FAX

FOOD AND DRUG ADMINISTRATION
DIVISION OF ONCOLOGY DRUG PRODUCTS
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

To: Sam Boddapati	**From:** Brenda Athey
Fax: 925-551-6472	**Fax:**
Phone: 925-560-0100	**Phone:** (301) 594-5767
Pages, including cover sheet: 13	**Date:** November 14, 2002
Re: PI for Mitoxytrex	

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination or other action based on the content of the communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

COMMENTS:

Additional revisions are included in this fax compared to the fax received on 11-13-02.

Please concur with these changes and submit in writing.

Thanks

/S/

MESSAGE CONFIRMATION

11/14/02 15:45

DATE	S.R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
11/14	05'26"	9259041921	CALLING	13	OK	0000

11/14/02 15:38 NO.003 001

FAX

FOOD AND DRUG ADMINISTRATION
DIVISION OF ONCOLOGY DRUG PRODUCTS
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

To: Sam Boddapati **From:** Brenda Athe

Fax: 925-551-6472 **Fax:**

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

Pages, including cover sheet: 13 **Date:** November 14, 2002

Re: PI for Mitoxantrone

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination or other action based on the content of the communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

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

FAX

FOOD AND DRUG ADMINISTRATION
DIVISION OF ONCOLOGY DRUG PRODUCTS
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

To: Sam Boddapati	**From:** Brenda Atkins
Fax: (925) 551-6472	**Fax:** (301) 594-0498
Phone: (925) 560-0100	**Phone:** (301) 594-5767
Pages, including cover sheet: 16 pages	**Date:** November 8, 2002
Re: Labeling Revisions	

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination or other action based on the content of the communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

COMMENTS:

Dear Sam:

Please see the attached labeling as submitted via e-mail on today at 6:08 PM (EST). Please note that the last page of this fax are the revised vial and Carton labels

Thanks

/S/

MESSAGE CONFIRMATION

11/08/02 18:46

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
11/03	05'55"	9259041921	CALLING	16	OK	0000

11/08/02 18:38 NO.009 D01

FAX

FOOD AND DRUG ADMINISTRATION
DIVISION OF ONCOLOGY DRUG PRODUCTS
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

To: SAM BODDAPATI **From:** BRENDA ATKINS

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

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

Pages, including cover sheet: 16 pages **Date:** NOVEMBER 8, 2002

Re: LABELING REVISIONS

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination or other action based on the content of the communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 20 May 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MITOExtra™ (mitomycin for injection)

SUBJECT: **Copy of Regulatory Letter**

Please refer to your resubmission of NDA 50-763 dated March 20, 2002, received March 21, 2002 and to your May 13, 2002 amendment, received May 14, 2002.

A copy of the May 20, 2002 FDA regulatory letter regarding your submissions is attached. A paper copy is forthcoming via U.S. Postal Service.

Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

filed in DFS 5-20-02

Attachment – 2 pages

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

MESSAGE CONFIRMATION

05/20/02 14:53

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
05/20	00'51"	9259041921	CALLING	03	OK	0000

05/20/02 14:51 NO.098 D01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 20 May 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MITOExtra™ (mitomycin for injection)

SUBJECT: Copy of Regulatory Letter

Please refer to your resubmission of NDA 50-763 dated March 20, 2002, received March 21, 2002 and to your May 13, 2002 amendment, received May 14, 2002.

A copy of the May 20, 2002 FDA regulatory letter regarding your submissions is attached. A paper copy is forthcoming via U.S. Postal Service.

#3

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 30 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Request for safety and effectiveness data**

Please refer to your submissions dated March 20, and May 13, 2002. Please respond to the following requests for information **as soon as possible**.

In a final rule effective August 10, 1998, FDA amended 21 CFR 314.50(d)(5)(v) and 314.50.50(d)(5)(vi)(a) to require sponsors to present safety and effectiveness data "by gender, age, and racial subgroups" in an NDA. Please see our previous requests for this analysis on October 17 and October 28, 2002. This is required to facilitate completion of the NDA review.

Please telephone me if you will be unable to provide this by fax and officially to the NDA **by close of business on November 1, 2002.**

/S/
Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

Faxed in DFS 10-30-02

Response received 11-6-02

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

MESSAGE CONFIRMATION

10/30/02 18:13

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
10/30	00'31"	9259041921	CALLING	01	OK	0000

10/30/02 18:12 NO.067 P01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 30 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Request for safety and effectiveness data**

Please refer to your submissions dated March 20, and May 13, 2002. Please respond to the following requests for information **as soon as possible.**

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 30 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Requests for information re. PK**

Please refer to your submissions dated March 20, and May 13, 2002. Please respond to the following requests for information **as soon as possible.**

Please provide the site locations of the patients who had PK data submitted to study ME2. We also need the number of patients per each site who had PK and patient initials and patient identifier number for any patients who had PK if they were from site 8.

Please submit your response by facsimile and officially to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

Filed in DFS
10-30-02
response rec'd 11-6-02

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

MESSAGE CONFIRMATION

10/30/02 17:49

DATE	S.R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
10/30	00'29"	9259041921	CALLING	01	OK	0000

10/30/02 17:48 NO.066 D01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 30 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Requests for information re. PK**

Please refer to your submissions dated March 20, and May 13, 2002. Please respond to the following requests for information **as soon as possible.**

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 30 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Requests for information**

Please refer to your submissions dated March 20, and May 13, 2002. Please respond to the following requests for information **as soon as possible**.

