

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-553

CHEMISTRY REVIEW(S)

ANDA 76-553

**Medroxyprogesterone Acetate
Injectable Suspension USP
150 mg/mL
1 mL Vial
Single Dose**

Gensia Sicor Pharmaceuticals

Kenneth J. Furnkranz

CDER/OGD/DC1

Chemistry Review #1

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Chemistry Review Data Sheet

1. ANDA 76-553
2. REVIEW #: 1
3. REVIEW DATE: 7-May-2003
4. REVIEWER: Kenneth J. Furnkranz
5. PREVIOUS DOCUMENTS: None

Previous Documents

Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed*

*Original ANDA Submission
Telephone Amendment

Document Date

27-November-2002
2-January-2003

7. NAME & ADDRESS OF APPLICANT:

Name: Gensia Sicor Pharmaceuticals, Inc.
19 Hughes
Address: Irvine, CA 92618

Representative: Elvia O. Gustavson

Telephone: 949-455-4700

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A

b) Non-Proprietary Name (USAN): Medroxyprogesterone Acetate

CHEMISTRY REVIEW

Chemistry Review Data Sheet

9. LEGAL BASIS FOR SUBMISSION:

Innovator Product: Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL vial

Innovator Company: Pharmacia & Upjohn

NDA#: 20-246

Patent Expiration Date: No patents that claim the listed drug

Exclusivity: No marketing Exclusivity exists

Gensia states that their drug product has the same active and inactive ingredients, dosage form, strength, route of administration and conditions of use, as the Reference Listed Drug; Pharmacia & Upjohn; Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL vial (refer to p. 1-18 for a comparison chart).

10. PHARMACOL. CATEGORY: Prevention of Pregnancy

11. DOSAGE FORM: Injectable Suspension Code: 704

12. STRENGTH/POTENCY: 150 mg/mL

13. ROUTE OF ADMINISTRATION: Intramuscular Code: 005

14. Rx/OTC DISPENSED: Rx OTC

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

SPOTS product – Form Completed

Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Medroxyprogesterone Acetate: pregn-4-ene-3,20-dione,17- (acetyloxy)-6-methyl-,(6 α)-

Molecular Formula: C₂₄H₃₄O₄

Molecular Weight: 386.53

CHEMISTRY REVIEW

Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
—	III	—————	—————	4	N/A		
—	II	—————	—————	1	Deficient	~4/14/03	

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)

B. Other Documents: None

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Pending		
EES	Pending		
Methods Validation	N/A (USP monograph ds/dp)		
Labeling	Deficient	3/24/03	A.Payne/J.Grace
Bioequivalence	Pending		
EA	Acceptable	4/28/03	K. Furnkranz
Radiopharmaceutical	N/A		

CHEMISTRY REVIEW

Chemistry Review Data Sheet

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. Yes No If no, explain reason(s) below:

**APPEARS THIS WAY
ON ORIGINAL**

The Chemistry Review for ANDA 76-553

The Executive Summary

I. Recommendations

- A. Recommendation and Conclusion on Approvability: The ANDA is not approvable pending clarification of MINOR Chemistry issues.
- B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable: None identified at this time.

II. Summary of Chemistry Assessments

- A. Description of the Drug Product(s) and Drug Substance(s): The Medroxyprogesterone Acetate drug substance is an odorless white to off-white crystalline powder. It is stable in air and melts between 200°C and 210°C. It is freely soluble in chloroform, soluble in acetone and dioxane, sparingly soluble in alcohol and methanol, and slightly soluble in ether and insoluble in water. It is manufactured _____ . The drug substance and its impurities have been characterized using the standard analytical techniques of _____ etc. A USP Reference Standard exists.

The drug substance and drug product have a USP Monograph. The USP Monograph and the established ANDA analytical methods submitted by GensiaSicor are the basis for the regulatory methods for the drug substance and drug product. The methods do not need to be validated in a FDA laboratory.

The drug product is a white, aqueous suspension. It is formulated with known compendial excipients to form the drug product. The drug product is based on the Reference Listed Drug; Pharmacia & Upjohn; Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL in a 2 mL vial.



CHEMISTRY REVIEW

Executive Summary Section

The vial drug product is packaged in an individual carton or a series of 10 vials in a shelf-tray. The drug product is labeled for storage between 20°C and 25°C (see USP).

