CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-716

MICROBIOLOGY REVIEW

Product Quality Microbiology Review
Review for HFD 550

14-June-2005

NDA:	21-716/N-000-BI
Drug Product Name:	HYDASE™
Non-proprietary Drug Product Classification:	Hyaluronidase Injection, USP
Review Number:	3
Subject of this Review	
Submission Date:	June 3, 2005
Receipt Date:	June 8, 2005
Consult Date:	June 10, 2005
Date Assigned for Review:	June 13, 2005
Submission History (for amendments only)	
Date(s) of Previous Submission(s):	October 17, 2003, January 12, 2005
Date(s) of Previous Micro Review(s):	March 12, 2004 March 25, 2005
Applicant/Sponsor	
Name:	Prima Pharm, Inc.
Address:	3443 Tripp Court Suite A San Diego, CA 92121
Representative:	Zak Hassanein
Telephone:	(858) 259-0717 x 303
Name of Reviewer:	Stephen E. Langille, Ph.D.
Conclusion:	Recommended for approval

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION:** Amendment to original application

2. **SUBMISSION PROVIDES FOR:** Responses to microbiology deficiencies identified in the second review

3. **MANUFACTURING SITE:** Primapharm, Inc
3443 Tripp Court
San Diego, CA 92121.

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**

- Aqueous injection
- Intravenous
- 150 units/mL

5. **METHOD(S) OF STERILIZATION:** ———

6. **PHARMACOLOGICAL CATEGORY:** Aid for drug absorption and dispersion

B. **SUPPORTING/RELATED DOCUMENTS:** None

C. **REMARKS:** This is a 505b2 submission and a priority review.

filename: N021716R3.DOC

Executive Summary

I. Recommendations

A. Recommendation on Approvability -
NDA 21-716 is recommended for approval from the standpoint of product quality microbiology.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -
Not applicable

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -
HYDASE™ is derived from bull testes and ——— processed at Prima Pharm Inc., San Diego, CA.

B. Brief Description of Microbiology Deficiencies -
No deficiencies were identified based upon the information provided.

C. Assessment of Risk Due to Microbiology Deficiencies -
Not applicable

III. Administrative

A. Reviewer's Signature _____
Stephen E. Langille, Ph.D.

B. Endorsement Block
James McVey

C. CC Block
In DFS

7 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

Withheld Track Number: Microbiology- 1

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/s/

Stephen Langille
6/15/05 11:27:20 AM
MICROBIOLOGIST

James McVey
6/15/05 02:05:39 PM
MICROBIOLOGIST

Product Quality Microbiology Review
Review for HFD 550

25-March-2005

NDA:	21-716/N-000-AZ
Drug Product Name:	HYDASE™
Non-proprietary Drug Product Classification:	Hyaluronidase Injection, USP
Review Number:	2
Subject of this Review	
Submission Date:	January 12, 2005
Receipt Date:	January 14, 2005
Consult Date:	January 18, 2005
Date Assigned for Review:	January 25, 2005
Submission History (for amendments only)	
Date(s) of Previous Submission(s):	October 17, 2003
Date(s) of Previous Micro Review(s):	March 12, 2004
Applicant/Sponsor	
Name:	Prima Pharm, Inc.
Address:	3443 Tripp Court Suite A San Diego, CA 92121
Representative:	Zak Hassanein
Telephone:	(858) 259-0717 x 303
Name of Reviewer:	Stephen E. Langille, Ph.D.
Conclusion:	Approvable pending revision

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Amendment to original application

2. SUBMISSION PROVIDES FOR: Responses to microbiology deficiencies identified in the first review

3. MANUFACTURING SITE: Primapharm, Inc
3443 Tripp Court
San Diego, CA 92121.

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:

- Aqueous injection
- Intravenous
- 150 units/mL

5. METHOD(S) OF STERILIZATION: ———

6. PHARMACOLOGICAL CATEGORY: Aid for drug absorption and dispersion

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: This is a 505b2 submission and a priority review.

filename: N021716R2.DOC

Executive Summary

I. Recommendations

A. Recommendation on Approvability -
NDA 21-716 is approvable pending the resolution of microbiological deficiencies.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -
Not applicable

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -
HYDASE™ is derived from bull testes and ——— , processed at Prima Pharm Inc., San Diego, CA.

B. Brief Description of Microbiology Deficiencies -
The applicant failed to provide adequate information regarding:

- [ ]

C. Assessment of Risk Due to Microbiology Deficiencies -
Failure to address the microbiology deficiencies could result in ——— contamination of the drug product.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Stephen E. Langille, Ph.D.
David Hussong, Ph.D.

C. CC Block
In DFS

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_____ § 552(b)(5) Draft Labeling

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/s/

Stephen Langille
3/25/05 04:20:15 PM
MICROBIOLOGIST

David Hussong
3/25/05 04:29:11 PM
MICROBIOLOGIST

Product Quality Microbiology Review
Review for HFD 550

12-March-2004

NDA:	21-716
Drug Product Name:	HYDASE™
Non-proprietary Drug Product Classification:	Hyaluronidase Injection, USP
Review Number:	1
Subject of this Review	
Submission Date:	October 17, 2003
Receipt Date:	October 20, 2003
Consult Date:	October 30, 2003
Date Assigned for Review:	November 11, 2003
Submission History (for amendments only)	
Date(s) of Previous Submission(s):	Not applicable
Date(s) of Previous Micro Review(s):	Not applicable
Applicant/Sponsor	
Name:	PrimaPharm, Inc.
Address:	3443 Tripp Court Suite A San Diego, CA 92121
Representative:	Zak Hassanein
Telephone:	(858) 259-0717 x 303
Name of Reviewer:	Stephen E. Langille, Ph.D.
Conclusion:	Approvable pending revision

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUPPLEMENT: Original Submission

2. SUPPLEMENT PROVIDES FOR: Not applicable

3. MANUFACTURING SITE: Primapharm, Inc
3443 Tripp Court
San Diego, CA 92121.

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:

- Aqueous injection
- Intravenous
- 150 units/mL

5. METHOD(S) OF STERILIZATION: ———

6. PHARMACOLOGICAL CATEGORY: Aid for drug absorption and dispersion

B. SUPPORTING/RELATED DOCUMENTS:

C. REMARKS: This is a 505b2 submission and a priority review.

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Executive Summary

I. Recommendations

A. Recommendation on Approvability -
NDA 21-716 is approvable pending the resolution of microbiological deficiencies.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -
Not applicable

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -
HYDASE™ is derived from bull testes and [redacted] processed at PrimaPharm Inc., San Diego, CA.

B. Brief Description of Microbiology Deficiencies -
The Applicant failed to provide important information regarding the health of the cattle prior to slaughter, the location of manufacturing equipment, media fill protocols, filter validation, container closure/equipment sterilization validation, and environmental monitoring.

C. Assessment of Risk Due to Microbiology Deficiencies -
Failure to address the microbiology deficiencies could result in a high risk of microbial and [redacted] contamination of the drug product.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Stephen E. Langille, Ph.D.
Peter Cooney, Ph.D.

C. CC Block
In DFS

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/s/

Stephen Langille
3/12/04 01:35:44 PM
MICROBIOLOGIST

Peter Cooney
3/22/04 07:55:57 AM
MICROBIOLOGIST