- Please state if you **do** or **do not have** a plan for pediatric development for this drug.
- For study ME2 we do not have your "120-day Safety Update" analysis. In your discussion of safety, you do not specify the date of data cut-off or how mature was the follow-up. Please clarify and provide additional data as necessary. Please respond **as soon as possible.**

Please submit your response by facsimile and officially to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/
Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

Filed in DFS
10-30-02
Response received 11-6-02

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MESSAGE CONFIRMATION

10/30/02 09:36

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
10/32	00'31"	9259041921	CALLING	01	OK	0000

10/30/02 09:35 NO.061 D01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 30 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Requests for information**

Please refer to your submissions dated March 20, and May 13, 2002. Please respond to the following requests for information **as soon as possible.**

- Please state if you do or do not have

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 28 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoZytrex™ (Mitomycin for Injection)

SUBJECT: **Requests for Carton, Vial Labels and Package Insert Revisions**

Please refer to your submissions dated March 20, May 13, and October 4, 2002. Please respond to the following requests **as soon as possible.**

1. **Uniform Storage Statement for Carton and Vial Labels and Package Insert:**
   For a drug product which is demonstrated to be stable at 25°C/60% RH or 30°C/60% RH and intended to be stored at Controlled Room Temperature, the recommended labeling statement is :

2. **Package Insert**
   The IV fluid stability table under statement 3 (under Stability in the DOSAGE AND ADMINISTRATION section):

filed in DFS
10-28-02
response recd 11-4-02

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The table should be revised to read:

IV Fluid	Stability
5% Dextrose Injection	no more than 4 hours
0.9% Sodium Chloride Injection	no more than 48 hours
Sodium Lactate Injection	no more than 24 hours

Please submit your response by facsimile and officially to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

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MESSAGE CONFIRMATION

10/28/02 16:55

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
10/28	00'46"	9259041921	CALLING	02	OK	0000

10/28/02 16:54 NO.046 P01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 28 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoZytrex™ (Mitomycin for Injection)

SUBJECT: **Requests for Carton, Vial Labels and Package Insert Revisions**

Please refer to your submissions dated March 20, May 13, and October 4, 2002. Please respond to the following requests **as soon as possible.**

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 28 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Request for Analyses of Efficacy and Safety information**

Please refer to your submissions dated March 20, May 13, 2002 and October 24, 2002. Please respond to the following request for information **as soon as possible.**

Your submission of October 24, 2002 provided the demographic data on race of the study participants. Have you provided an "Applicant's Efficacy and Safety Analyses of Effects of Gender, Age, Race, or Ethnicity"? We cannot locate this information in your NDA resubmission. Please direct us as to where it can be located; or if you have not submitted this information, then you should submit **as soon as possible.**

Please submit your response by facsimile and officially to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

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

/s/
Brenda Atkins
10/28/02 11:56:18 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 17 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Missing demographic information**

Please refer to your submissions dated March 20 and May 13, 2002. Please respond to the following request for information **as soon as possible**.

As you know, we are required to evaluate an "Applicant's Efficacy and Safety Analyses of Effects of Gender, Age, Race, or Ethnicity." The demographic data that you have provided does not appear to make reference to race. Is that information available? We are unable to locate any reference(s) to race in the clinical parts of this NDA.

Please submit your response by facsimile and officially to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

Filed in DFS

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MESSAGE CONFIRMATION

10/17/02 10:56

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
10/17	00'30"	9259041921	CALLING	01	OK	0000

10/17/02 10:55 NO.003 P01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 17 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Missing demographic information**

Please refer to your submissions dated March 20 and May 13, 2002. Please respond to the following request for information **as soon as possible.**

Atkins, Brenda J

From: Scher, Nancy
Sent: Wednesday, October 16, 2002 6:21 PM
To: Atkins, Brenda J
Cc: Scher, Nancy; Griebel, Donna J
Subject: NDA MitoExtra

Brenda,

I cannot find any reference to race in the clinical parts of this NDA.

Please send a fax Thursday advising them that we are required to evaluate an "Applicant's Efficacy and Safety Analyses of Effects of Gender, Age, Race, or Ethnicity." The demographic data they have provided does not appear to make reference to race. Is that information available?

Thanks.

Nancy S. Scher, MD, FACP
Division of Oncology Drug Products
HFD-150
1451 Rockville Pike
Rockville, MD 20852

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 01 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Chemistry requests for information**

Please refer to your submissions dated March 20 and May 13, 2002. Please respond to the following requests for information **as soon as possible.**

The role of 2-hydroxypropyl β-cyclodextrin, whether strictly an excipient or a pharmacologically active complexing agent (functional excipient) remains unclear. The data provided in Research Report No. 3 (prepared by J. Blanchard, Ph.D., University of Arizona, Tables 2 through 5) indicates that as the concentration of mitomycin C and 2-hydroxypropyl β-cyclodextrin decrease, the complex dissociates (in both Sterile Water for Injection solution and in normal saline solution). We question whether there is minimal complexing between mitomycin C and 2-hydroxypropyl β-cyclodextrin in diluted infusion solutions (40 µg/mL). If this is the case, please explain the function of 2-hydroxypropyl β-cyclodextrin in the drug formulation. Please explain the advantage of this formulation versus the available formulation(s).

Please submit your responses officially to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

Filed in DFS

responded 10-4-02

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Redacted 1

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secret and/or

confidential

commercial

information

MESSAGE CONFIRMATION

10/01/02 10:36

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
10/01	00'33"	9259041921	CALLING	01	OK	0000

10/01/02 10:34 NO.002 D01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 01 October 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Chemistry requests for information**

Please refer to your submissions dated March 20 and May 13, 2002. Please respond to the following requests for information **as soon as possible.**

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 27 September 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Request for information**

Please refer to your submission dated March 20, received March 21, 2002. Please submit via facsimile a copy of the reference (previously appended to the NDA) by Blanchard, et al (of the University of Arizona) at your earliest convenience.

Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/
Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

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filed in DFS
9-27-02

MESSAGE CONFIRMATION

09/27/02 12:18

DATE	S.R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
09/27	00'28"	9259041921	CALLING	01	OK	0000

09/27/02 12:17 NO.118 D01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 27 September 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Request for information**

Please refer to your submission dated March 20, received March 21, 2002. Please submit via facsimile a copy of the reference (previously appended to the NDA) by Blanchard, et al (of the University of Arizona) at your earliest convenience.

Atkins, Brenda J

From: Hsieh, Yung Ao
Sent: Friday, September 27, 2002 9:26 AM
To: Atkins, Brenda J
Subject: Re: NDA 50-763 Resubmission

Brenda,

Could you request the applicant to fax us a copy of the reference (previously appended to the NDA) by Blanchard, et al (of the University of Arizona) at his earliest convenience ? Thanks.

