CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-790

CHEMISTRY REVIEW(S)

NDA 21-790

REVIEW # 3

Dacogen™ (decitabine) for INJECTION

JOSEPHINE M. JEE
REVIEW CHEMIST

DIVISION OF ONCOLOGY
DRUG PRODUCTS
HFD-150

CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-790

2. REVIEW: # 3

3. REVIEW DATE: 09-FEB-2006

4. REVIEWER: Josephine M. Jee

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Pre-NDA Meeting	15-AUG-2003

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
	27-MAY-2004
NDA 21-790 - (Rolling Submission - CMC)	21-AUG-2004
Amendment	23-NOV-2004
Amendment	03-DEC-2004
Amendment	23-DEC-2004
Amendment	01-JUN-2005
Amendment	04-AUG-2005
Amendment	14-NOV-2005
Amendment	21-DEC-2005
Amendment (MGI Carton, bottle, and PI)	21-FEB-2006
Amendment (email, MGI Carton Label and container label)	20-MAR-2006
Amendment (email, MGI Carton Label and Container Label)	23-MAR-2006

7. NAME & ADDRESS OF APPLICANT:

Name: SuperGen – changed on 23-DEC-2005 to **MGI Pharma**

Address: 5775 West Old Shakopee Road, Suite 100
Bloomington, MN 55437-3174

8. DRUG PRODUCT NAME/CODE/TYPE:

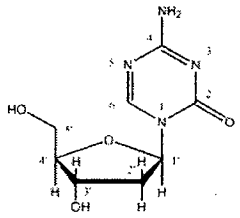
a) Proprietary Name: Dacogen™
b) Non-Proprietary Name (USAN): Decitabine
c) Code Name/# (ONDC only): NSC-127716
d) CAS Registry Number: 2353335
e) Chemical Name (IUPAC): 4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-1,3,5-triazin-2(1*H*)-one
f) Chem. Type/Submission Priority (ONDC only):
   - Chem. Type: 1
   - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: N/A
10. PHARMACOL. CATEGORY: Myelodysplastic Syndrome
11. DOSAGE FORM: Lyophilized Powder for Injection
12. STRENGTH/POTENCY: 50 mg/ vial
13. ROUTE OF ADMINISTRATION: Intravenous

14. Rx/OTC DISPENSED: __X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM): N/A

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
4-Amino-1-(2-deoxy-ß-D-erythro-pentofuranosyl)-1,3,5-triazin-2(1*H*)-one



Molecular Formula: $C_8H_{12}N_4O_4$ Molecular Weight/Mass: 228.21 daltons

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	III			1	Adequate	11-MAY-2005	J.Jee
	III			1	Adequate	10-MAY-2005	J.Jee
				1	Adequate	16-JUN-2005	J.Jee
	III			1	Adequate	02-JAN-2002	R.Kasliwal, Ph.D.
	V			1	7	03-MAY-2005	Brenda Pillari, Ph.D.
	III			1	Adequate	17-JUN-2005	J.Jee
	V			7	DMF not reviewed		See NDA 21-790, Micro. Review by

							J. Barletta, Ph.D.

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
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6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	IND 33,929	Decitabine Injectables
EOP 2 Meeting	IND 33.929	Pre-NDA Meeting Package

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	Not Applicable		
EES	Acceptable	24-JAN-2006	Office of Compliance
Pharm/Tox	Acceptable	22-JUN-2005	M. Anwar Goheer, Ph.D.
Biopharm	Acceptable/ Phase IV Commitments	23-JUN-2005	R. Ramchandani , PhD
Methods Validation	Pending		To be validated upon approval of NDA
DMETS	Dacogen™ - Acceptable	23-JUN-2005	Kimberly Curly, RPh
EA	Acceptable *	17-JUN-2005	Josephine Jee
Microbiology	Approval	15-JUL-2005	J. Barletta, Ph.D

* A requests for categorical exclusion under 21 CFR 25.31 (b) is submitted in the application. The applicant provided adequate justification for the claim of categorical exclusion.

The Chemistry Review for NDA 21-790

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This application is recommended for approval from the standpoint of Chemistry, Manufacturing and Controls (CMC). The deficiencies identified in Review No. 1 and Review No. 2 related to the drug substance and drug product have been addressed by the applicant. In addition, deficiencies identified in the package labeling insert, carton label and container label have been addressed on 23-MAR-2006.

