placebo.

Patients who died on study:

ME2-04-08-27  
ME2-04-01-02  
ME2-04-04-05  
ME2-04-05-02  
ME2-04-07-00  
ME2-04-08-13  
ME2-04-08-21  
ME2-04-09-06  
ME2-04-09-08

Patients who discontinued treatment  
due to adverse events:

ME2-04-02-01  
ME2-04-04-01  
ME2-04-04-04  
ME2-04-05-04  
ME2-04-05-05  
ME2-04-05-007  
ME2-04-07-002  
ME2-04-07-005  
ME2-04-07-006  
ME2-04-07-007  
ME2-04-08-05  
ME2-04-08-06  
ME2-04-08-14  
ME2-04-08-26  
ME2-04-08-30  
ME2-04-09-01  
ME2-04-09-03  
ME2-04-11-04

LAP  
9/13/02



November 13, 2002

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

**Sub: NDA 50-763  
Mitozytrex™ (Mitomycin for Injection)  
AMENDMENT  
Package Insert**

Dear Dr. Pazdur:

We carefully reviewed the Package Insert for Mitozytrex™ which you forwarded to us by email today. We concur with the text in full.

We await your response tomorrow, November 14<sup>th</sup>.

Sincerely,

Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs

*PI referred to in this  
letter revisited dated  
11-13-02*

13 pages redacted from this section of  
the approval package consisted of draft labeling



4140 Dublin Boulevard, Suite 200, Dublin, CA 94568

# Fax

**To:** Ms. Brenda Atkins **From:** Sam Boddapati

---

**Company:** Project Manager; Div of Oncology **Company:** SuperGen, Inc.

---

**Fax:** 301-594-0498 **Fax:** (925) 551-6472

---

**Phone:** 301-594-5767 **Phone:** (925) 560-0100

---

**Date:** November 14, 2002 **Pages:** 6

---

**Re:** NDA 50-763/Mitozytrex (Mitomycin for Injection)—Package Insert

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**CC:**

---

PLEASE REPLY  URGENT  HARD COPY TO FOLLOW

**Sub: NDA 50-763**  
**Mitozytrex™ (Mitomycin for injection)**  
**Package Insert**

Dear Ms. Atkins:

We carefully reviewed the Package Insert for Mitozytrex™ which you forwarded to us by fax today with minor revisions on pages 3, 4, 6 and 8. We concur with the text in full.

Sincerely,

Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs



November 14, 2002

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

**Sub: NDA 50-763  
Mitozytrex™ (Mitomycin for Injection™  
New proposed name, formerly MitoExtra™)  
AMENDMENT  
Package Insert**

Dear Dr. Pazdur:

We carefully reviewed the Package Insert for Mitozytrex™ which you forwarded to us by fax today with minor revisions on pages 3, 4, 6 and 8. We concur with the text in full.

Sincerely,

A handwritten signature in black ink, appearing to read "S. Boddapati", with a long horizontal flourish extending to the right.

Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338  
Expiration Date: March 31, 2003  
See OMB Statement on page 2.

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT SuperGen, Inc.	DATE OF SUBMISSION November 14, 2002
TELEPHONE NO. (include Area Code) (925) 560-0100	FACSIMILE (FAX) Number (include Area Code) (925) 551-6472
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)  4140 Dublin Blvd., Suite 200 Dublin, CA 94568	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) NDA 50-763	
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) mitomycin for injection	PROPRIETARY NAME (trade name) IF ANY Mitozytrex™ (formerly MitoExtra™)
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any) 7-amino-9a-methoxymitosane	CODE NAME (if any)
DOSEAGE FORM: vial	STRENGTHS: 5mg/vial
ROUTE OF ADMINISTRATION: Intravenous	
(PROPOSED) INDICATION(S) FOR USE:  See attachment	

