CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-841

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 1

2. ANDA # 75-841

3. NAME AND ADDRESS OF APPLICANT
Whitney Pharmaceuticals Inc.
8300 Boone Blvd., Suite 533
Vienna, VA 22182

4. LEGAL BASIS FOR SUBMISSION: The Reference Listed Drug is Novartis Pharmaceutical Corporation's Aredia®® (Pamidronate Disodium for Injection.

Whitney filed a Paragraph IV Certification under 505(j)(2)(B) & 21 CFR 314.95 to Novartis claiming the patent #US 4711880 to be invalid.

Whitney has also filed a suitability petition for approval to market a liquid injectable product (the innovator product is a dry lyophilized powder for injection) under an ANDA (Docket #99P-2252/CP1; 1/12/00), and the suitability petition was accepted (letter dated 4/18/00).

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME: Pamidronate Disodium Injection, 3 mg/mL, 6 mg/mL, and 9 mg/mL; 10 mL vials.

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

FIRM:

2/28/00	ANDA Submission
6/20/00	Patent Amendment (Notice of Paragraph IV Certification sent to Innovator on 6/6/00

FDA:

5/30/00	Receipt of ANDA/Acceptable for Filing
7/12/00	Bioequivalence Review; No further questions
7/19/00	Labeling Review/Deficiencies noted

OTHER:

8/28/00	Notice of filing of Patent Infringement lawsuit on 7/24/00 by Novartis against Faulding and Whitney.

10. PHARMACOLOGICAL CATEGORY Treatment for mild to severe hypercalcemia, moderate to severe Paget's disease, and treatment of osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma.

11. Rx or OTC: Rx

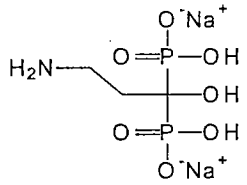
12. RELATED IND/NDA/DMF(s)

Novartis:	NDA #20-036	Reference Listed Drug
	DMF #	
	DMF #	

13. DOSAGE FORM
Injection

14. POTENCY
3 mg/mL; 30 mg/10 mL vial
6 mg/mL; 60 mg/10 mL vial
9 mg/mL; 90 mg/10 mL vial

15. CHEMICAL NAME AND STRUCTURE
Pamidronate Disodium. $C_3H_9NNa_2O_7P_2$. 279.1. Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt. 109552-15-0. Suppressant. USAN 1993, page 475.



16. RECORDS AND REPORTS N/A

17. COMMENTS: This ANDA is for a liquid injectable for IV Infusion, whereas the listed drug is a lyophilized product. Manufacture of the product involves

- Bio Waiver granted on 7/12/00
- Labeling review was found deficient on 7/19/00.
- EER pending.
- Microbiological Review pending.
- Method Validation will be necessary.

18. CONCLUSIONS AND RECOMMENDATIONS: N/A MAJOR Amendment.

19. REVIEWER:
Kenneth J. Furnkranz

DATE COMPLETED: 10/12/00
DATE REVISED: 10/16/00

Redacted 26

Page(s) of trade secret and /or confidential commercial information

1. **CHEMISTRY REVIEW NO.** 2

2. **ANDA #** 75-841

3. **NAME AND ADDRESS OF APPLICANT**

Point Holdings Inc.
529 Fifth Avenue
New York, NY 10017

U.S. AGENT

Faulding Pharmaceuticals
Attention: Heike Masser, Ph.D.
200 Elmora Avenue
Elizabeth, NJ 07207

4. **LEGAL BASIS FOR SUBMISSION:** The RLD Aredia°® (Pamidronate Disodium for Injection); Novartis Pharmaceutical Corporation

Whitney filed a Paragraph IV Certification under 505(j)(2)(B) & 21 CFR 314.95 to Novartis claiming the patent #US 4711880 to be invalid.

Whitney has also filed a suitability petition for approval to market a liquid injectable product (the innovator product is a dry lyophilized powder for injection) under an ANDA (Docket #99P-2252/CP1; 1/12/00), and the suitability petition was accepted (letter dated 4/18/00).

ANDA was transferred to Point Holdings Inc. from Whitney Pharmaceuticals on November 14, 2000.

5. **SUPPLEMENT(s):** N/A 6. **PROPRIETARY NAME:** N/A

7. **NONPROPRIETARY NAME:** Pamidronate Disodium Injection.