J. Barletta, Ph.D. also recommended for approval on 15-JUL-2005 from the standpoint of Microbiology.

All outstanding issues on carton and container and package insert labeling have been adequately addressed in the amendment dated 23-MAR-2006.

Note: The applicant notified the Agency of the Transfer of Ownership on 21-DEC-2005 from SuperGen to MGI Pharma, Inc., 5775 West Old Shakopee Road, Suite 100, Bloomington, MN 55437-3174, effective 23-DEC-2005.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Decitabine is an analogue of the natural nucleoside 2'- deoxycytidine. It is a fine, white, crystalline powder with the molecular formula of $C_8H_{12}N_4O_4$ and molecular weight of 228.21. Its chemical name is 4-amino-1-(2-deoxy-ß-D-erythro-pentofuranosyl)-1,3,5-triazin-2(1*H*)-one.

Decitabine is slightly soluble in ethanol/water (50/50), methanol/water (50/50) and methanol; sparingly soluble in water; and soluble in dimethylsulfoxide (DMSO).
The drug substance is [redacted] and 36 months of supportive stability data were provided. A retest period of [redacted] will be established based on submitted data.

Dacogen™ (decitabine) for Injection is a white to almost white sterile lyophilized powder supplied in a clear colorless glass vial. Each 20 mL, single dose, glass vial contains 50 mg decitabine, 68 mg Monobasic Potassium Phosphate (Potassium Dihydrogen Phosphate) and 11.6 mg Sodium Hydroxide, packaged in cartons of 1 vial.

Dacogen™ should be reconstituted with 10 mL Sterile Water for Injection, the solution should be immediately further diluted with 0.9% Sodium Chloride Injection, 5% Dextrose Injection or Lactated Ringer's Injection to a final drug concentration of 0.1 - 1.0 mg/mL and

administered within 15 minutes. If not to be administered within 15 minutes, Dacogen should be aseptically reconstituted with 10 mL of Sterile Water for Injection (WFI) and further diluted with cold infusion solutions (0.9% Sodium Chloride Injection, 5% Dextrose Injection or Lactated Ringer's Injection) to a concentration of 0.1 - 1.0 mg/mL and stored at 2 to 8°C (36 to 46°F) for up to a maximum of 7 hours prior to administration.

The drug product vials should be stored at 25°C (77°F) with excursion permitted to 15 – 30°C (59 - 86°F) in the original package and protected from light. SuperGen proposed an expiry dating period of 3 years based on 36 months of long-term stability data for — NDA qualifying lots (primary stability data) and — supportive stability data lots, all the data provided were within specifications.

B. Description of How the Drug Product is Intended to be Used

The product is intended to be used for the treatment of myelodysplastic syndrome. Dacogen™ (decitabine) Lyophilized Powder Injection will be administered intravenously. The recommended Dacogen dose is 15 mg/m^2 administered by continuous intravenous infusion over three hours repeated every eight hours for three days. Subsequently, this cycle should be repeated every six weeks. It is recommended that patients be treated for a minimum of 4 cycles. Treatment may be continued as long as the patients continues to benefit.

C. Basis for Approvability or Not-Approval Recommendation

The microbiological review was found to be acceptable and recommended approval on 15-JUL-2005

The identified deficiencies in Review No. 1 for drug substance and drug product have been addressed by the applicant on 01-JUN-2005. However, a comment was communicated to the applicant in July 2005 concerning ———————— The applicant adequately responded on 14-NOV-2005. Adequate validation data to support the proposed regulatory methods were provided. Stability data are adequate to support a 36 month expiry period and the applicant formally requests a three year expiry dating period when stored at room temperature conditions of 20-25°C (68-77°F), with excursions between 15°C and 30°C (59°F and 86°F). All manufacturing facilities for decitabine drug substance and Dacogen™ (decitabine) Lyophilized Powder Injection are found to be acceptable by the Office of Compliance on 24-JAN-2006.

NDA 21-790 is approvable from a CMC perspective, pending adequate changes to the labels and labeling issues as outlined on pages 30 and 31. Comments were communicated to MGI on 13-MAR-2006. MGI submitted revised container and carton labels on 20-MAR-2006; however The changes made for the container l submission was incomplete and comments were sent to MGI on 20-MAR-2006. The final acceptable carton and container labels were submitted on 23-MAR-2006. **This application is recommended for approval from the standpoint of Chemistry, Manufacturing and Controls (CMC).**

III. Administrative

A. Reviewer's Signature

See electronic signatures in Division File System (DFS).