APPLICATION INFORMATION

APPLICATION TYPE (check one)	<input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50)	<input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
	<input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR part 601)	
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE	<input type="checkbox"/> 505 (bX1)	<input checked="" type="checkbox"/> 505 (bX2)
IF AN ANDA, OR 505 (bX2), 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)	<input type="checkbox"/> ORIGINAL APPLICATION	<input checked="" type="checkbox"/> AMENDMENT TO A PENDING APPLICATION
	<input type="checkbox"/> PRESUBMISSION	<input type="checkbox"/> RESUBMISSION
	<input type="checkbox"/> ANNUAL REPORT	<input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT
	<input type="checkbox"/> LABELING SUPPLEMENT	<input type="checkbox"/> EFFICACY SUPPLEMENT
	<input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT	<input type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION		
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY	<input type="checkbox"/> CBE	<input type="checkbox"/> CBE-30
	<input type="checkbox"/> PRIOR APPROVAL (PA)	

REASON FOR SUBMISSION

Response to information request, message from Agency on 11/13/02

PROPOSED MARKETING STATUS (check one)	<input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx)	<input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
---------------------------------------	---	---

NUMBER OF VOLUMES SUBMITTED 1	THIS APPLICATION IS	<input checked="" type="checkbox"/> PAPER	<input type="checkbox"/> PAPER AND ELECTRONIC	<input type="checkbox"/> ELECTRONIC
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ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)  
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 attachment

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

This application contains the following items: (Check all that apply)

<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling (check one) <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d)(1), 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g. 21 CFR 314.50 (e)(2)(i), 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d)(2), 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d)(3), 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g. 21 CFR 314.50 (d)(5), 21 CFR 601-2)
<input type="checkbox"/>	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g. 21 CFR 314.50 (d)(6), 21 CFR 601-2)
<input type="checkbox"/>	11. Case report tabulations (e.g. 21 CFR 314.50 (f)(1), 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g. 21 CFR 314.50 (f)(2), 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (c)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 308 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (1)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3387)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input checked="" type="checkbox"/>	20. OTHER (Specify) Package Insert

**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 Parts 210 and 211, or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 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 Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 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 <i>S. Boddapati</i>	TYPED NAME AND TITLE Sam Boddapati, PhD, Senior Director, Regulatory Affairs	DATE 11/14/02
ADDRESS (Street, City, State, and ZIP Code) 4140 Dublin Blvd., Suite 200 Dublin, CA 94568		Telephone Number ( 925 ) 560-0100

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:

Food and Drug Administration  
CDER, HFD-99  
1401 Rockville Pike  
Rockville, MD 20852-1448

Food and Drug Administration  
CDER, HFD-94  
12420 Parklawn Dr., Room 3048  
Rockville, MD 20852

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.



DUPLICATE

November 4, 2002

ORIG AMENDMENT

BL

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

RECEIVED

NOV - 5 2002

HFD-150 / CDER

**Sub: NDA 50-763**  
**Mitozytrex™ (Mitomycin for Injection)**  
**(New proposed name, formerly MitoExtra™)**  
**AMENDMENT**  
**Requests for Carton, Vial Labels and Package Insert Revisions**

Dear Dr. Pazdur:

Reference is made to NDA 50-763 for **Mitozytrex™** (new proposed trade name, formerly **MitoExtra™**) submitted December 10, 1997 and amendment submitted October 21, 2002. Reference is also made to the fax communication dated October 28, 2002 from Ms. Brenda Atkins requesting Carton and Vial Labels and Package Insert revisions.

We are providing revised labels as requested in the fax communication:

1. Revised storage statement for Carton and Vial Labels and Package Insert
2. Revised IV fluid stability table in the Package Insert

Should you require any additional information, please contact the undersigned at 925-560-0100.

Sincerely,

Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs

12 pages redacted from this section of  
the approval package consisted of draft labeling

**18** pages redacted from this section of  
the approval package consisted of draft labeling

DUPLICATE



May 21, 2002

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

ORIG AMENDMENT

BL

RECEIVED

MAY 22 2002

HFD-150 / CDER

Sub: NDA 50-763  
MITOExtra™ (Mitomycin for Injection)  
Telephone Amendment

Dear Dr. Pazdur:

Reference is made to the above NDA for MITOExtra™ (Mitomycin for Injection) submitted on December 10, 1997 and amendment dated March 20, 2002. Reference is also made to the May 14, 2002 telephone request from Ms. Brenda Atkins, Project Manager for the submission of the proposed vial and carton labeling in MS Word format on a diskette.