Y. A. Hsieh

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 15 September 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Requests for information**

Please refer to your submission dated March 20, received March 21, 2002. Please respond to the following requests for information.

1. No case report forms were provided for patients #25 and 26 at Site11 who had SAE's. Please provide these and indicate whether the SAEs were included in the summary tables.

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

Please submit your responses officially to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

filed in DFS
9-15-02

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MESSAGE CONFIRMATION

09/15/02 12:21

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
09/15	00'30"	9259041921	CALLING	01	OK	0000

09/15/02 12:20 NO.056 P01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 15 September 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Requests for information**

Please refer to your submission dated March 20, received March 21, 2002. Please respond to the following requests for information.

1. No case report forms were provided for patients #25 and 26 [illegible]

Atkins, Brenda J

From: Scher, Nancy
Sent: Friday, September 13, 2002 6:45 PM
To: Atkins, Brenda J
Cc: Griebel, Donna J; Scher, Nancy
Subject: NDA 50-763, MitoExtra

Brenda,

Please send a fax to the company requesting information about the following:

1. No case resport forms were provided for patients #25 and 26 at Site11 who had SAE's. Please provide these and indicate whether the SAEs were included in the summary tables.

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

Thank you.

Nancy S. Scher, MD, FACP
Division of Oncology Drug Products
HFD-150
1451 Rockville Pike
Rockville, MD 20852

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 06 September 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Numerical Inconsistencies in the ME2 Study Report**

Please refer to your submission dated March 20, received March 21, 2002. Please respond to the following requests for clarification.

We note inconsistencies in the patient distribution data for the number of courses completed as cited in the Study Report on pages 0098, 0099, and 0110.

Also, there are inconsistencies in the calculations for per cent of patients who had disease progression or stable disease, as reported on pages 0066 and 0156. On page 0104 there is a discrepancy between the narrative (44% progression/49% response or stable) and the table on the same page (49% progression/(1+10+34) 45% response or stable).

Please provide us with corrections and submit your responses officially to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

rec'd 9-15-02

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

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MESSAGE CONFIRMATION

09/06/02 09:12

DATE	S.R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
09/06	00'32"	9259041921	CALLING	01	OK	0000

09/06/02 09:11 NO.029 001

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 06 September 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Numerical Inconsistencies in the ME2 Study Report**

Please refer to your submission dated March 20, received March 21, 2002. Please respond to the following requests for clarification.

Atkins, Brenda J

From: Scher, Nancy
Sent: Thursday, September 05, 2002 7:54 PM
To: Atkins, Brenda J
Cc: Rothmann, Mark D; Scher, Nancy; Griebel, Donna J
Subject: NDA50763

Brenda,

Mark and I have discussed several numerical inconsistencies in the Study Report. Would you please fax SuperGen my comments?

"We note inconsistancies in the patient distribution data for the number of courses completed, as cited in the Study Report on pages #0098, 0099, and 0110.

Also, there are inconsistancies in the calculations for per cent of patients who had disease progression or stable disease, as reported on pages 0066 and page 0156. On page 0104 there is a discrepancy between the narrative (44% progression/49% response or stable) and the table on the same page (49% progression/(1+10+34) 45% response or stable).

Please provide us with corrections."

Thanks, Brenda.

Nancy S. Scher, MD, FACP
Division of Oncology Drug Products
HFD-150
1451 Rockville Pike
Rockville, MD 20852

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 22 July 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Investigators and Sites**

Please refer to your submission dated March 20, received March 21, 2002. Page 0070, xi of your submission, containing a final report of a trial entitled "Clinical Protocol No. ME2, Protocol for a Study of the Tolerance and Efficacy of MitoExtra™ in Patients with Solid Tumors who Have Failed Previous Therapy", stated that there were a total of 13 investigators that participated in the multicenter trial. The list of investigators is located on pages 0071, xii and 0072, xiii.

Please provide clarification on the following:

1. We note that there are 12 investigators and site number 10 is missing. Please clarify this discrepancy.
2. Site number 5 listed two locations, i.e. Shreveport, Louisiana and Park Ridge, Illinois. Is this correct?
3. What were the exact number of sites and investigators?

Please submit your response to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

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MESSAGE CONFIRMATION

07/22/02 07:57
ID=FDA-DODP

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
07/22	00'32"	9259041921	CALLING	01	OK	0000

07/22/02 07:56 FDA-DODP → 919255516472 NO.007 D01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 22 July 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Investigators and Sites**

Please refer to your submission dated March 20, received March 21, 2002. Page 0070, xi of your submission, containing a final report of a trial entitled "Clinical Protocol No. ME2, Protocol for a Study of the Tolerance and Efficacy of MitoExtra™ in Patients with Solid Tumors who Have Failed

N5076

LIST OF PARTICIPATING INVESTIGATORS

(All have filed financial disclosure forms)

Site No.	Investigator (No. of Patients Treated)
1	***Luis Meza, M.D.*** (5 patients) Southwest Oncology Research 155 hospital Drive, Ste.101 Lafayette, LA 70503 (318) 234-4535
2	***Hal Gerstein, M.D.*** (3 patients) Medical Oncology and Hematology 170 Great Neck Road Ste.100 Great Neck, NY 11022 (516) 773-3708
3	***Clarence B. Vaughn, M.D.*** (6 patients) Southfield Oncology Institute 21751 West Eleven Mile Road Southfield, MI 48076 (248) 356-2828
4	***Arnold Wax, M.D.*** (6 patients) 3920 South Eastern Ave., Ste 200 Las Vegas, NV 89119 (702) 369-4604
5	***John B. Craig, M.D.*** (8 patients) Schumpert Cancer Treatment Center One St. Mary Place Shreveport LA 71101 (318) 681-4139 Lutheran General Cancer Center 1700 Luther Lane Park Ridge Park Ridge ,IL 60068-1174 (847) 723-2620
6	***Gary Cota MD*** (1 patient enrolled) LA Hematology/Oncology Group 1245 Wilshire #303 Los Angeles, CA 90017 (213) 977-1214