Josephine Jee, Review Chemist (Branch V), Division of Pre-Marketing Assessment III & Manufacturing Science

B. Endorsement Block

See electronic signatures in DFS

Ravi. S. Harapanhalli, Ph.D., Branch Chief (Branch V), Division of Pre-Marketing Assessment III & Manufacturing Science

C. CC Block

See DFS

27 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

Withheld Track Number: Chemistry- 3

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

/s/

Josephine Jee
3/24/2006 08:51:25 AM
CHEMIST

Ravi Harapanhalli
3/24/2006 12:55:23 PM
CHEMIST

NDA 21-790

REVIEW # 2

Dacogen™ (decitabine) for INJECTION

JOSEPHINE M. JEE
REVIEW CHEMIST

DIVISION OF ONCOLOGY
DRUG PRODUCTS
HFD-150

CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-790

2. REVIEW: # 2

3. REVIEW DATE: 19-AUG-2005

4. REVIEWER: Josephine M. Jee

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Pre-NDA Meeting	15-AUG-2003

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
NDA 21-790 - (Rolling Submission - CMC)	27-MAY-2004
Amendment	21-AUG-2004
Amendment	23-NOV-2004
Amendment	03-DEC-2004
Amendment	23-DEC-2004
Amendment	01-JUN-2005
Amendment	04-AUG-2005

7. NAME & ADDRESS OF APPLICANT:

Name: SuperGen

Address: 4140 Dublin Boulevard, Suite 200
Dublin, CA 94568

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Dacogen™

b) Non-Proprietary Name (USAN): Decitabine

c) Code Name/# (ONDC only): NSC-127716

d) CAS Registry Number: 2353335

e) Chemical Name (IUPAC): 4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-1,3,5-triazin-2(1*H*)-one

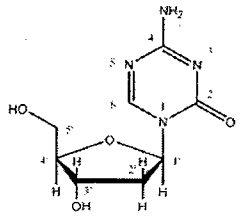
f) Chem. Type/Submission Priority (ONDC only):
- Chem. Type: 1
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: N/A
10. PHARMACOL. CATEGORY: Myelodysplastic Syndrome
11. DOSAGE FORM: Lyophilized Powder for Injection
12. STRENGTH/POTENCY: 50 mg/ vial
13. ROUTE OF ADMINISTRATION: Intravenous

14. Rx/OTC DISPENSED: __X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM): N/A

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
4-Amino-1-(2-deoxy-ß-D-erythro-pentofuranosyl)-1,3,5-triazin-2(1*H*)-one



Molecular Formula: $C_8H_{12}N_4O_4$ Molecular Weight/Mass: 228.21 daltons

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	III			1	Adequate	11-MAY-2005	J.Jee
	III			1	Adequate	10-MAY-2005	J.Jee
				1	Adequate	16-JUN-2005	J.Jee
	III			1	Adequate	02-JAN-2002	R.Kasliwal, Ph.D.
	V			1	7	03-MAY-2005	Brenda Pillari, Ph.D.
				1	Adequate	17-JUN-2005	J.Jee
				7	DMF not reviewed		See NDA 21-790, Micro. Review by J. Barletta, Ph.D.

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	IND 33,929	Decitabine Injectables
EOP 2 Meeting	IND 33.929	Pre-NDA Meeting Package

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics			
EES	Acceptable	15-JUL-04	Office of Compliance
Pharm/Tox	Acceptable	22-JUN-2005	M. Anwar Goheer, Ph.D.
Biopharm	Pending		R. Ramchandani , PhD
Methods Validation	Pending		To be validated upon approval of NDA
DMETS	Dacogen™ - Acceptable	23-JUN-2005	Kimberly Curly, RPh
EA	Acceptable	17-JUN-2005	Josephine Jee
Microbiology	Approvable	02-MAY-2005	J. Barletta, Ph.D

The Chemistry Review for NDA 21-790

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This application is recommended for approvablel from the standpoint of Chemistry, Manufacturing and Controls (CMC). The deficiencies identified in Review No. 1 related to the drug substance and drug product have been addressed by the applicant. However, there are two additional comments to be communicated to SuperGen.

