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RESEARCH**

APPLICATION NUMBER:

21-790

MICROBIOLOGY REVIEW

Product Quality Microbiology Review
Review for HFD 150
15 JUL 2005

NDA: 21-790/BI

Drug Product Name: Dacogen™
Non-proprietary Decitabine (for injection)
Drug Product Priority Classification: 1S

Review Number: 2

Dates of Submission(s) Covered by this Review:

Letter	Stamp	Consult Sent	Assigned to Reviewer
01 JUN 2005	02 JUN 2005	06 JUN 2005	06 JUN 2005
13 JUN 2005	14 JUN 2005	20 JUN 2005	20 JUN 2005

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
13 JUN 2005	#1: 02 MAY 2005	11 JUN 2005
24 JUN 2005	#2: 11 JUN 2005	11 JUN 2005

Applicant/Sponsor:

Name: SuperGen, Inc.
Address: 4140 Dublin Blvd., Suite 200
Dublin, CA 94568
Representative: Audrey F. Jakubowski, Ph.D.
Sr. Vice President Regulatory Affairs
and Quality Chief Regulatory and
Quality Officer
Telephone: (925) 560-0100 (X352)
(410) 827-9450
ajakubowski@supergen.com

Name of Reviewer:

Janet Barletta, Ph.D.

Conclusion:

Recommended for approval based on
microbiological product quality

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUPPLEMENT:** Original NDA submission
 2. **SUPPLEMENT PROVIDES FOR:** Not applicable
 3. **MANUFACTURING SITE:** Pharmachemie B.V.
Swensweg 5, Haarlem
The Netherlands
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Sterile lyophilized powder
 - Intravenous infusion
 - 50 mg/vial
 5. **METHOD(S) OF STERILIZATION:** _____
 6. **PHARMACOLOGICAL CATEGORY:** Therapy for myelodysplastic syndrome (MDS)
- B. **SUPPORTING/RELATED DOCUMENTS:** _____, Type V (June 2003).
Required information was provided in NDA. DMF was not reviewed.
- C. **REMARKS:** The applicant's responses to the first review of NDA 21-790 were filed electronically on June 1 and June 13, 2005. Decitabine, the active ingredient in Dacogen, has been granted Orphan Drug Status (February 22, 1999) and Fast Track designation on May 9, 2003. The proposal for a rolling NDA was submitted March 26, 2004 and accepted April 21, 2004.

filename: N021790r2.doc

Executive Summary**I. Recommendations**

- A. Recommendation on Approvability** - NDA 21-790 is recommended for approval based on microbiological product quality.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** - N/A

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – _____ processed lyophilized powder manufactured at Pharmachemie B.V., Haarlem, the Netherlands.
- B. Brief Description of Microbiology Deficiencies** - No deficiencies were identified based upon the information provided.
- C. Assessment of Risk Due to Microbiology Deficiencies** – N/A

III. Administrative

- A. Reviewer's Signature** _____
Janet Barletta, Ph.D.
- B. Endorsement Block**
James L. McVey/Microbiology Team Leader
- C. CC Block**
In DFS
Original NDA 21-790 (review #2)
DFS

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this page is the manifestation of the electronic signature.**

/s/

Janet Barletta
7/15/05 04:13:57 PM
MICROBIOLOGIST

James McVey
7/18/05 07:00:47 AM
MICROBIOLOGIST

Product Quality Microbiology Review

Review for HFD 150

02 MAY 2005

NDA: 21-790

Drug Product Name: Dacogen™
Non-proprietary Decitabine (for injection)
Drug Product Priority Classification: 1S

Review Number: 1

Dates of Submission(s) Covered by this Review:

<u>Letter</u>	<u>Stamp</u>	<u>Consult Sent</u>	<u>Assigned to Reviewer</u>
29 OCT 2004	1 NOV 2004	28 JAN 2005	14 FEB 2005

Applicant/Sponsor:

Name: SuperGen, Inc.
Address: 4140 Dublin Blvd., Suite 200
Dublin, CA 94568
Representative: Audrey F. Jakubowski, Ph.D.
Sr. Vice President Regulatory Affairs
and Quality Chief Regulatory and
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(410) 827-9450
ajakubowski@supergen.com

Name of Reviewer: Janet Barletta, Ph.D.

Conclusion: Approvable pending revision

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUPPLEMENT:** Original NDA submission
 2. **SUPPLEMENT PROVIDES FOR:** Not applicable
 3. **MANUFACTURING SITE:** Pharmachemie B.V.
Swensweg 5, Haarlem
The Netherlands
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Sterile lyophilized powder
 - Intravenous infusion
 - 50 mg/vial
 5. **METHOD(S) OF STERILIZATION:** _____
 6. **PHARMACOLOGICAL CATEGORY:** Therapy for myelodysplastic syndrome (MDS)
- B. **SUPPORTING/RELATED DOCUMENTS:** _____ Type V (June 2003).
Required information was provided in NDA. DMF was not reviewed.
- C. **REMARKS:** NDA 21-790 was filed electronically. Decitabine, the active ingredient in Dacogen, has been granted Orphan Drug Status (February 22, 1999) and Fast Track designation on May 9, 2003. The proposal for a rolling NDA was submitted March 26, 2004 and accepted April 21, 2004.

filename: N021790r1.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability** - NDA 21-790 is approvable pending the revision of microbiological deficiencies.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** - N/A

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – An _____ lyophilized powder will be manufactured at Pharmachemie B.V., Haarlem, the Netherlands.

- B. Brief Description of Microbiology Deficiencies** - The applicant should provide additional information regarding:

1. A validation data summary establishing the minimum _____
2. Validation data summaries for one current (2004) re-qualification for both the _____

4. validation data summaries for the sterilization of filtration and filling equipment;
5. A validation data summary for the : _____
6. Specification of batch numbers and correction of inaccurate sample numbers (Section E.1.) used for the _____ Test. Quantification of the limit of sensitivity of detection of the positive control used in the : _____

- C. Assessment of Risk Due to Microbiology Deficiencies** – Additional information regarding sterilization validation is necessary to insure product sterility.

III. Administrative

- A. Reviewer's Signature** _____
Janet Barletta, Ph.D.
- B. Endorsement Block**
James L. McVey/Microbiology Team Leader
- C. CC Block**
cc:
Original NDA N021790r1.doc
DFS

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this page is the manifestation of the electronic signature.**

/s/

Janet Barletta
5/2/05 02:32:18 PM
MICROBIOLOGIST

James McVey
5/2/05 02:48:24 PM
MICROBIOLOGIST