LIST OF PARTICIPATING INVESTIGATORS

Site No.	Investigator (No. of Patients Treated)
7	***Francisco Gonzales, M.D.*** (8 patients) USC School of Medicine Center for Cancer Treatment and Research Palmetto Richland Memorial Hospital Seven Medical Park, Suite 202 Columbia, SC 29203 (803) 434-3673
8	
9	***John J. Petrus, M.D.*** (9 patients) The Cancer Center 224 West Exchange Street Ste. 150 Akron, OH 44302 (330) 384-6431
11	***Kai-Yiu Yeung, M.D.*** (28 patients)* Oncology-Hematology Associates 8926 Woodyard Road, Suite 201 Clinton, MD 20735 (301) 868-7911
12	***Jerome Rubin, M.D.*** (2 patients) 700 Cass Street, Suite 122 Monterey, CA 93940 (831) 375-4777

LIST OF PARTICIPATING INVESTIGATORS

Site No.	Investigator (No. of Patients Treated)
13	***John MacDonald, M.D.*** (9 patients)* Saint Vincent's Hospital 153 West 11th Street New York, NY 10011 (212) 604-2219
14	***Grant Swanson, M.D.*** (1 patient) Monterey Bay Oncology 261 El Dorado #202 Monterey, CA 93940-2911 (831) 375-4105

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 30 August 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Chemistry Deficiencies - Please address as soon as possible**

Please refer to your submission dated March 20, received March 21, 2002. And to your amendment dated May 21, 2002. We have the following comments and requests. Your timely responses are appreciated so that we can continue our review of this application.

A. The following comments pertain to your responses provided in the amendment dated 20-March-02:

1. **Item 23 (page 2240)**: Results of the determination whether the peak eluted with an ——— should be submitted for review as soon as possible.

2. **Item 28 (page 2273)**: The proposed expiration dating is usually based on the full term data of 3 batches of drug products. Additionally, the statistical analysis based solely on potency is not adequate to support the proposed shelf life. A statistical analysis to show that the levels of impurities will remain within the proposed limits for 24 months should be submitted.

File in DFS

Aperson acknowledged receipt of fax 8-30-02 response recd 10-21

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3. **Item 28 (page 2270)**: The response is not acceptable. We wish to remind you that Janssen's data demonstrated that no degradation of HPβCD takes place when tested by itself or formulated with itraconazole under the testing conditions described in Janssen's NDA. SuperGen has theorized that mitomycin molecule is bound to the external surface of HPβCD. Data of reconstituted MITOExtra stored at — and at — (pages 2275 through 2279) indicated that the mitomycin is stable for 3 months under refrigerated condition and for 1 week under room temperature storage. However, to support the safety of MITOExtra, data to demonstrate the stability of HPβCD in the drug product formulation and reconstituted infusion solutions should be submitted for review.

4. **Item 30 (page 2280)**: The data should be submitted for review as soon as possible. Stability Study of MITOExtra for injection, 5 mg per vial, Lot No. 973669 reconstituted with Water for Injection and Diluted with 5% Dextrose Injection, USP, dated 3-Nov-99 (— , indicated that the study protocol — — Study Protocol MME-4/26/99-02 also includes the testing of extractables and stated that the results will be reported separately (page 2284).

5. **Item 32 (page 2286)**: The response is not acceptable. The — study (dated 3-Nov-01) indicated that . Experimental data only support the use of a 24-h utility time.

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 20 1. I 0(g)(2) for guidance.
   b) Replace the "CAUTION: Federal law prohibits dispensing without prescription." Statement with "Rx Only".

2. **Package Insert:**
   Under **Stability** in the **DOSAGE AND ADMINISTRATION** section:
   a) The first statement:

   revised to read:

b) The IV fluid stability table under statement 3:

should be revised to read:

IV Fluid	Stability
5% Dextrose Injection	Approximately 4 hours
0.9% Sodium Chloride Injection	Approximately 48 hours
Sodium Lactate Injection	Approximately 24 hours

Please submit your response to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

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MESSAGE CONFIRMATION

08/30/02 09:30

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
08/30	01'13"	9259041921	CALLING	03	OK	0000

08/30/02 09:25 NO.012 D01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 30 August 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Chemistry Deficiencies - Please address as soon as possible**

Please refer to your submission dated March 20, received March 21, 2002. And to your amendment dated May 21, 2002. We have the following comments and requests. Your timely responses are appreciated so that we can continue our review of this application.

DATE: May 1, 2002 **MEETING:** 45-Day Filing
TIME: 2:00 PM **NDA#:** 50-763 Resubmission in response to 12-11-98 NA letter
ROOM: CR B **DRUG:** MITOExtra™ (Mitomycin for Injection

Chem/Ther Type: 3 S New Dosage form or formulation, including a new strength, where the drug has already been approved or marketed in the U.S. by the same or another manufacturer. The indication may be the same as that of the already marketed drug product or may be new. A drug with changes in its inactive ingredients such that clinical studies (as opposed to bioequivalence studies) are required is considered to be a Type 3.

CONTACT: Brenda Atkins **PHONE#:** 4-5767 **e-mail:** AtkinsB

PURPOSE: 45 DAY FILING MEETING is the meeting at which the review team determines, based on the recommendations of each reviewer, whether the NDA contains sufficient information to permit a substantive review. If accepted for filing, consults are identified, and a review management plan, including a timeline, is developed.

AGENDA

(15 min) 1. **Discussion Points / Potential problems with review** IS RESUBMISSION A COMPLETE RESPONSE?

a. Medical — Fileable pending receipt of CRFs and Financial Disclosure information. Dr. Pazdur agreed with the bioavailablity but questions "what is the advantage over BMS's drug? Shows less extravasation?

b. Chemistry — Fileable

c. Pharm/Tox — Fileable

d. Clinical Pharmacology and Biopharmaceutics — Fileable

b. Statistical — Fileable

(5 min) 2. **Identify Consults**

a. Medical
--DSI. ΛΛΛΛΛΛΛΛ Yes (done 5-10-02)

b. - As per 12-11-98 NA letter Labeling and Nomenclature Committee will review the proposed name, MITOEXTRA™, for appropriateness. The use of the suffix "Extra" might convey clinical benefits that are not or cannot be substantiated by data, or may be considered inappropriate.