The pending microbiological issues are adequately corrected (see J. Barletta, Ph.D.'s Review No. 2, dated 15-JUL-2005). It is recommended for approval based on microbiological product quality.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Dacogen™ (decitabine) for Injection contains decitabine, an analogue of the natural nucleoside 2'-deoxycytidine. Decitabine is a fine, white, crystalline powder with the molecular formula of $C_8H_{12}N_4O_4$ and molecular weight of 228.21. Its chemical name is 4-amino-1-(2-deoxy-ß-D-erythro-pentofuranosyl)-1,3,5-triazin-2(1*H*)-one.

Decitabine is slightly soluble in ethanol/water (50/50), methanol/water (50/50) and methanol; sparingly soluble in water; and soluble in dimethylsulfoxide (DMSO).
The drug substance is ——————————————————
——— and 36 months of supportive stability data were provided. A retest period of ——
——— will be established based on submitted data.

Dacogen™ (decitabine) for Injection is a white to almost white sterile lyophilized powder supplied in a clear colorless glass vial. Each 20 mL, single dose, glass vial contains 50 mg decitabine, 68 mg Monobasic Potassium Phosphate (Potassium Dihydrogen Phosphate) and 11.6 mg Sodium Hydroxide, packaged in cartons of 1 vial (NDC 62701-200-01).

Dacogen™ should be reconstituted with 10 mL Sterile Water for Injection, the solution should be immediately further diluted with 0.9% Sodium Chloride Injection, 5% Dextrose Injection or Lactated Ringer's Injection to a final drug concentration of 0.1 - 1.0 mg/mL and administered within 15 minutes. If not administered within 15 minutes, Dacogen should be aseptically reconstituted with 10 mL of Sterile Water for Injection (WFI) and further diluted with cold infusion solutions (0.9% Sodium Chloride Injection, 5% Dextrose Injection or

Lactated Ringer's Injection) to a concentration of 0.1 - 1.0 mg/mL and stored at 2 to 8°C (36 to 46°F) for up to a maximum of 7 hours prior to administration.

The drug product vials should be stored at 25°C (77°F) with excursion permitted to 15 – 30°C (59 - 86°F) in the original package and protected from light. SuperGen did not formally propose an expiry dating period; however, SuperGen provided 36 months of long-term

stability data for — NDA qualifying lots (primary stability data) and — supportive stability data lots, all the data provided were within specifications.

B. Description of How the Drug Product is Intended to be Used

The product is intended to be used for the treatment of myelodysplastic syndrome. Dacogen™ (decitabine) Lyophilized Powder Injection will be administered intravenously. The recommended Dacogen dose is 15 mg/m^2 administered by continuous intravenous infusion over three hours repeated every eight hours for three days. Subsequently, this cycle should be repeated every six weeks. It is recommended that patients be treated for a minimum of 4 cycles. Treatment may be continued as long as the patients continues to benefit.

C. Basis for Approvability or Not-Approval Recommendation

Microbiology recommended (15-JUL-2005) approval based on microbiological product quality. The identified deficiencies in Review No. 1 for drug substance and drug product have been addressed by the applicant. However, there are two new comments to be communicated to the applicant.

Adequate validation data to support the proposed regulatory methods were provided. Stability data are adequate to support a 36 month expiry period. SuperGen formally proposed a three year expiry dating period when stored at room temperature conditions of 20-25°C (68-77°F), with excursions between 15°C and 30°C (59°F and 86°F).

. All manufacturing facilities for decitabine drug substance and Dacogen™ (decitabine) Lyophilized Powder Injection are found to be acceptable by the Office of Compliance.

NDA 21-790 is recommended for approvable from a CMC standpoint.

III. Administrative

A. Reviewer's Signature

See electronic signatures in Division File System (DFS).

B. Endorsement Block

See electronic signatures in DFS

C. CC Block

See DFS

21 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

Withheld Track Number: Chemistry- 2

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

/s/

Josephine Jee
8/19/2005 07:03:05 PM
CHEMIST

Nallaperumal Chidambaram
8/29/2005 05:17:02 PM
CHEMIST
See memo to file dated August 29, 2005

NDA 21-790

REVIEW # 1

Dacogen™ (decitabine) for INJECTION

JOSEPHINE M. JEE
REVIEW CHEMIST

DIVISION OF ONCOLOGY
DRUG PRODUCTS
HFD-150

CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-790

2. REVIEW: # 1

3. REVIEW DATE: 20-JUN-2005

4. REVIEWER: Josephine M. Jee

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Pre-NDA Meeting	15-AUG-2003

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
NDA 21-790 - (Rolling Submission - CMC)	27-MAY-2004
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- Chem. Type: 1
- Submission Priority: S