Enclosed, we are providing a copy of our vial and carton labeling in Adobe Acrobat (PDF file) format. Please note that these labels will be sent to the printers in this format, which cannot be converted to MS Word format.

Should you require additional information, please contact the undersigned at 925-560-0100.

Sincerely,

A handwritten signature in black ink, appearing to read "S. Boddapati", with a long horizontal flourish extending to the right.

Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338  
Expiration Date: March 31, 2003  
See OMB Statement on page 2.

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT SuperGen, Inc.	DATE OF SUBMISSION May 21, 2002
TELEPHONE NO. (Include Area Code) 925-560-0100	FACSIMILE (FAX) Number (Include Area Code) 925-551-6472
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 4140 Dublin Blvd., Suite 200 Dublin, CA 94568	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) NDA #50-763		
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) mitomycin for injection	PROPRIETARY NAME (trade name) IF ANY MITOExtra(TM)	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 7-amino-9a-methoxymitosane		CODE NAME (If any)
DOSAGE FORM: vial	STRENGTHS: 5 mg/vial	ROUTE OF ADMINISTRATION: Intravenous

(PROPOSED) INDICATION(S) FOR USE:

See attachment

APPLICATION INFORMATION

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input checked="" type="checkbox"/> 505 (b)(2)
IF AN ANDA, OR 505 (B)(2), 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) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO A PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION _____
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> PRIOR APPROVAL (PA)

REASON FOR SUBMISSION

Response to request for electronic copies of labeling, May 14, 2002

PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input type="checkbox"/> PAPER <input checked="" type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)

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)

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 report 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 314.50 (l)(3))
- 18. User Fee Cover Sheet (Form FDA 3397)
- 19. Financial Information (21 CFR Part 54)
- 20. OTHER (Specify)

**CERTIFICATION**

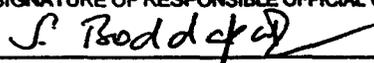
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. 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 Parts 210 and 211, or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 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 Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 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 Sam Boddapati, PhD Senior Director, Regulatory Affairs	DATE May 21, 2002
ADDRESS (Street, City, State, and ZIP Code) 4140 Dublin Blvd., Suite 200 Dublin, CA 94568		Telephone Number ( 925 ) 560-0100

**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:**

Food and Drug Administration  
CDER, HFM-99  
1401 Rockville Pike  
Rockville, MD 20852-1448

Food and Drug Administration  
CDER, HFD-94  
12420 Parklawn Dr., Room 3046  
Rockville, MD 20852

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.

## **ATTACHMENT 1**

### **(PROPOSED) INDICATION(S) FOR USE .**

MITOExtra™ is not recommended as single-agent, primary therapy. It has been shown to be useful in the therapy of disseminated adenocarcinoma of the stomach or pancreas in proven combinations with other approved chemotherapeutic agents and as palliative treatment when other modalities have failed. MITOExtra is not recommended to replace appropriate surgery and/or radiotherapy.

**APPEARS THIS WAY  
ON ORIGINAL**

1 pages redacted from this section of  
the approval package consisted of draft labeling



September 20, 2002

Richard Pazdur, M.D.  
 Director  
 Division of Oncology Drug Products (HFD 150)  
 Document Control Room 2061  
 Center for Drug Evaluation and Research  
 Food and Drug Administration  
 1451 Rockville Pike  
 Rockville, Maryland 20852-1448

**Sub: NDA 50-763  
 MITOExtra™ (Mitomycin for Injection)  
 AMENDMENT—Alternative Trade Name(s)**

Dear Dr. Pazdur:

Reference is made to the above NDA for MITOExtra™ (Mitomycin for Injection) submitted on December 10, 1997 and the amendment submitted on September 12, 2002 for alternate proposed trade names: \_\_\_\_\_ and \_\_\_\_\_ Reference is also made to the telephone request dated September 18, 2002 by Ms. Brenda Atkins, Project Manager, Division of Oncology Drug Products to Dr. Sam Boddapati, SuperGen, Inc to submit additional trade names without the \_\_\_\_\_ suffix.