8. **SUPPLEMENT(s) PROVIDE(s) FOR:** N/A

9. **AMENDMENTS AND OTHER DATES:**

FIRM:

2/28/00	ANDA Submission
11/16/00	TofO to Point Holdings Inc.
3/30/01	Microbiological Amendment
4/4/01	Micro Amendment Update Correspondence
4/6/01	ANDA MAJOR Chemistry Amendment
4/10/01	Method Validation Update correspondence
8/7/01	Orig ANDA Amendment; Additional Batch sizes.

FDA:

5/30/00	Receipt of ANDA/Acceptable for Filing
7/12/00	Bioequivalence Review; No further questions
7/19/00	Labeling Review/Deficiencies noted
8/10/00	Bio review completed. No further questions.
10/31/00	N/A MAJOR Chemistry Deficiencies
1/3/01	Acknowledgement of TofO.
2/12/01	N/A MAJOR Micro deficiencies

OTHER:

6/20/00	Patent Amendment (Notice of Paragraph IV Certification sent to Innovator on 6/6/00
8/28/00	Notice of filing of Patent Infringement lawsuit on 7/24/00 by Novartis against Faulding and Whitney.
10/25/00	Notification of FDA of Notice of Voluntary Dismissal of lawsuit dated 10/3/00.
11/16/00	TofO of ANDA from Whitney to Point Holdings
11/16/00	Appointment of US Agent; Faulding Pharm.
12/8/00	Confirmation of TofO and appointment of US Agent

10. **PHARMACOLOGICAL CATEGORY** Treatment for mild to severe hypercalcemia, moderate to severe Paget's disease, and treatment of osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma.

11. **Rx or OTC:** Rx

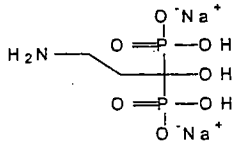
12. **RELATED IND/NDA/DMF(s)**

Novartis:	NDA #20-036	Reference Listed Drug
	DMF #	
	DMF #	

13. **DOSAGE FORM**
Injection

14. **POTENCY**
3 mg/mL; 30 mg/10 mL vial
6 mg/mL; 60 mg/10 mL vial
9 mg/mL; 90 mg/10 mL vial

15. **CHEMICAL NAME AND STRUCTURE**
Pamidronate Disodium. $C_3H_9NNa_2O_7P_2$. 279.1. Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt. 109552-15-0. Suppressant. USAN 1993, page 475.



16. **RECORDS AND REPORTS N/A**

17. **COMMENTS:** This ANDA is for a liquid injectable for IV Infusion. The listed drug is a lyophilized product. Manufacture of the product involves [redacted]

- Bio Waiver granted on 7/12/00
- Labeling review was found deficient on 7/10/01.
- EER pending. [redacted] added as [redacted]
- Microbiological Review is currently pending.
- Method Validation will be necessary.

18. **CONCLUSIONS AND RECOMMENDATIONS:** N/A MINOR Amendment.

19. **REVIEWER:** Kenneth J. Furnkranz

DATE COMPLETED: 9/5/01
DATE REVISED: 9/12/01

APPEARS THIS WAY
ON ORIGINAL

Redacted 22

Page(s) of trade secret and /or confidential commercial information

1. **CHEMISTRY REVIEW NO.** 3

2. **ANDA #** 75-841

3. **NAME AND ADDRESS OF APPLICANT**

Point Holdings Inc.
529 Fifth Avenue
New York, NY 10017

U.S. AGENT

Faulding Pharmaceuticals
Attention: Heike Masser, Ph.D.
200 Elmora Avenue
Elizabeth, NJ 07207

4. **LEGAL BASIS FOR SUBMISSION:** The RLD Aredia°® (Pamidronate Disodium for Injection); Novartis Pharmaceutical Corporation

Whitney filed a Paragraph IV Certification under 505(j)(2)(B) & 21 CFR 314.95 to Novartis claiming the patent #US 4711880 to be invalid.

Whitney has also filed a suitability petition for approval to market a liquid injectable product (the innovator product is a dry lyophilized powder for injection) under an ANDA (Docket #99P-2252/CP1; 1/12/00), and the suitability petition was accepted (letter dated 4/18/00).