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

Medroxyprogesterone Acetate Injectable Suspension USP is approved for intramuscular injection as a contraceptive agent for the prevention of pregnancy.

C. Basis for Approvability or Not-Approval Recommendation

The ANDA is currently Not Approvable. The following sections contain deficiencies:

- 20. COMPONENTS AND COMPOSITION
- 22. SYNTHESIS
- 25. MANUFACTURING AND PROCESSING
- 28. LABORATORY CONTROLS
- 29. STABILITY
- 32. LABELING

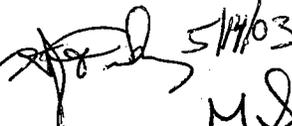
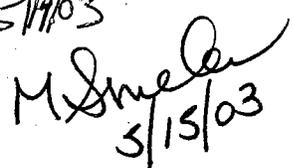
III. Administrative

A. Reviewer's Signature



B. Endorsement Block

Kenneth J. Furnkranz, R/C/5/7/03
M. Smela, T/L
P. Chen, P/M

 5/14/03
 5/15/03
 5/14/03

C. CC Block

ANDA #76-553
ANDA DUP
DIV FILE
Field Copy

F/T by: gp/5/13/03

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TYPE OF LETTER: NOT APPROVABLE – MINOR Amendment

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of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #1

CHEMISTRY REVIEW

Chemistry Assessment Section

cc: ANDA #76-553
ANDA DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-625/K.Furnkranz, R/C/5/7/03

HFD-625/M.Smela, T/L5/8/03

HFD-617/P.Chen, P/M/5/11/03

F/T by: gp/5/13/03

V:\FIRMSAM\Gensia\LTRS&REV\76553Rev01.kjf.doc

TYPE OF LETTER: NOT APPROVABLE – MINOR Amendment

[Handwritten signatures and dates]
5/14/03
M. Smela 5/15/03
P. Chen 5/14/03

**APPEARS THIS WAY
ON ORIGINAL**



ANDA 76-553

**Medroxyprogesterone Acetate
Injectable Suspension USP
150 mg/mL
1 mL Vial
Single Dose**

Sicor Pharmaceuticals

Kenneth J. Furnkranz

CDER/OGD/DC1

Chemistry Review #2

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Chemistry Review Data Sheet

1. ANDA 76-553
2. REVIEW #: 2
3. REVIEW DATE: 22-September-2003
REVISED: 8-October-2003
4. REVIEWER: Kenneth J. Furnkranz
5. PREVIOUS DOCUMENTS: None

Previous Documents

Original ANDA Submission
Telephone Amendment
Labeling Amendment

Document Date

27-November-2002
2-January-2003
25-April-2003

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

ANDA MINOR Amendment
New Correspondence

Document Date

28-July-2003
2-July-2003

7. NAME & ADDRESS OF APPLICANT:

Name: Sicor Pharmaceuticals, Inc.
19 Hughes

Address: Irvine, CA 92618

Representative: Elvia O. Gustavson

Telephone: 949-455-4700

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A



Chemistry Review Data Sheet

b) Non-Proprietary Name (USAN): Medroxyprogesterone Acetate

9. LEGAL BASIS FOR SUBMISSION:

Innovator Product: Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL vial

Innovator Company: Pharmacia & Upjohn

NDA#: 20-246

Patent Expiration Date: No patents that claim the listed drug

Exclusivity: No marketing Exclusivity exists

Sicor states that their drug product has the same active and inactive ingredients, dosage form, strength, route of administration and conditions of use, as the Reference Listed Drug; Pharmacia & Upjohn; Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL vial (refer to p. 1-18 for a comparison chart).

