

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
21945Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

18 December 2008

NDA: 21-945/BC

Drug Product Name

Proprietary: Gestiva (Cytoc)

Non-proprietary: 17 λ α -Hydroxyprogesterone Caproate Injection

Drug Product Priority Classification: P

Review Number: 2

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
31 October 2008	3 NOVEMBER 2008	5 November 2008	5 November 2008

Applicant/Sponsor

Name: Hologics, Inc. (Cytoc Corporation)

Address: 1240 Elko Drive
Sunnyvale, CA 94089

Representative: Catherine Williams

Telephone: 408-745-5128

Name of Reviewer: James L. McVey

Conclusion: The label storage and use conditions (5 weeks at room temperature) are supported by the data provided.

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** original resubmission, amendment
 2. **SUBMISSION PROVIDES FOR:** response to Information Request dated 16 October 2008.
 3. **MANUFACTURING SITE:** Baxter Pharmaceutical Solutions LLC
927 South Curry Pike
Bloomington, IN
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** 250 mg/mL, 1 mL IV/dose, 5 doses in 5 mL glass vial
 5. **METHOD(S) OF STERILIZATION:** (b) (4).
 6. **PHARMACOLOGICAL CATEGORY:** indicated for prevention of recurrent pre-term birth

B. **SUPPORTING/RELATED DOCUMENTS:** N.A.

C. **REMARKS:** The first microbiologist's review recommended approval. Additional review of the label hold time was requested. Clearly the least risk of growth due to in-use contamination would be accomplished if this product had been provided in a unit dose configuration. The USP <51> antimicrobial effectiveness test period of 4 weeks is exceeded by 1 week for this label and does not address the possibility of several sequential contamination events. The data for this five dose configuration demonstrates an adequate level of preservative throughout the expiration period.

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Executive Summary

I. Recommendations

- A. Recommendation on Approvability - Approve**
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - N.A.**

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -** The product is held for 5 weeks at room temperature after initial penetration because the treatment calls for weekly injection for 5 sequential weeks.
- B. Brief Description of Microbiology Deficiencies –** None.
- C. Assessment of Risk Due to Microbiology Deficiencies –** N.A.

III. Administrative

- A. Reviewer's Signature** _____
Microbiologist: **James L. McVey**
- B. Endorsement Block** _____
Microbiology Supervisor: **David Hussong, Ph.D.**
- C. CC Block**
N/A

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/s/

James McVey
12/18/2008 02:47:50 PM
MICROBIOLOGIST

David Hussong
12/18/2008 02:54:35 PM
MICROBIOLOGIST

I concur with the reviewer's recommendation that the preservative
system is adequate for the product's use-period as
described in the label.

Product Quality Microbiology Review

17 June 2008

NDA: 21-945/AZ-000

Drug Product Name

Proprietary:

Gestiva.

Non-proprietary:

17 alpha-Hydroxyprogesterone
Caproate Injection.

Drug Product Priority Classification: Priority

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
24 APR 2008	25 APR 2008	16 MAY 2008	19 MAY 2008

Applicant/Sponsor

Name:

Cytec Corporation

Address:

1240 Elko Dr.
Sunnyvale, CA 94089-2212

Representative:

Catherine Williams

Telephone:

408-745-5128

Name of Reviewer:

John W. Metcalfe, Ph.D.

Conclusion:

Recommended for Approval.

Product Quality Microbiology Data Sheet

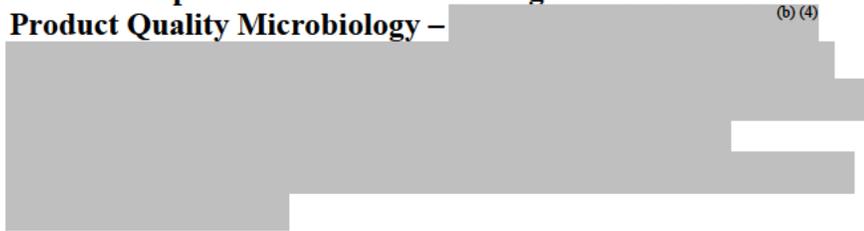
- A.
1. **TYPE OF SUBMISSION:** Resubmission: Major Amendment.
 2. **SUBMISSION PROVIDES FOR:** A change to the (b) (4) process.
 3. **MANUFACTURING SITE:** Baxter Pharmaceutical Solutions LLC
927 South Curry Pike
Bloomington, IN.
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Solution in 5 mL glass vial. **This is a multi-dose container consisting of five 1 mL doses.**
 - Intramuscular injection.
 - 250 mg/mL.
 5. **METHOD(S) OF STERILIZATION:** (b) (4).
 6. **PHARMACOLOGICAL CATEGORY:** Indicated for prevention of recurrent pre-term birth.
- B. **SUPPORTING/RELATED DOCUMENTS:** Microbiology Review of NDA 21-945, dated 07 AUG 2006.
- C. **REMARKS:**
In response to an inspection of the BPS manufacturing facility by the Medicines and Healthcare Products Regulatory Agency, the applicant has modified certain aspects of the drug product's (b) (4) manufacturing process. This review is limited to the proposed modifications made to the (b) (4) manufacturing process.

Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** – NDA 21-945/AZ-000 is recommended for approval on the basis of microbiological product quality.
- 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** –  (b) (4)
- B. **Brief Description of Microbiology Deficiencies** – There are no microbiology deficiencies identified.
- C. **Assessment of Risk Due to Microbiology Deficiencies** – Not applicable.

III. Administrative

- A. **Reviewer's Signature** _____
John W. Metcalfe, Ph.D.
- B. **Endorsement Block** _____
Stephen Langille, Ph.D.
- C. **CC Block**
N/A

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/s/

John Metcalfe
6/18/2008 11:52:36 AM
MICROBIOLOGIST

Stephen Langille
6/19/2008 07:30:45 AM
MICROBIOLOGIST

Product Quality Microbiology Review

07 August 2006

NDA: 21-945

Drug Product Name

Proprietary: Gestiva.

Non-proprietary: 17 alpha-Hydroxyprogesterone
Caproate Injection.

Drug Product Priority Classification: Priority.

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
14 APRIL 2006	20 APRIL 2006	2 MAY 2006	4 MAY 2006

Applicant/Sponsor

Name: Adeza Biomedical

Address: 1240 Elko Dr.
Sunnyvale, CA. 94089

Representative: Catherine Williams

Telephone: 408-745-5128

Name of Reviewer: John W. Metcalfe, Ph.D.

Conclusion: Recommended for approval.

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original New Drug Application.
 2. **SUBMISSION PROVIDES FOR:** A new drug.
 3. **MANUFACTURING SITE:** Baxter Pharmaceutical Solutions LLC
927 South Curry Pike
Bloomington, IN.
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Solution in 5 mL glass vial. **This is a multi-dose container consisting of five 1 mL doses.**
 - Intramuscular injection.
 - 250 mg/mL.
 5. **METHOD(S) OF STERILIZATION:** (b) (4).
 6. **PHARMACOLOGICAL CATEGORY:** Indicated for prevention of recurrent pre-term birth.
- B. **SUPPORTING/RELATED DOCUMENTS:** Type V DMF (b) (4), *Information on the Sterile Processing Facility in Bloomington, IN.* Note: this reviewer located all of the necessary manufacturing process information related to microbiological drug product quality in the application. For this reason, there was no reason to review DMF (b) (4).
- C. **REMARKS:**
A phone call was placed to Catherine Williams, applicant representative for the purpose of conveying the following two information requests:
- Please provide more detail regarding the incubation temperature and duration relative to environmental microbiological monitoring samples.
 - Do you have validation data supportive of the (b) (4) (b) (4). It is stated in a table in Module 3.2.P.3.4.5 that this (b) (4) “pending completion of process validations”. Is this information found in the application?
- A teleconference took place between Robb Hesley, Mark D’Andrea (both applicant representatives) and this reviewer on 07 August 2006. The teleconference provided the information requested above. The information provided was found to be sufficient by this reviewer, and is incorporated into appropriate sections of this review.

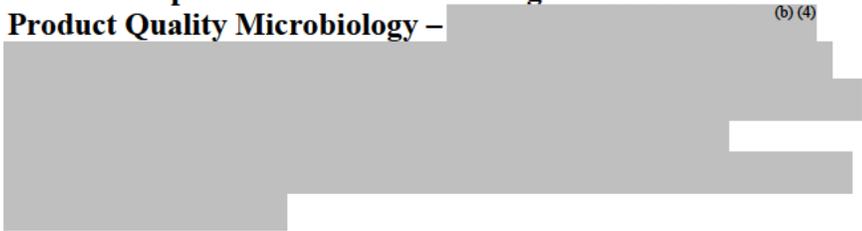
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Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** – NDA 21-945 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** – (b) (4)

- B. **Brief Description of Microbiology Deficiencies** – There are no microbiology deficiencies identified.
- C. **Assessment of Risk Due to Microbiology Deficiencies** – Not applicable.

III. Administrative

- A. **Reviewer's Signature** _____
- B. **Endorsement Block**
Stephen E. Langille, Ph.D.
- C. **CC Block**
N/A

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/s/

John Metcalfe
8/9/2006 11:19:10 PM
MICROBIOLOGIST

Stephen Langille
8/10/2006 08:06:31 AM
MICROBIOLOGIST