We are herewith submitting alternate trade names in the order of preference as described below:

**First Choice:** Mitozytrex

**Second Choice:** \_\_\_\_\_

**Third Choice:** \_\_\_\_\_

We hope that one of these names will be acceptable to FDA's Labeling and Nomenclature committee.

Should you require any additional information, please contact the undersigned at 925-560-0100.

Sincerely,

for  
 Sam Boddapati, Ph.D.  
 Senior Director, Regulatory Affairs

**ATTACHMENT 1**

**(PROPOSED) INDICATION(S) FOR USE**

MITOExtra™ is not recommended as single-agent, primary therapy. It has been shown to be useful in the therapy of disseminated adenocarcinoma of the stomach or pancreas in proven combinations with other approved chemotherapeutic agents and as palliative treatment when other modalities have failed. MITOExtra is not recommended to replace appropriate surgery and/or radiotherapy.

APPEARS THIS WAY  
ON ORIGINAL



DUPLICATE

November 4, 2002

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

ORIG AMENDMENT

BL

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NOV - 5 2002

HFD-150 / CDER

**Sub: NDA 50-763**  
**Mitozytrex™ (Mitomycin for Injection)**  
**(New proposed name, formerly MitoExtra™)**  
**AMENDMENT**  
**Requests for Carton, Vial Labels and Package Insert Revisions**

Dear Dr. Pazdur:

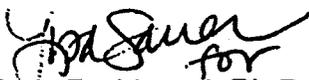
Reference is made to NDA 50-763 for **Mitozytrex™** (new proposed trade name, formerly MitoExtra™) submitted December 10, 1997 and amendment submitted October 21, 2002. Reference is also made to the fax communication dated October 28, 2002 from Ms. Brenda Atkins requesting Carton and Vial Labels and Package Insert revisions.

We are providing revised labels as requested in the fax communication:

1. Revised storage statement for Carton and Vial Labels and Package Insert
2. Revised IV fluid stability table in the Package Insert

Should you require any additional information, please contact the undersigned at 925-560-0100.

Sincerely,

  
for  
Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs

4

           pages redacted from this section of  
the approval package consisted of draft labeling

DUPLICATE



November 6, 2002

SUPPL NEW CORRESP

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

SNC

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NOV - 7 2002  
HFD-150 / CDER

Sub: NDA 50-763  
Mitozytrex™ (Mitomycin for Injection)  
(New proposed name, formerly MitoExtra™)  
AMENDMENT  
Requests for information

Dear Dr. Pazdur:

Reference is made to NDA 50-763 for Mitozytrex™ (new proposed trade name, formerly MitoExtra™) submitted December 10, 1997 and amendment submitted May 13, 2002. Reference is also made to the fax communication dated October 30, 2002 from Ms. Brenda Atkins requesting information regarding a pediatric development plan and a "120-day Safety Update."

SuperGen does not have a plan for the pediatric development of this drug at this time.

The final clinical study report for protocol ME2 was submitted in our March 20, 2002 Amendment. There is no additional safety information.

Should you require any additional information, please contact the undersigned at 925-560-0100.

Sincerely,

Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338  
Expiration Date: March 31, 2003  
See OMB Statement on page 2.

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT SuperGen, Inc.	DATE OF SUBMISSION November 6, 2002
TELEPHONE NO. (Include Area Code) 925-560-0100	FACSIMILE (FAX) Number (Include Area Code) 925-551-6472
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 4140 Dublin Blvd., Suite 200 Dublin, CA 94568	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)  
NDA 50-763

ESTABLISHED NAME (e.g., Proper name, USP/USAN name) mitomycin for injection	PROPRIETARY NAME (trade name) IF ANY Mitozytrex(TM)	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 7-amino-9a-methoxymitosane	CODE NAME (If any)	
DOSAGE FORM: vial	STRENGTHS: 5 mg/vial	ROUTE OF ADMINISTRATION: Intravenous