ANDA was transferred to Point Holdings Inc. from Whitney Pharmaceuticals on November 14, 2000.

5. **SUPPLEMENT(s):** N/A 6. **PROPRIETARY NAME:** N/A

7. **NONPROPRIETARY NAME:** Pamidronate Disodium Injection.

8. **SUPPLEMENT(s) PROVIDE(s) FOR:** N/A

9. **AMENDMENTS AND OTHER DATES:**

FIRM:

2/28/00	ANDA Submission
11/16/00	TofO to Point Holdings Inc.
3/30/01	Microbiological Amendment
4/4/01	Micro Amendment Update Correspondence
4/6/01	ANDA MAJOR Chemistry Amendment
4/10/01	Method Validation Update correspondence
8/7/01	Orig ANDA Amendment; Additional Batch sizes.
10/17/01	ANDA MINOR Chemistry Amendment

FDA:

5/30/00	Receipt of ANDA/Acceptable for Filing
7/12/00	Bioequivalence Review; No further questions
7/19/00	Labeling Review/Deficiencies noted
8/10/00	Bio review completed. No further questions.
10/31/00	N/A MAJOR Chemistry Deficiencies
1/3/01	Acknowledgement of TofO.
2/12/01	N/A MAJOR Micro deficiencies
9/18/01	N/A MINOR Chemistry Deficiencies

OTHER:

6/20/00	Patent Amendment (Notice of Paragraph IV Certification sent to Innovator on 6/6/00
8/28/00	Notice of filing of Patent Infringement lawsuit on 7/24/00 by Novartis against Faulding and Whitney.
10/25/00	Notification of FDA of Notice of Voluntary Dismissal of lawsuit dated 10/3/00.
11/16/00	TofO of ANDA from Whitney to Point Holdings
11/16/00	Appointment of US Agent; Faulding Pharm.
12/8/00	Confirmation of TofO and appointment of US Agent
9/5/01	MV Package sent out.

10. **PHARMACOLOGICAL CATEGORY** Treatment for mild to severe hypercalcemia, moderate to severe Paget's disease, and treatment of osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma.

11. **Rx or OTC:** Rx

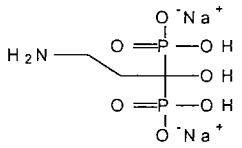
12. **RELATED IND/NDA/DMF(s)**

Novartis:	NDA #20-036	Reference Listed Drug
[redacted]	DMF # [redacted]	[redacted]
[redacted]	DMF # [redacted]	[redacted]

13. **DOSAGE FORM**
Injection

14. **POTENCY**
3 mg/mL; 30 mg/10 mL vial
6 mg/mL; 60 mg/10 mL vial
9 mg/mL; 90 mg/10 mL vial

15. **CHEMICAL NAME AND STRUCTURE**
Pamidronate Disodium. $C_3H_9NNa_2O_7P_2$. 279.1. Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt. 109552-15-0. Suppressant. USAN 1993, page 475.



16. **RECORDS AND REPORTS N/A**

17. **COMMENTS:** This ANDA is for a liquid injectable for IV Infusion. The listed drug is a lyophilized product. Manufacture of the product involves [redacted]

- Bio Waiver granted on 7/12/00.
- EER is Acceptable for all listed firms as per the 8/29/01 EER. [redacted] added as [redacted]
- Awaiting Labeling Review of revised labeling of 10/17/01.
- Microbiological Review is pending as of 11/26/01 for the 3/30 and 4/4/01 ANDA Amendments.
- Method Validation is necessary. MV package was sent out on 9/5/01. We await the results at this time.

18. **CONCLUSIONS AND RECOMMENDATIONS:** **Chemistry Closed.**

19. **REVIEWER:** Kenneth J. Furnkranz

DATE COMPLETED: 11/26/01
DATE REVISED: 12/7/01
Date Revised: 12/12/01

Redacted 17

Page(s) of trade secret and /or confidential commercial information

1. **CHEMISTRY REVIEW NO.** 4

2. **ANDA #** 75-841

3. **NAME AND ADDRESS OF APPLICANT**
Faulding Pharmaceuticals
Attention: Jatin Shah, Ph.D.
650 From Road
Mack-Call Centre II
Paramus, NJ 07652

4. **LEGAL BASIS FOR SUBMISSION:** The RLD Aredia®® (Pamidronate Disodium for Injection); Novartis Pharmaceutical Corporation

Whitney filed a Paragraph IV Certification under 505(j)(2)(B) & 21 CFR 314.95 to Novartis claiming the patent #US 4711880 to be invalid.