(5 min) 3. **Set Division Goals:**

a. P = 9-21-02 (Saturday) /9-20-02 (Friday)
b. ODAC date: ????????
c. Timing preference for team meetings: 1/2/3/4/5-Mo; Labeling, pre- & post-ODAC
d. Target date for first completed reviews: M_____/ C_____/CPB_____/S_____/ Other_____
e. Division vs Temple sign-off? Temple
f. Target date for Action Letter: _____

(5 min) 4. **Other Issues**

a. Dr. Pazdur was a clinical investigator for one of the clinical study(ies). Dr. Williams will be attending future meetings
b.

DATE: May 1, 2002 **MEETING:** 45-Day Filing
TIME: 2:00 PM **NDA#:** 50-763 Resubmission in response to 12-11-98 NA letter
ROOM: CR B **DRUG:** MITOExtra™ (Mitomycin for Injection

Chem/Ther Type: 3 S New Dosage form or formulation, including a new strength, where the drug has already been approved or marketed in the U.S. by the same or another manufacturer. The indication may be the same as that of the already marketed drug product or may be new. A drug with changes in its inactive ingredients such that clinical studies (as opposed to bioequivalence studies) are required is considered to be a Type 3.

CONTACT: Brenda Atkins **PHONE#:** 4-5767 **e-mail:** AtkinsB

PURPOSE: 45 DAY FILING MEETING is the meeting at which the review team determines, based on the recommendations of each reviewer, whether the NDA contains sufficient information to permit a substantive review. If accepted for filing, consults are identified, and a review management plan, including a timeline, is developed.

(5 min) 5. **Fileability** **RESPONSE**

a. Medical..... YES NO

b. Chemistry..... YES NO

c. Clinical Pharmacology and Biopharmaceutics YES NO

d. Pharm/Tox YES NO
e. Statistical YES NO

(5 min) 6. **Subsequent Meetings/Milestones** - see table on back

(5 min) 7. **ACTION ITEMS**

	Who	When
a. Schedule of meetings/milestones	Brenda	by
b. 45-day minutes	Brenda	by
c. E-mail to Leah Ripper re. finan disclosure	Brenda	asap (done)
d. Micro consult	YHsieh/Brenda	asap (done)
e. DSI consult	MO/Brenda	asap (done)
f. Tradename consult	Brenda	asap (done)

FAX

FOOD AND DRUG ADMINISTRATION
DIVISION OF ONCOLOGY DRUG PRODUCTS
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

To: Khin M. U, M.D.	**From:** Brenda Atkins, PM
Fax: (301) 827-5290	**Fax:** (301) 594-0498
Phone: (301) 827-7395	**Phone:** (301) 594-5767.
Pages, including cover sheet: 4	**Date:** October 23, 2002

Re: CRFs at Site 11 - NDA 50-763 MITOExtra

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COMMENTS:

Dr. U:

We thought you might want to review Supervalu's response to request for more information.

Please comment.

Thanks. /S/ PM

MESSAGE CONFIRMATION

10/23/02 08:24

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
10/23	01'25"	93018275290	CALLING	04	OK	0000

10/23/02 08:22 NO.028 D01

FAX

FOOD AND DRUG ADMINISTRATION
DIVISION OF ONCOLOGY DRUG PRODUCTS
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

To: Khin M. U, M.D. **From:** Brenda Atkins, PM

Fax: (301) 827-5290 **Fax:** (301) 594-0498

Phone: (301) 827-7395 **Phone:** (301) 594-5767.

Pages, including cover sheet: 4 **Date:** October 23, 2002

Re: CRFs at Site 11 - NDA 50-763 Mito Extra

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination or other action based on the content of the communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

Redacted 6

pages of trade

secret and/or

confidential

commercial

information

SuperGen
THE KEY TO LIFE

FACSIMILE COVER SHEET

Date: July 26, 2002

From: Ken Matto for Audrey Takubowski Extension: 313

☑ Corporate Headquarters: 4140 Dublin Boulevard, Suite 200, Dublin, CA 94568
Voice: (925) 560-0100 Fax: ~~(925) 551-6470~~ 925-551-6472

☐ SPRI: 1059 Serpentine Lane, Pleasanton, CA 94566
Voice: (925) 484-4400 Fax: (925) 461-1734

To: Ms. Brenda Atkins

Company: Div of Oncology Drug Products - Food and Drug Administration

Fax No.: (301) 594-0498

Phone No.: (301) 594-5767

Number of Pages (Including cover): _____

Original to follow: ☑ Yes ☐ No via mail

Comments:

Notice of confidentiality

Information contained in this fax is privileged and confidential information of the addressed and intended for the use of the addressee above. If you are neither recipient nor the employee or agent responsible for delivering this message to the intended recipient, you are hereby notified that any disclosures, copying, distribution, or the selling of any action in reliance on the contents of this transmittal is strictly prohibited. If you received this telecopy in error, please immediately notify us by telephone (925) 560-0100 to arrange return of the original document to us. Thank You.

SuperGen®
THE KEY TO LIFE

July 25, 2002

Ms. Brenda Atkins
Regulatory Project Manager
Division of Oncology Drug Products
Food and Drug Administration
1451 Rockville Pike
Rockville, Maryland 20852-1448

Dear Ms. Atkins:

Re: NDA/DRUG: 50-763/ MitoExtra™ (Mitomycin for Injection)

Subject: Investigators and Sites Facsimile Correspondence dated July 22, 2002.

As stated in our study report, there are a total of thirteen (13) principal investigators. A complete listing is provided in this submission as Attachment 1 and it replaces page xii of the final study report entitled "Clinical Protocol No. ME2, Protocol for a Study of the Tolerance and Efficacy of MitoExtra™ in Patients with Solid Tumors who Have Failed Previous Therapy", which was submitted to this NDA on March 20, 2002. We also provide as Attachment II in this submission a revised Appendix 1.5.1, List of Investigators, which replaces pages 259-261 of the original study report. The revised documents (Attachments I and II) incorporate the changes listed below. The reason for each change is provided here.