(PROPOSED) INDICATION(S) FOR USE:  
see attachment

APPLICATION INFORMATION

APPLICATION TYPE (check one)  
 NEW DRUG APPLICATION (21 CFR 314.50)     ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)  
 BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

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

IF AN ANDA, OR 505 (b)(2), 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     EFFICACY SUPPLEMENT  
 LABELING SUPPLEMENT     CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT     OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION \_\_\_\_\_

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY     CBE     CBE-30     PRIOR APPROVAL (PA)

REASON FOR SUBMISSION  
response to fax from Agency, dated October 30, 2002

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

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

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)  
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 attachment

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

This application contains the following items: (Check all that apply)

- 1. Index
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- 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 report 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 314.50 (l)(3))
- 18. User Fee Cover Sheet (Form FDA 3397)
- 19. Financial Information (21 CFR Part 54)
- 20. OTHER (Specify) *pediatric and safety update information*

**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 Parts 210 and 211, or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 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 Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 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 <i>Sam Boddapati</i>	TYPED NAME AND TITLE Sam Boddapati, PhD Senior Director, Regulatory Affairs	DATE 11/6/2002
ADDRESS (Street, City, State, and ZIP Code) 4140 Dublin Blvd., Suite 200 Dublin, CA 94568		Telephone Number ( 925 ) 560-0100

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:

Food and Drug Administration  
CSER, HFM-99  
1401 Rockville Pike  
Rockville, MD 20852-1448

Food and Drug Administration  
CDER, HFD-94  
12420 Parklawn Dr., Room 3046  
Rockville, MD 20852

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.



DUBUINICATE

September 27, 2002

ORIG AMENDMENT

BM

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

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SEP 30 2002

HFD-150 / CDER

**Sub: NDA 50-763  
MITOExtra™ (Mitomycin for Injection)  
AMENDMENT-- Requests for Information**

Dear Dr. Pazdur:

Reference is made to the above NDA for MITOExtra™ (Mitomycin for Injection) submitted on December 10, 1997, amendment submitted on March 20, 2002 and fax communication dated September 15, 2002 requesting 1) case report forms for patients #25 and 26; and 2) clarification on hormone-refractory cancer in 3 patients.

Please see the following for our responses to the requested clarification on the 2 items in the fax dated September 15, 2002.

- 1): *No case report forms were provided for patients #25 and 26 at Site 11 who has SAE's. Please provide these and indicate whether the SAEs were included in the summary tables.*

**Response:**

Copies of case report forms for patients 4-11-25 ( — ) and 4-11-26 are provided in Attachment 1.

Patient 4-11-25 ( — ) had a SAE form dated 7/11/00 but these was no SAE reported for this patient on the form or in the database. Therefore there was no reason to list this patient in the SAE summary table. Patient 4-11-26 ( — ) has a SAE report completed retrospectively on 7/21/00 for the unrelated death due to disease progression which occurred on 3/20/00. This event was in the database and is listed in the summary table.

2): *Please provide evidence that the 3 patients with prostate cancer who received MitoExtra as initial chemotherapy had hormone-refractory cancer.*

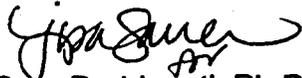
**Response:**

The documentation for patients with LHRH agonist hormone refractory prostate cancer is provided in Attachment 2. There were three patients (4-08-15; WAX-004; 4-11-07) with date of progressive disease specified on the Prior Therapy case report form, and these were included as hormone refractory in the database.

Two other patients were clearly reported as LHRH agonist hormone refractory (4-08-25; 4-08-27). However, progression date was specified in other parts of the CRFs and therefore these patients were not specified as hormone refractory in the database. Three additional patients (4-08-05; 4-11-10; 4-08-08) were refractory to antiandrogens or unknown hormones and they were not defined as classically hormone refractory.

Should you require any additional information, please contact the undersigned at 925-560-0100.