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14. Rx/OTC DISPENSED: __X_Rx ___OTC

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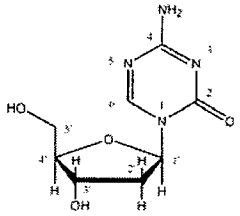

Molecular Formula: $C_8H_{12}N_4O_4$ Molecular Weight/Mass: 228.21 daltons

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	III			1	Adequate	10-MAY-2005	J.Jee
			t	1	Adequate	16-JUN-2005	J.Jee
	III			1	Adequate	02-JAN-2002	R.Kasliwal, Ph.D.
	V			1	7	03-MAY-2005	Brenda Pillari, Ph.D.
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Pharm/Tox	Acceptable	22-JUN-2005	M. Anwar Goheer, Ph.D.
Biopharm	Pending		R. Ramchandani , PhD
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EA	Acceptable	17-JUN-2005	Josephine Jee
Microbiology	Approvable	02-MAY-2005	J. Barletta, Ph.D

The Chemistry Review for NDA 21-790

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This application is approvable from the standpoint of Chemistry, Manufacturing and Controls (CMC). A number of deficiencies related to the drug substance and drug product have been identified and conveyed to the applicant to address. In addition, pending microbiological issues are yet to be satisfactorily addressed.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

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The drug substance is [redacted] and 36 months of supportive stability data were provided. A [redacted] will be established based on submitted data.

Dacogen™ (decitabine) for Injection is a white to almost white sterile lyophilized powder supplied in a clear colorless glass vial. Each 20 mL, single dose, glass vial contains 50 mg decitabine, 68 mg Monobasic Potassium Phosphate (Potassium Dihydrogen Phosphate) and 11.6 mg Sodium Hydroxide, packaged in cartons of 1 vial (NDC 62701-200-01).

Dacogen™ should be reconstituted with 10 mL Sterile Water for Injection, the solution should be immediately further diluted with 0.9% Sodium Chloride Injection, 5% Dextrose Injection or Lactated Ringer's Injection to a final drug concentration of 0.1 - 1.0 mg/mL and administered within 15 minutes. If not administered within 15 minutes, Dacogen should be aseptically reconstituted with 10 mL of Sterile Water for Injection (WFI) and further diluted with cold infusion solutions (0.9% Sodium Chloride Injection, 5% Dextrose Injection or Lactated Ringer's Injection) to a concentration of 0.1 - 1.0 mg/mL and stored at 2 to 8°C (36 to 46°F) for up to a maximum of 7 hours prior to administration.

The drug product vials should be stored at 25°C (77°F) with excursion permitted to 15 – 30°C (59 - 86°F) in the original package and protected from light. SuperGen did not formally propose an expiry dating period; however, SuperGen provided 36 months of long-term

stability data for — NDA qualifying lots (primary stability data) and — supportive stability data lots, all the data provided were within specifications.

B. Description of How the Drug Product is Intended to be Used

The product is intended to be used for the treatment of myelodysplastic syndrome. Dacogen™ (decitabine) Lyophilized Powder Injection will be administered intravenously. The recommended Dacogen dose is 15 mg/m^2 administered by continuous intravenous infusion over three hours repeated every eight hours for three days. Subsequently, this cycle should be repeated every six weeks. It is recommended that patients be treated for a minimum of 4 cycles. Treatment may be continued as long as the patients continues to benefit.

C. Basis for Approvability or Not-Approval Recommendation

NDA 21-790 is approvable from a CMC standpoint at this time due to deficiencies noted for drug substance and drug product. In addition, microbiology is yet to provide an acceptable recommendation.

Adequate validation data to support the proposed regulatory methods were provided. Stability data are adequate to support a 36 month expiry period; however, SuperGen did not formally propose any expiry dating period. All manufacturing facilities for decitabine drug substance and Dacogen™ (decitabine) Lyophilized Powder Injection are found to be acceptable by the Office of Compliance.

III. Administrative

A. Reviewer's Signature

See electronic signatures in Division File System (DFS).

B. Endorsement Block

See electronic signatures in DFS

C. CC Block

See DFS

80 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

Withheld Track Number: Chemistry- 1

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