Attachment I– List of Participating Investigators, page xii (revised)

a) Site 5 lists a second address ( ). After a thorough review of our records, we conclude that this was a word processing error. There was no alternate location for Site 5 and this address does not correspond with any investigator in this study, so this address has been removed in Attachment I.

b) Site 10 is not included in this listing. SuperGen was interviewing an investigator who was tentatively assigned Site 10. However, this investigator did not finally agree to participate in the study so Site 10 never became an actual study site.

Attachment II– List of Participating Investigators, Appendix 1.5.1, pages 259-261 (revised)

a) Site 5 shows Dr. John B. Craig as the principal investigator, which is correct. However, Dr. Craig was replaced as the principal investigator because he became ill and was unable to continue in this role. Dr. Alan Grosbach became the new principal investigator. His name is included next to Dr. Craig's in Appendix 1.5.1, page 259 in our original submission and in Attachment II.

b) Site 8 lists both Dr. , Dr. Keith Thompson. Dr. was the original principal investigator and Dr. Thompson was one of the original sub investigators when the site was initiated. Following monitoring visits by SuperGen, site compliance was found to be lacking and Dr. Thompson was designated by his IRB to replace Dr. .

c) On the same form, page 261, Site 14 identifies Dr. Grant Swanson as the principal investigator. His name is followed by the names of four other physicians. The revised Appendix 1.5.1, List of Investigators shows these names deleted because these names were put on this list in error. These physicians were considered, but never contracted to perform this study. They were never given drug for the study and never enrolled a patient in this study.

In direct response to your questions:

1) There were 13 principal investigators and Site 10 was never activated, so the number was not used.

2) The first location (Schumpert Cancer Treatment Center) is correct. The second location , was listed in error.

3) The study had 13 principal investigators who were located at 13 sites. Some investigators had sub-investigators, and there were satellite sites where patients who participated in this study were seen. These are listed on the respective Form 1572s.

If you have any other questions regarding this information, please contact Dr. Audrey F. Jakubowski at (925) 560-0100 x352.

Sincerely,

Audrey F. Jakubowski

Audrey F. Jakubowski, Ph.D.
Vice President – Regulatory Affairs

Attachment I

LIST OF PARTICIPATING INVESTIGATORS

Page 1 of 3

Site No.	Investigator (No. of Patients Treated)
1	Luis Meza, M.D. (5 patients) Southwest Oncology Research 155 hospital Drive, Ste.101 Lafayette, LA 70503 (318) 234-4535
2	Hal Gerstein, M.D. (3 patients) Medical Oncology and Hematology 170 Great Neck Road Ste.100 Great Neck, NY 11022 (516) 773-3708
3	Clarence B. Vaughn, M.D. (6 patients) Southfield Oncology Institute 21751 West Eleven Mile Road Southfield, MI 48076 (248) 356-2828
4	Arnold Wax, M.D. (6 patients) 3920 South Eastern Ave., Ste 200 Las Vegas, NV 89119 (702) 369-4604
5	John B. Craig, M.D. (8 patients) Schumpert Cancer Treatment Center One St. Mary Place Shreveport LA 71101 (318) 681-4139
6	Cary Gots, M.D. (1 patient) LA Hematology/Oncology Group 1245 Wilshire #303 Los Angales, CA 90017 (213) 977-1214

Source: TABLE 1.2, Appendix 2.

LIST OF PARTICIPATING INVESTIGATORS

Page 2 of 3

Site No.	Investigator (No. of Patients Treated)
7	Francisco Gonzales, M.D. (8 patients) USC School of Medicine Center for Cancer Treatment and Research Palmetto Richland Memorial Hospital Seven Medical Park, Suite 202 Columbia, SC 29203 (803) 434-3673
8	
9	John J. Petrus, M.D. (9 patients) The Cancer Center 224 West Exchange Street Ste. 150 Akron, OH 44302 (330) 384-6431
11	Kai-Yin Yeung, M.D. (28 patients)* Oncology-Hematology Associates 8926 Woodyard Road, Suite 201 Clinton, MD 20735 (301) 868-7911
12	Jerome Rubin, M.D. (2 patients) 700 Cass Street, Suite 122 Monterey, CA 93940 (831) 375-4777

*Site No. 11 also enrolled 6 patients who were never treated.

LIST OF PARTICIPATING INVESTIGATORS

Page 3 of 3

Site No.	Investigator (No. of Patients Treated)
13	John MacDonald, M.D. (9 patients)* Saint Vincent's Hospital 153 West 11th Street New York, NY 10011 (212) 604-2219
14	Grant Swanson, M.D. (1 patient) Monterey Bay Oncology 261 El Dorado #202 Monterey, CA 93940-2911 (831) 375-4105

*Site No. 13 also enrolled 1 patient who was never treated.

Attachment II

LIST OF INVESTIGATORS

1. Luis Meza, M.D.
Southwest Oncology Research
155 Hospital Drive, Ste.101
Lafayette, LA 70503
(318) 234-4535

2. Hal Gerstein, M.D.
Medical Oncology and Hematology
170 Great Neck Road Ste.100
Great Neck, NY 11022
(516) 773-3708

3. Clarence B. Vaughn, MD
Southfield Oncology Institute
21751 West Eleven Mile Road
Southfield , MI 48076
(248) 356-2828

4. Arnold Wax, M.D.
3920 South Eastern Ave., Ste 200
Las Vegas, NV 89119
(702) 369-4604

5. John B. Craig, M.D.
Schumpert Cancer Treatment Center
One St. Mary Place
Shreveport, LA 71101
(318) 681-4139

5. Alan Grosbach, M.D.
Schumpert Cancer Treatment Center
One St. Mary Place
Shreveport, LA 71101
(318) 681-4139

6. **Cary Gota, M.D.**
LA Hematology/Oncology Group
1245 Wilshire #303
Los Angeles, CA 90017
(213)977-1214

7. **Francisco Gonzales, M.D.**
USC School of Medicine
Center for Cancer Treatment and Research
Palmetto Richland Memorial Hospital
Seven Medical Park, Suite 202
Columbia, SC 29203
(803) 434-3673

8.