10. PHARMACOL. CATEGORY: Prevention of Pregnancy

11. DOSAGE FORM: Injectable Suspension Code: 704

12. STRENGTH/POTENCY: 150 mg/mL

13. ROUTE OF ADMINISTRATION: Intramuscular Code: 005

14. Rx/OTC DISPENSED: Rx OTC

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

SPOTS product – Form Completed

Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Medroxyprogesterone Acetate: pregn-4-ene-3,20-dione,17- (acetyloxy)-6-methyl-,(6 α)-

Molecular Formula: C₂₄H₃₄O₄

Molecular Weight: 386.53



CHEMISTRY REVIEW



Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
—	III	—	/	4	N/A		
—	II	—		1	Inadequate	~9/22/03	

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)

B. Other Documents: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Recommended for Approval	6/20/03	N. Nath/N. Sweeney
EES	Pending		
Methods Validation	Not Necessary	4/28/03	K.Furnkranz
Labeling	Approvable	5/28/03	A.Payne/J.Grace
Bioequivalence	Pending		
EA	Acceptable	4/28/03	K. Furnkranz
Radiopharmaceutical	Not Applicable	4/28/03	K.Furnkranz

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ___ Yes ___X___ No If no, explain reason(s) below:

Priority "B" Review due to MINOR Amendment status.

The Chemistry Review for ANDA 76-553

The Executive Summary

I. Recommendations

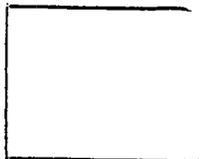
- A. **Recommendation and Conclusion on Approvability:** The ANDA is not approvable pending clarification of MINOR Chemistry issues as well as a pending Bioequivalence Review.
- B. **Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable:** None identified at this time.

II. Summary of Chemistry Assessments

- A. **Description of the Drug Product(s) and Drug Substance(s):** The Medroxyprogesterone Acetate drug substance is an odorless white to off-white crystalline powder. It is stable in air and melts between 200°C and 210°C. It is freely soluble in chloroform, soluble in acetone and dioxane, sparingly soluble in alcohol and methanol, and slightly soluble in ether and insoluble in water. It is manufactured _____ . The drug substance and its impurities have been characterized using the standard analytical techniques _____ etc. A USP Reference Standard exists.

The drug substance and drug product have a USP Monograph. The USP Monograph and the established ANDA analytical methods submitted by Sicor are the basis for the regulatory methods for the drug substance and drug product. The methods do not need to be validated in a FDA laboratory.

The drug product is a white, aqueous suspension. It is formulated with known compendial excipients to form the drug product. The drug product is based on the Reference Listed Drug; Pharmacia & Upjohn; Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL in a 2 mL vial.





Executive Summary Section

The vial drug product is packaged in an individual carton or a series of 10 vials in a shelf-tray. The drug product is labeled for storage between 20°C and 25°C (see USP).

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

Medroxyprogesterone Acetate Injectable Suspension USP is approved for intramuscular injection as a contraceptive agent for the prevention of pregnancy.

C. Basis for Approvability or Not-Approval Recommendation

The ANDA is currently Not Approvable pending MINOR Chemistry Issues and Bioequivalence Review.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Kenneth J. Furnkranz, Review Chemist/10/8/03
M.Smela, Team Leader/10/8/03
P.Chen, Project Manager

C. CC Block

ANDA #76-553
ANDA DUP
DIV FILE
Field Copy

F/T by: ard/10/9/03

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TYPE OF LETTER: NOT APPROVABLE – MINOR Amendment

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confidential commercial

information from

CHEMISTRY REVIEW #2



CHEMISTRY REVIEW



Chemistry Assessment Section

1. The CGMP status of the firms referenced in the ANDA is currently being evaluated by our Office of Compliance. A satisfactory evaluation is required for approval.
2. Your bioequivalence information is pending review.

Sincerely yours,

M. Patel for 10/10/03

Rashmikant M. Patel, Ph.D.

Director

Division of Chemistry I

Office of Generic Drugs

Center for Drug Evaluation and Research

**APPEARS THIS WAY
ON ORIGINAL**



CHEMISTRY REVIEW



Chemistry Assessment Section

cc: ANDA #76-553
ANDA DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-625/K.Furnkranz, Review Chemist/10/8/03