Sincerely,



Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs





DUPLICATE

ORIG AMENDMENT

BC

June 13, 2002

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products (HFD 150)  
Document Control Room 2061  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852-1448

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JUN 17 2002

HFD-150 / CDER

**Sub: NDA 50-763  
MITOExtra™ (Mitomycin for Injection)  
AMENDMENT**

Dear Dr. Pazdur:

Reference is made to the above NDA for **MITOExtra™** (mitomycin for injection) submitted on December 10, 1997, amendment submitted on March 20, 2002 and fax communication dated June 10, 2002 regarding the 'Environmental Impact Analysis' for MITOExtra.

We are herewith enclosing categorical exclusion claim for environmental impact analysis, since our NDA will not increase the use of the active moiety.

Should you require any additional information, please contact the undersigned at 925-560-0100.

Sincerely,

for  
Sam Boddapati, Ph.D.  
Senior Director, Regulatory Affairs

*6-20-02  
Send to mail to DOR  
notifying that if we do  
will be the reviewer  
for the amendment*

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT SuperGen, Inc.	DATE OF SUBMISSION June 13, 2002
TELEPHONE NO. (Include Area Code) 925-560-0100	FACSIMILE (FAX) Number (Include Area Code) 925-551-6472
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 4140 Dublin Blvd., Suite 200 Dublin, CA 94568	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)  
NDA 50-763

ESTABLISHED NAME (e.g., Proper name, USP/USAN name) mitomycin for injection, USP	PROPRIETARY NAME (trade name) IF ANY MITOExtra(TM)	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any) 7-amino-9a-methoxymitosane	CODE NAME (if any)	
DOSAGE FORM: vial	STRENGTHS: 5 mg/vial	ROUTE OF ADMINISTRATION: Intravenous

(PROPOSED) INDICATION(S) FOR USE:

see attachment

APPLICATION INFORMATION

APPLICATION TYPE (check one)  NEW DRUG APPLICATION (21 CFR 314.50)  ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)  BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

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

IF AN ANDA, OR 505 (b)(2), 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  EFFICACY SUPPLEMENT  LABELING SUPPLEMENT  CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT  OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION \_\_\_\_\_

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY  CBE  CBE-30  PRIOR APPROVAL (PA)

REASON FOR SUBMISSION

Response to information request, Agency fax dated June 10, 2002

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

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

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)  
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 attachment

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

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 report 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 314.50 (l)(3))
- 18. User Fee Cover Sheet (Form FDA 3397)
- 19. Financial Information (21 CFR Part 54)
- 20. OTHER (Specify) Environmental Assessment Exclusion Claim

**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 Parts 210 and 211, or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 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 Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 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 <i>Jasa Sauer</i> for Sam Boddapati, PhD	TYPED NAME AND TITLE Sam Boddapati, PhD Senior Director, Regulatory Affairs	DATE June 13, 2002
ADDRESS (Street, City, State, and ZIP Code) 4140 Dublin Blvd., Suite 200 Dublin, CA 94568		Telephone Number ( 925 ) 560-0100

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:

Food and Drug Administration  
CBER, HFM-99  
1401 Rockville Pike  
Rockville, MD 20852-1448

Food and Drug Administration  
CDER, HFD-94  
12420 Parklawn Dr., Room 3046  
Rockville, MD 20852

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.

**ATTACHMENT 1**

**(PROPOSED) INDICATION(S) FOR USE**

MITOExtra™ is not recommended as single-agent, primary therapy. It has been shown to be useful in the therapy of disseminated adenocarcinoma of the stomach or pancreas in proven combinations with other approved chemotherapeutic agents and as palliative treatment when other modalities have failed. MITOExtra is not recommended to replace appropriate surgery and/or radiotherapy.

**APPEARS THIS WAY  
ON ORIGINAL**

**ENVIRONMENTAL IMPACT ANALYSIS**

**CATEGORICAL EXCLUSION CLAIM**

We are requesting a categorical exclusion from an environment impact analysis for the drug product MITOExtra (mitomycin for injection). Since our NDA will not increase the use of the active moiety, this action qualifies for a categorical exclusion from the requirement to prepare an environmental assessment according to 21 CFR § 25.31 (a).

To the best of our knowledge, no extraordinary circumstances exist that would warrant the preparation of an environmental assessment.

**APPEARS THIS WAY  
ON ORIGINAL**