8. **Keith A. Thompson, M.D.**
Alabama Oncology
4145 Carmichael Road
Montgomery, AL 36106
(334) 273-7000

9. **John J. Petrus, M.D.**
The Cancer Center
224 West Exchange Street Ste. 150
Akron, OH 44302
(330)384-6431

11. **Kai-Yin Yeung, M.D.**
Oncology-Hematology Associates
8926 Woodyard Road, Suite 201
Clinton, MD 20735
(301) 868-7911

12. Jerome Rubin, M.D.-05
700 Cass Street, Suite 122
Monterey, CA 93940
(831)375-4777

13. John Macdonald, M.D.-02
Saint Vincent's Hospital
153 west 11th Street
New York, NY 10011
(212) 604-2219

14. Grant Swanson, M.D.-06
Monterey Bay Oncology
261 El Dorado #202
Monterey, CA 93940-2911
(831) 375-4105

Redacted 3

pages of trade secret and/or confidential commercial information

MEMORANDUM

Date: November 13, 2002

To: NDA 50-763

From: Yung-Ao Hsieh, Ph.D., Chemistry Reviewer, HFD-810 through Rebecca H. Wood, Ph.D., Chemistry Team Leader, HFD-810

Subject: NDA 50-763 Mitozytrex (mitomycin for injection, USP)

The resubmission of NDA 50-763, dated March 20, 2002 was found acceptable from a CMC perspective (see CMC review dated 12-Nov-02).

OPDRA consult (dated 12-Nov-02) indicated that the proposed trade name of Mitozytrex is acceptable. The resubmission is recommended for approval.

APPEARS THIS WAY
ON ORIGINAL

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

/s/

Yung-Ao Hsieh
11/12/02 04:17:21 PM
CHEMIST

Rebecca Wood
11/12/02 04:22:22 PM
CHEMIST

SuperGen
THE KEY TO LIFE
4140 Dublin Boulevard, Suite 200, Dublin, CA 94568

Fax

To:	Ms. Brenda Atkins	**From:**	Sam Boddapati
Company:	Div of Oncology; FDA	**Company:**	SuperGen, Inc.
Fax:	301-594-0498	**Fax:**	(925) 551-6472
Phone:	301-594-5767	**Phone:**	(925) 560-0100
Date:	May 24, 2002	**Pages:**	3
Re:	NDA 50-763: MITOExtra (mitomycin for injection)		
CC:			

☐ PLEASE REPLY ☐ URGENT ☐ HARD COPY TO FOLLOW

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

Dear Ms. Atkins:

Reference is made to the resubmission of our NDA 50-763 dated March 20, 2002 and your fax communication dated May 23, 2002 regarding the — testing facility for MITOExtra.

We would like to point out that the — testing is carried out by — and not by — Please see the attached response.

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

Sincerely,

S. Boddapati

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

SuperGen®, Inc.
NDA: 50-763 MITOExtra™ (Mitomycin for Injection)

CHEMISTRY

Our district office has notified us that —— , does not plan to conduct — testing on your new drug product. Please submit the name(s) of alternate — tester(s) for CGMP qualification.

Response:

Although —— carries out some analytical testing for us on MITOExtra™, they do not conduct — testing on our product. Such testing is carried out by —— during —— , testing. Attached is a representative — test report, which was issued by ——

Thus, should CGMP qualification be required, it is — who should be contacted regarding such an inspection.

APPEARS THIS WAY
ON ORIGINAL

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information

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 23 May 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Alternative site for — testing**

Please refer to your resubmission of NDA 50-763 dated March 20, 2002, received March 21, 2002.

Our district office has notified us that — does not plan to conduct — testing on your new drug product. Please submit the name(s) of alternate — tester(s) for CGMP qualification. We wish to remind you that delays in resolving this issue may withhold approval of your NDA resubmission.

Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/

Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

5-28-02

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MESSAGE CONFIRMATION

05/23/02 12:25

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
05/23	00'30"	9259041921	CALLING	01	OK	0000

05/23/02 12:24 NO.005 P01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 23 May 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Alternative site for —— testing**

Please refer to your resubmission of NDA 50-763 dated March 20, 2002, received March 21, 2002.

Atkins, Brenda J

From: Hsieh, Yung Ao
Sent: Wednesday, May 22, 2002 3:19 PM
To: Atkins, Brenda J
Subject: RE: 50763

Yes, no problem. See you tomorrow.

-----Original Message-----
From: Atkins, Brenda J
Sent: Wednesday, May 22, 2002 3:16 PM
To: Hsieh, Yung Ao
Subject: RE: 50763

I am working from home today. Can this wait until I return tomorrow?

Brenda

-----Original Message-----
From: Hsieh, Yung Ao
Sent: Wednesday, May 22, 2002 3:10 PM
To: Atkins, Brenda J
Cc: Wood, Rebecca H
Subject: FW: 50763

Brenda,

Please check with SuperGen to see (1) if they are aware of this problem, and (2) they have any alternative site(s) for — testing. As indicated in the e-mail, this is an issue serious enough to withhold approval of the NDA.

Y. A. Hsieh

-----Original Message-----
From: Alcock, Patricia L
Sent: Wednesday, May 22, 2002 12:04 PM
To: Hsieh, Yung Ao
Cc: Patel, Hasmukh B; Ferguson, Shirnette D
Subject: FW: 50763

Please note that EES will be updated today - a withhold will be placed on — : - as you can see from the email from the district, — does not plan on conducting — testing on finished marketed product - this would complete the EER process. Does the applicant have another alternate — tester? Otherwise - this will lead to a withhold for the overall application.

-----Original Message-----
From: Pagano, Debra L
Sent: Wednesday, May 22, 2002 11:34 AM
To: Alcock, Patricia L
Subject: RE: 50763

At the present time they have absolutely no plans to conduct — testing on finished marketed products. They would like to however there are no plans in place - can imagine putting together a — testing suite, etc. in a matter of a few months. I suggest that CDER somehow communicate this to the applicant that there is a withhold placed on — so that they can decide what to do.

Deb

-----Original Message-----
From: Alcock, Patricia L
Sent: Wednesday, May 22, 2002 9:34 AM
To: Pagano, Debra L
Subject: 50763

Ok - one more thing - does this CTL lab know when they will be ready for inspection? Just trying to assess the UF date w/ the 11-02 goal date p-

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 10 June 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Request to Address Environmental Impact**

Please refer to your resubmission of NDA 50-763 dated March 20, 2002, received March 21, 2002.