HFD-625/M.Smela, Team Leader/10/8/03

HFD-617/P.Chen, Project Manager 10/9/03

F/T by:ard/10/9/03

V:\FIRMSAM\Gensia\LTRS&REV\76553Rev02.kjf.doc

TYPE OF LETTER: NOT APPROVABLE – **MINOR** Amendment

[Handwritten signatures and dates]
10/10/03
M. Smela 10/10/03
P. Chen 10/10/03

**APPEARS THIS WAY
ON ORIGINAL**



ANDA 76-553

**Medroxyprogesterone Acetate
Injectable Suspension USP**

150 mg/mL

1 mL Vial

Single Dose

Sicor Pharmaceuticals

Kenneth J. Furnkranz

CDER/OGD/DC1

Chemistry Review #3



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II. Summary of Chemistry Assessments.....	6
A. Description of the Drug Product(s) and Drug Substance(s).....	6
B. Description of How the Drug Product is Intended to be Used	7
C. Basis for Approvability or Not-Approval Recommendation	7
III. Administrative.....	7
A. Reviewer's Signature	7
B. Endorsement Block	7
C. CC Block.....	7
Chemistry Assessment	8



Chemistry Review Data Sheet

1. ANDA 76-553
2. REVIEW #: 3
3. REVIEW DATE: 18-November-2003
REVISED:
4. REVIEWER: Kenneth J. Furnkranz
5. PREVIOUS DOCUMENTS: None

Previous Documents

Original ANDA Submission
Telephone Amendment
Labeling Amendment
New Correspondence
ANDA MINOR Amendment

Document Date

27-November-2002
2-January-2003
25-April-2003
2-July-2003
28-July-2003

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

ANDA MINOR Amendment

Document Date

16-October-2003

7. NAME & ADDRESS OF APPLICANT:

Name: Sicor Pharmaceuticals, Inc.
19 Hughes
Address: Irvine, CA 92618

Representative: Elvia O. Gustavson

Telephone: 949-455-4700

8. DRUG PRODUCT NAME/CODE/TYPE:



Chemistry Review Data Sheet

- a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Medroxyprogesterone Acetate

9. LEGAL BASIS FOR SUBMISSION:

Innovator Product: Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL vial
Innovator Company: Pharmacia & Upjohn
NDA#: 20-246
Patent Expiration Date: No patents that claim the listed drug
Exclusivity: No marketing Exclusivity exists

Sicor states that their drug product has the same active and inactive ingredients, dosage form, strength, route of administration and conditions of use, as the Reference Listed Drug; Pharmacia & Upjohn; Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL vial (refer to p. 1-18 for a comparison chart).

10. PHARMACOL. CATEGORY: Prevention of Pregnancy

11. DOSAGE FORM: Injectable Suspension Code: 704

12. STRENGTH/POTENCY: 150 mg/mL

13. ROUTE OF ADMINISTRATION: Intramuscular Code: 005

14. Rx/OTC DISPENSED: Rx OTC

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

SPOTS product – Form Completed

Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Medroxyprogesterone Acetate: pregn-4-ene-3,20-dione,17- (acetyloxy)-6-methyl-,(6 α)-

Molecular Formula: C₂₄H₃₄O₄

Molecular Weight: 386.53



CHEMISTRY REVIEW



Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
---	III	-----	/	4	N/A		
---	II	-----		1	Adequate	~11/18/03	

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)

B. Other Documents: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Recommended for Approval	7/10/03	N. Nath/N. Sweeney
EES	Pending		
Methods Validation	Not Necessary	4/28/03	K.Furnkranz
Labeling	Approvable	5/28/03	A.Payne/J.Grace
Bioequivalence	Pending		
EA	Acceptable	4/28/03	K. Furnkranz
Radiopharmaceutical	Not Applicable	4/28/03	K.Furnkranz

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ___ Yes ___X___ No If no, explain reason(s) below:

Priority "B" Review due to MINOR Amendment status.

The Chemistry Review for ANDA 76-553

The Executive Summary

I. Recommendations

- A. **Recommendation and Conclusion on Approvability: The ANDA is Not Approvable pending Minor CMC issues, EES and Bioequivalence Review.**
- B. **Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable: None identified at this time.**

II. Summary of Chemistry Assessments

- A. **Description of the Drug Product(s) and Drug Substance(s):** The Medroxyprogesterone Acetate drug substance is an odorless white to off-white crystalline powder. It is stable in air and melts between 200°C and 210°C. It is freely soluble in chloroform, soluble in acetone and dioxane, sparingly soluble in alcohol and methanol, and slightly soluble in ether and insoluble in water. It is manufactured _____
_____. The drug substance and its impurities have been characterized using the standard analytical techniques of _____ etc. A USP Reference Standard exists.