Faulding has also filed a Suitability Petition to allow submission of a liquid injectable product (the innovator product is a dry lyophilized powder for injection) under an ANDA (Docket #99P-2252/CP1; 1/12/00), and the Suitability Petition was accepted (letter dated 4/18/00).

ANDA was transferred to Point Holdings Inc. from Whitney Pharmaceuticals on November 14, 2000.

On October 1, 2001, Point Holdings transferred all rights and ownership of ANDA 75-841 to Faulding Pharmaceutical Co., 1 New England Avenue, Piscataway, NJ 08854.

5. **SUPPLEMENT(s):** N/A 6. **PROPRIETARY NAME:** N/A

7. **NONPROPRIETARY NAME:** Pamidronate Disodium Injection.

8. **SUPPLEMENT(s) PROVIDE(s) FOR:** N/A

9. **AMENDMENTS AND OTHER DATES:**
FIRM:

2/28/00	ANDA Submission
11/16/00	TofO to Point Holdings Inc.
3/30/01	Microbiological Amendment
4/4/01	Micro Amendment Update Correspondence
4/6/01	ANDA MAJOR Chemistry Amendment
4/10/01	Method Validation Update correspondence
8/7/01	Orig ANDA Amendment; Additional Batch sizes.
10/17/01	ANDA MINOR Chemistry Amendment
10/26/01	TofO to Faulding Pharmaceutical Co.
11/28/01	Receipt of ANDA 75-841 by Faulding Pharm. Co.
1/30/02	Change of Corporate Address

*3/19/02	ANDA MINOR Chemistry Amendment Response
*3/19/02	Relinquishment of "180 Day Exclusivity".
*3/22/02	Submission of duplicate copy of the 3/19/02 "Relinquishment of 180 Day Exclusivity" letter.
4/1/02	ANDA New Correspondence (Methods Validation)

FDA:

5/30/00	Receipt of ANDA/Acceptable for Filing
7/12/00	Bioequivalence Review; No further questions
7/19/00	Labeling Review/Deficiencies noted
8/10/00	Bio review completed. No further questions.
10/31/00	N/A MAJOR Chemistry Deficiencies
1/3/01	Acknowledgement of TofO.
2/12/01	N/A MAJOR Micro deficiencies
9/18/01	N/A MINOR Chemistry Deficiencies
12/19/01	N/A MINOR Chemistry Deficiencies
12/27/01	Receipt and acknowledgement of TofO to Faulding

OTHER:

6/20/00	Patent Amendment (Notice of Paragraph IV Certification sent to Innovator on 6/6/00
8/28/00	Notice of filing of Patent Infringement lawsuit on 7/24/00 by Novartis against Faulding and Whitney.
10/25/00	Notification of FDA of Notice of Voluntary Dismissal of lawsuit dated 10/3/00.
11/16/00	TofO of ANDA from Whitney to Point Holdings
11/16/00	Appointment of US Agent; Faulding Pharm.
12/8/00	Confirmation of TofO and appointment of US Agent
9/5/01	MV Package sent out.
2/28/02	Telecon re binding of Pamidronate with metal ions and background information for the telecon dated 2/25/02.

10. **PHARMACOLOGICAL CATEGORY** Treatment for mild to severe hypercalcemia, moderate to severe Paget's disease, and treatment of osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma.

11. **Rx or OTC:** Rx

12. **RELATED IND/NDA/DMF(s)**

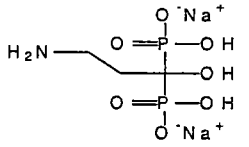
Novartis:	NDA #20-036	Reference Listed Drug
[redacted]	DMF # [redacted]	[redacted]
[redacted]	DMF # [redacted]	[redacted]

13. **DOSAGE FORM**
Injection

14. **POTENCY**
3 mg/mL; 30 mg/10 mL vial
6 mg/mL; 60 mg/10 mL vial
9 mg/mL; 90 mg/10 mL vial

15. **CHEMICAL NAME AND STRUCTURE**

Pamidronate Disodium. $C_3H_9NNa_2O_7P_2$. 279.1. Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt. 109552-15-0. Suppressant. USAN 1993, page 475.