All applications (e.g., NDAs) requesting agency action require the submission of an environmental assessment (EA) or a claim of categorical exclusion. The Environmental Impact Analysis requesting a categorical exclusion that you submitted on December 3, 1998 is not acceptable. If your new drug application qualifies for a categorical exclusion, you should file a categorical exclusion claim stating that the action requested qualifies for a categorical exclusion from the requirement to prepare an environmental assessment and citing the particular categorical exclusion that is claimed. Additionally, you should declare that to your knowledge, no extraordinary circumstances exist that would warrant the preparation of an EA. Please refer to the EA Industry Guidance at http://www.fda.gov/cder/guidance/1730fnl.pdf.

Please submit your response officially to the NDA. Please feel free to contact me on (301) 594-5767 if you have any questions regarding the contents of this transmission.

/S/
Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products

-filed in DFS 6-10-02

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MESSAGE CONFIRMATION

06/10/02 08:29

DATE	S,R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
06/10	00'34"	9259041921	CALLING	01	OK	0000

06/10/02 08:28 NO.109 P01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 10 June 2002

TO: Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Phone (925) 560-0100
Fax (925) 551-6472

FROM: Brenda J. Atkins, Regulatory Project Manager
Ph: (301) 594-5767/Fx: (301) 594-0498

NDA/DRUG: 50-763/MitoExtra™ (Mitomycin for Injection)

SUBJECT: **Request to Address Environmental Impact**

Please refer to your resubmission of NDA 50-763 dated March 20, 2002, received March 21, 2002. –

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Peter Cooney, Ph.D., Office of Pharmaceutical Science
Office of New Drug Chemistry, Microbiology Team, HFD-805
Parklawn Room 18B08
Phone: (301) 827-7340/Fax: (301) 443-9281

FROM:
Yung-Ao Hsieh, Ph.D.; Review Chemist
Division of Oncology Drug Products (DODP), HFD-150
Brenda J. Atkins, Project Manager, DODP, HFD-150
Phone: (301) 594-5767/Fax: (301) 594-0498

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
May 6, 2002		50-763	NDA Resubmission	March 20, 2002

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
MitoExtra (Mitomycin for Injection)	UF Goal Date 9-21-02	Cytotoxic	August 1, 2002

NAME OF FIRM: SuperGen, Inc.

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL	☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: The amendment provides responses to microbiological deficiencies cited in the NA letter dated 11-Dec-98. Please review responses to microbiological deficiencies (Items 33 to 42). Thanks.

Attachments: NDA 50-763 AZ
NA Letter dated 11-Dec-98

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) ☒ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

/s/

Yung-Ao Hsieh
5/6/02 04:10:25 PM

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information			
NDA 50-763	Efficacy Supplement Type SE-	Supplement Number	
Drug: Mitozytrex™ (mitomycin for injection)		Applicant: SuperGen, Inc.	
RPM: Brenda J. Atkins		HFD-150	Phone # 301-594-5767
Application Type: ( ) 505(b)(1) (✓) 505(b)(2)		Reference Listed Drug (NDA #, Drug name):	

❖ Application Classifications:	
• Review priority	( ) Standard (✓) Priority
• Chem class (NDAs only)	3-S
• Other (e.g., orphan, OTC)	
❖ User Fee Goal Dates	November 14, 2002
❖ Special programs (indicate all that apply)	(✓) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	( ) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation (✓) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (✓) No
• This application is on the AIP	( ) Yes ( ) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	(✓) Verified 11-12-02
❖ Patent	
• Information: Verify that patent information was submitted	(✓) Verified 11-12-02
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	( ) Verified
❖ Exclusivity Summary (approvals only)	11-14-02
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	

General Information	
Actions	
• Proposed action	(✓) AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	NA 12-11-98
• Status of advertising (approvals only)	(✓) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	( ) Yes ( ) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	( ) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	11-13-02 (Sponsored concurred 11-13-02)
• Most recent applicant-proposed labeling	11-11-02
• Original applicant-proposed labeling	12-10-1997
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	DDMAC/07-23-02 ONS/11-12-02
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	11-11-02 (Sponsor concurred during 11-12-02 teleconference)
• Applicant proposed	12-10-97
• Reviews	11-12-02 (Chemistry review)
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	None
• Documentation of discussions and/or agreements relating to post-marketing commitments	
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	See action package (MEMORANDUM AND TELECONS TAB)
❖ Memoranda and Telecons	See action package (MEMORANDUM AND TELECONS TAB)
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	None
• Pre-NDA meeting (indicate date)	None
• Pre-Approval Safety Conference (indicate date; approvals only)	None
• Other	None
❖ Advisory Committee Meeting	
• Date of Meeting	None
• 48-hour alert	None
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	

Clinical and Summary Information	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	
❖ Clinical review(s) *(indicate date for each review)*	
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	
❖ Statistical review(s) *(indicate date for each review)*	
❖ Biopharmaceutical review(s) *(indicate date for each review)*	09-12-02
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	
• Bioequivalence studies	09-16-02
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	08-29-02, 11-12-02, 11-13-02
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	08-29-02
• Review & FONSI *(indicate date of review)*	
• Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	07-02-02
❖ Facilities inspection (provide EER report)	Date completed: (✓) Acceptable ( ) Withhold recommendation
❖ Methods validation	( ) Completed ( ) Requested ( ) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	11-08-02
❖ Nonclinical inspection review summary	
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	
❖ CAC/ECAC report	

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

Form Approved: OMB No. 0910-0297
Expiration Date: February 29, 2004.

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS

SuperGen, Inc.
4140 Dublin Blvd., Suite 200
Dublin, CA 94568

2. TELEPHONE NUMBER *(Include Area Code)*

(925) 560-0100

3. PRODUCT NAME

MITOExtra(TM)

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

NDA 50-763

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

☐ YES ☒ NO

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

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER

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

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☒ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☐ YES ☒ NO

(See item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes 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:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, 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.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Gina Savio for Sam Boddapati, PhD	Sam Boddapati, PhD Senior Director, Regulatory Affairs	March 26, 2002

FORM FDA 3397 (4/01)

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