The drug substance and drug product have a USP Monograph. The USP Monograph and the established ANDA analytical methods submitted by Sisor are the basis for the regulatory methods for the drug substance and drug product. The methods do not need to be validated in a FDA laboratory.

The drug product is a white, aqueous suspension. It is formulated with known compendial excipients to form the drug product. The drug product is based on the Reference Listed Drug; Pharmacia & Upjohn; Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL in a 2 mL vial.





Executive Summary Section

The vial drug product is packaged in an individual carton or a series of 10 vials in a shelf-tray. The drug product is labeled for storage between 20°C and 25°C (see USP).

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

Medroxyprogesterone Acetate Injectable Suspension USP is approved for intramuscular injection as a contraceptive agent for the prevention of pregnancy.

C. Basis for Approvability or Not-Approval Recommendation

The ANDA is currently Not Approvable pending minor CMC issues, EES and Bioequivalence Review.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Kenneth J. Furnkranz, Review Chemist/11/24/03
M.Smela, Team Leader
P.Chen, Project Manager

C. CC Block

ANDA #76-553
ANDA DUP
DIV FILE
Field Copy

F/T by: gp/11/26/03
V:\FIRMSAM\Gensia\LTRS&REV\76553Rev03.kjf.doc
NOT APPROVABLE; MINOR Amendment

Redacted 13 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #3



CHEMISTRY REVIEW



Chemistry Assessment Section

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

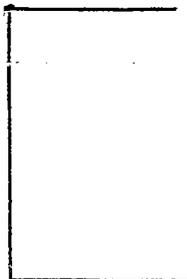
ANDA: 76-553

APPLICANT: SICOR Pharmaceuticals, Inc.

DRUG PRODUCT: Medroxyprogesterone Acetate Injectable Suspension USP,
150 mg/mL, 1 mL vials

The deficiency presented below represents a MINOR deficiency:

A. Deficiency:



B. In addition to responding to the deficiency presented above, please note and acknowledge the following comments in your response:

1. The CGMP status of the firms referenced in the ANDA is currently being evaluated by our Office of Compliance. A satisfactory evaluation is required for approval.
2. Your bioequivalence information is pending review.
3. Please provide any additional stability data that is available.

Sincerely yours,

M. Smela for 12/1/03

Rashmikant M. Patel, Ph.D.

Director

Division of Chemistry I

Office of Generic Drugs

Center for Drug Evaluation and Research



CHEMISTRY REVIEW



Chemistry Assessment Section

**APPEARS THIS WAY
ON ORIGINAL**

cc: ANDA #76-553
ANDA DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-625/K.Furnkranz, Review Chemist/11/24/03

HFD-625/M.Smela, Team Leader/11/24/03

HFD-617/P.Chen, Project Manager/11/25/03

F/T by: gp/11/26/03

V:\FIRMSAMGENSIALTRS&REV\76553Rev03.kjf.doc

TYPE OF LETTER: NOT APPROVABLE – MINOR Amendment

[Handwritten signatures and dates]
12/1/03
M. Smela 12/1/03
12/1/03



ANDA 76-553

**Medroxyprogesterone Acetate
Injectable Suspension USP
150 mg/mL
1 mL Vial
Single Dose**

Sicor Pharmaceuticals

Kenneth J. Furnkranz

CDER/OGD/DC1

Chemistry Review #4



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B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable	6
II. Summary of Chemistry Assessments.....	6
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Chemistry Review Data Sheet

1. ANDA 76-553
2. REVIEW #: 4
3. REVIEW DATE: 14-January-2004
REVISED:
4. REVIEWER: Kenneth J. Furnkranz
5. PREVIOUS DOCUMENTS: None

Previous DocumentsDocument Date

Original ANDA Submission
Telephone Amendment
Labeling Amendment
New Correspondence
ANDA MINOR Amendment
ANDA MINOR Amendment

27-November-2002
2-January-2003
25-April-2003
2-July-2003
28-July-2003
16-October-2003

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) ReviewedDocument Date

ANDA MINOR Amendment

12-December-2003

7. NAME & ADDRESS OF APPLICANT:

Name: Sicor Pharmaceuticals, Inc.
19 Hughes
Address: Irvine, CA 92618

Representative: Elvia O. Gustavson
Telephone: 949-455-4700

8. DRUG PRODUCT NAME/CODE/TYPE:



Chemistry Review Data Sheet

- a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Medroxyprogesterone Acetate