16. **RECORDS AND REPORTS N/A**

17. **COMMENTS:** This ANDA is for a liquid injectable for IV Infusion. The listed drug is a lyophilized product. Manufacture of the product involves

- Bio Waiver granted on 7/12/00.
- EER is Acceptable for all listed firms as per the 8/29/01 EER
- Labeling is acceptable as per A.Payne/J.Grace 12/26/01.
- Microbiological Review is acceptable as per N.Nath (11/6/01) and L. Ensor (1/4/02).
- Method Validation is necessary. MV package was sent out on 9/10/01. Samples have not been received by the District Laboratory as of 4/1/02. We await the results at this time.

18. **CONCLUSIONS AND RECOMMENDATIONS: APPROVE**

19. **REVIEWER:** Kenneth J. Furnkranz

DATE COMPLETED: 4/10/02
DATE REVISED: 4/12/02

Redacted 16

Page(s) of trade secret and /or confidential commercial information

APPROVAL SUMMARY PACKAGE

ANDA NUMBER: 75-841

FIRM: Faulding Pharmaceuticals
Attention: Jatin Shah, Ph.D.
650 From Road
Mack-Call Centre II
Paramus, NJ 07652

DOSAGE FORM: Injection

STRENGTH: 3 mg/mL; 30 mg/10 mL vial
6 mg/mL; 60 mg/10 mL vial
9 mg/mL; 90 mg/10 mL vial

DRUG: Pamidronate Disodium

CGMP STATEMENT/EIR UPDATED STATUS:
EER for all listed facilities (refer to Section #33 of the ANDA review) was found acceptable on 8/29/01.

The drug product is manufactured, processed, packaged, labeled and controlled by:

F.H. Faulding & Co., Ltd.
1-23 Lexia Place
Mulgrave, Victoria 3170
Australia

The Pamidronic Acid drug substance, which is used to manufacture the Pamidronate Disodium Injection drug product, is [redacted] by [redacted]

BIO STUDY: Faulding has requested a waiver from the performance of a bioequivalence study, and the request was found acceptable as per the bio review/letter issued to the firm on 7/12/00.

METHODS VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S): MV: Validation of the analytical methods used to analyze the drug substance and drug product will be performed by the San Juan District Laboratory. The methods were sent out for validation on 9/10/01. Samples have not been received by the San Juan District Laboratory as of 4/1/02. We await the results at this time. The drug product is listed in the current BP.

STABILITY - ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION? Containers used in the stability studies are identical to those listed in container section.

Vials (10 mL): Clear glass vial with a 20 mm neck finish and a [redacted] The vials are manufactured by [redacted]

Closure: [redacted] rubber stopper; [redacted]

Seal: 20 mm Aluminum, [redacted] Flip-Off Aluminum Seal; [redacted]

LABELING: The Final Printed Labeling was found acceptable as per A. Payne/J. Grace on 12/26/01. Refer to the Labeling Approval Summary in the ANDA (Vol. 2.1).

STERILIZATION VALIDATION (IF APPLICABLE): Micro review: The ANDA has been recommended for approval on the basis of sterility assurance as per the micro review of N. Nath/L. Ensor dated 1/4/02.

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.?): Faulding's exhibit batches and proposed commercial production batches are as indicated in the following table:

Production Batch Sizes			
Batch Type	Strength (all are 10 mL vials)		
	3 mg/mL	6 mg/mL	9 mg/mL
Exhibit Batches	[redacted]	[redacted]	[redacted]
Proposed Commercial Batch	[redacted]	[redacted]	[redacted]

The DMFs for the [redacted] are currently considered adequate.

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH WERE THEY MANUFACTURED VIA SAME PROCESS?) Stability batches were the

same as the exhibit batches. The exhibit/stability batches are manufactured via same manufacturing process.

cc: ANDA #75-841
HFD-600/Reading File
HFD-625/K.Furnkranz4/12/02
HFD-625/M.Smela TL
V:\firmsnz\whitney\ltrs&rev\75841.appsum.kjf.doc
Approval Summary

4/24/02

4/24/02