CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-841

MICROBIOLOGY REVIEW(S)

OFFICE OF GENERIC DRUGS, HFD-620

Microbiology Review #1

February 12, 2001

A. 1. **ANDA:** 75-841

APPLICANT: Point Holdings Inc.
529 Fifth Ave.
NY, NY 10017

2. PRODUCT NAME: Pamidronate Disodium Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 3 mg/mL, 6 mg/mL and 9 mg/mL in 10mL/20 mm vials, for IV infusion

4. METHOD(S) OF STERILIZATION: [redacted]

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

B. 1. DATE OF INITIAL SUBMISSION: February 28, 2000
Subject of this Review (Received April 19, 2000)

2. DATE OF NEW CORRESPONDENCE: December 8, 2000

3. RELATED DOCUMENTS:
DMF [redacted]
DMF [redacted]

4. ASSIGNED FOR REVIEW: January 19, 2001

C. COMMENTS: The 12/8/00 new correspondence submitted to the application (v.2.1) clarifies Faulding Pharmaceutical Co. as the regulatory agent and Point Holdings Inc. as the owner (previously owned by Whitney Pharmaceuticals Inc.) of the subject ANDA.

D. CONCLUSIONS: The submission is **not recommended** for approval on the basis of sterility assurance. Specific comments regarding the [redacted] process are provided in "E. Review Notes" and a Microbiologist's draft of deficiencies to be provided to the Applicant. The microbiology deficiencies represent major deficiencies.

Lynne A. Ensor 2/12/01
Lynne A. Ensor, Ph. D.

cc: Original **ANDA 75-841**
Duplicate ANDA
Division Copy
Field Copy
Drafted by L. Ensor, HFD 600 v:microrev\75841.doc
Initialed by A. High

(CSH) 12/20/01

E. REVIEW NOTES:

1. General Drug and Processing Descriptions. Each mL of the product contains:

Component	Quantity per mL		
	3 mg/mL	6 mg/mL	9 mg/mL
Pamidronic Acid (equiv to Pamidronic Disodium)	(3 mg)	(6 mg)	(9 mg)
Sodium Hydroxide			
Phosphoric Acid	For pH	For pH	For pH
WFI	Qs 1 mL	Qs 1 mL	Qs 1 mL

Six batches were produced in support of the ANDA. were used to produce the 3 strengths of the product:

Batch #	Batch Size	Strength		Page #
J014935R		3 mg/mL		390-450
J024935R		3 mg/mL		451-517
J014915R		6 mg/mL		519-580
J024915R		6 mg/mL		581-641
J014945R		9 mg/mL		642-702
J024945R		9 mg/mL		703-766

Environmental monitoring results provided for the production of the exhibit batches are within the applicant's acceptance specifications (p. 1323, v.1.4). Blank master batch records are provided (p.308 on, v.1.1)

Acceptable

2. Facility and Environmental Control Descriptions. The manufacturing, packaging, labeling, and the finished dosage form testing/stability testing of the drug product will be performed at:

F.H. Faulding & Co., Limit
1-23 Lexia Place
Mulgrave, Vicotria 3170
Australia

A description of the manufacturing facility is provided (p. 1197, v.1.4). Equipment locations and room classifications are indicated on the floor plans

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

Microbiology Comments to be Provided to the Applicant

ANDA: 75-841 APPLICANT: Point Holdings Inc.

DRUG PRODUCT: Pamidronate Disodium Injection, 3 mg/mL, 6 mg/mL and 9 mg/mL in 10mL vials

A. Microbiology Deficiencies:

1. Your WFI bioburden action limits are unclear and may be excessive (i.e., the WFI action limit is stated to be "2 successive episodes in which any microorganism cannot be classified as adventitious" - or - "if TMC cannot be classified as adventitious and is greater than [redacted] ; p. 1255, v.1.4). Please clarify your WFI bioburden action limits. For example, does the action limit of "2 successive episodes in which any microorganism cannot be classified as adventitious" mean that adventitious organisms are allowable and that any one excessive WFI bioburden result does not dictate action (i.e., if an extremely high WFI bioburden level is reported that no action will be taken if a successive result is not reported?)? Does the action limit of "if TMC cannot be classified as adventitious and is greater than [redacted] (p. 1255, v.1.4) mean that adventitious organisms are allowable and/or allowable at levels greater than [redacted].

2. Please clarify your bulk solution bioburden limit for production of commercial batches. Initially you state it to be [redacted] It is also stated that following the manufacture of the validation batches, the bioburden limit will be set at [redacted] and that "Faulding will notify the Agency of such changes by the appropriate regulatory submission within six months after approval (p. 1258, v.1.4)". Additionally, please note that the bulk drug solution bioburden action limit of [redacted] is approaching excessive levels. The limit should be based on historical knowledge of the process capability. Since all exhibit batches reported no bioburden in samples tested prior to [redacted] (p. 1323-1334, v.1.4), it is unclear why this higher limit is necessary.

3. Results are provided for only [redacted] Please provide initial validation results, including 3 consecutive and successful validation runs per [redacted] for vial [redacted]

4. Results are provided for only [redacted] validation. Please provide initial validation results, including 3 consecutive and successful validation runs per [redacted]

5. Results are provided for only [redacted] validation. Please provide initial validation results, including 3 consecutive and successful validation runs per [redacted].

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

Mary Fanning, M.D., Ph.D.
Associate Director of Medical Affairs
Office of Generic Drugs
Center for Drug Evaluation and Research

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OFFICE OF GENERIC DRUGS, HFD-620
Microbiology Review #2
November 6, 2001

A. 1. ANDA: 75-841

APPLICANT: Faulding Pharmaceuticals
11 Commerce Dr.
Cranford, NJ 07016

2. PRODUCT NAME: Pamidronate Disodium Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 3 mg/mL, 6 mg/mL and 9 mg/mL in 10mL/20 mm vials, I/V

4. METHOD(S) OF STERILIZATION: [redacted]

5. PHARMACOLOGICAL CATEGORY: Calcium balance

B. 1. DATE OF INITIAL SUBMISSION: February 28, 2000
(Received April 19, 2000)

2. DATE OF Amendment: March 30, 2001
Subject of this Review (April 2, 2001)

3. RELATED DOCUMENTS: None

4. ASSIGNED FOR REVIEW: November 5, 2001

C. COMMENTS: The subject amendment provides for the response to the microbiology deficiency letter dated February 22, 2001.

D. CONCLUSIONS: The submission is **recommended** for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes".

Nrapendra Nath 11/6/01
Nrapehdra Nath, Ph. D.

L. Ensor 1/4/02 (for 11/15/01)

cc. Original **ANDA**
Duplicate ANDA
Division Copy
Field Copy
Drafted by N.Nath, HFD 600 v: microrev\75-841a1.doc
Initialed by L. Ensor

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