9. LEGAL BASIS FOR SUBMISSION:

Innovator Product: Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL vial
Innovator Company: Pharmacia & Upjohn
NDA#: 20-246
Patent Expiration Date: No patents that claim the listed drug
Exclusivity: No marketing Exclusivity exists

Sicor states that their drug product has the same active and inactive ingredients, dosage form, strength, route of administration and conditions of use, as the Reference Listed Drug; Pharmacia & Upjohn; Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL vial (refer to p. 1-18 for a comparison chart).

10. PHARMACOL. CATEGORY: Prevention of Pregnancy

11. DOSAGE FORM: Injectable Suspension Code: 704

12. STRENGTH/POTENCY: 150 mg/mL

13. ROUTE OF ADMINISTRATION: Intramuscular Code: 005

14. Rx/OTC DISPENSED: Rx OTC

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

SPOTS product – Form Completed

Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Medroxyprogesterone Acetate: pregn-4-ene-3,20-dione,17- (acetyloxy)-6-methyl-,(6 α)-
Molecular Formula: C₂₄H₃₄O₄
Molecular Weight: 386.53

Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
_____	III	_____	/	4	N/A		
_____	II	_____		1	Adequate	~1/14/04	

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)

B. Other Documents: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Recommended for Approval	7/10/03	N. Nath/N. Sweeney
EES	Pending		
Methods Validation	Not Necessary	4/28/03	K.Furnkranz
Labeling	Approvable	5/28/03	A.Payne/J.Grace
Bioequivalence	Pending		
EA	Acceptable	4/28/03	K. Furnkranz
Radiopharmaceutical	Not Applicable	4/28/03	K.Furnkranz

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ___ Yes ___X___ No If no, explain reason(s) below:

Priority "B" Review due to MINOR Amendment status.

The Chemistry Review for ANDA 76-553

The Executive Summary

I. Recommendations

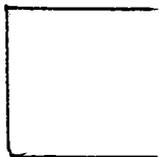
- A. Recommendation and Conclusion on Approvability: The ANDA is Approvable for CMC, pending EES and Bioequivalence Review.
- B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable: None identified at this time.

II. Summary of Chemistry Assessments

- A. Description of the Drug Product(s) and Drug Substance(s): The Medroxyprogesterone Acetate drug substance is an odorless white to off-white crystalline powder. It is stable in air and melts between 200°C and 210°C. It is freely soluble in chloroform, soluble in acetone and dioxane, sparingly soluble in alcohol and methanol, and slightly soluble in ether and insoluble in water. It is manufactured by _____ . The drug substance and its impurities have been characterized using the standard analytical techniques of _____ etc. A USP Reference Standard exists.

The drug substance and drug product have a USP Monograph. The USP Monograph and the established ANDA analytical methods submitted by Sicor are the basis for the regulatory methods for the drug substance and drug product. The methods do not need to be validated in a FDA laboratory.

The drug product is a white, aqueous suspension. It is formulated with known compendial excipients to form the drug product. The drug product is based on the Reference Listed Drug; Pharmacia & Upjohn; Depo-Provera®; Medroxyprogesterone Acetate Injectable Suspension, 150 mg/mL, 1 mL in a 2 mL vial.





Executive Summary Section

The vial drug product is packaged in an individual carton or a series of 10 vials in a shelf-tray. The drug product is labeled for storage between 20°C and 25°C (see USP).

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

Medroxyprogesterone Acetate Injectable Suspension USP is approved for intramuscular injection as a contraceptive agent for the prevention of pregnancy.

C. Basis for Approvability or Not-Approval Recommendation

The ANDA is currently Approvable pending EER and Bioequivalence Review.

III. Administrative

A. Reviewer's Signature:



B. Endorsement Block

Kenneth J. Furnkranz, Review Chemist

M. Smela, Team Leader

~~P. Chen, Project Manager~~

 1/16/04


1/16/04

C. CC Block

ANDA #76-553

ANDA DUP

DIV FILE

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Chemistry Completed (pending EER and Bioequivalence review).

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of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #4