

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
50-807

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

19 JUNE 2006

NDA: 50-807

Drug Product Name

Proprietary: N/A

Non-proprietary: Epirubicin Hydrochloride for Injection

Drug Product Priority Classification: S

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
15 JULY 2005	19 JUL 2005	03 AUG 2005	19 AUG 2005
16 JUNE 2006	19 JUNE 2006	N/A	N/A

Applicant/Sponsor

Name: Mayne Pharma (USA) Inc.
Address: Mack Cali Centre II, 2nd Floor
650 From Rd.
Paramus, NJ 07652
Representative: Steve Richardson
Telephone: 201-225-5514

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

Conclusion: Recommended for Approval.

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** An Original New Drug Application.
 2. **SUBMISSION PROVIDES FOR:** A new drug.
 3. **MANUFACTURING SITE:**
Mayne Pharma Pty. Ltd.
1 Lexia Place
Mulgrave, Victoria 3170
Australia
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Lyophilized powder for reconstitution.
 - Intravenous infusion.
 - 50 mg/vial; 200 mg/vial.
 5. **METHOD(S) OF STERILIZATION:** _____
 6. **PHARMACOLOGICAL CATEGORY:** Indicated as a component of adjuvant therapy in patients with evidence of axillary node tumor involvement following resection of primary breast cancer.

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

C. **REMARKS:**

A telephone call was placed by this reviewer to make the following information requests on 30 January 2006.

- Section A.3.2.P.3.5.C contains a report (DHO 515) summarizing the _____ for glassware. It is missing pages 3, 4, and 5. Please provide these pages.
- Does the NDA contain a container/closure integrity validation report? If so, where in the NDA are the container/closure integrity studies located?

An applicant representative (Mr. Michael Nebo) telephoned this reviewer on 31 January 2006 with answers to the requested information. The information is incorporated into appropriate sections of this review.

A second teleconference took place between this reviewer and Steve Richardson (applicant representative) on 19 April 2006 to discuss the performance of an additional microbiological based study. The proposed labeling states that the reconstituted product can be held for a 24 hour period at room temperature. This reviewer queried the applicant (see DFS FAX to applicant dated 13 March 2006)

as to whether they have data to support the fact that the reconstituted drug product is incapable of supporting microbial growth at room temperature over the stated time period. (It is assumed that a drug product is no longer sterile following the delivery of the diluent, therefore it is important that the product not be able to support microbial growth during the stated hold time.) To date (19 April 2006), the applicant has not performed such studies.

During the 19 April 2006 teleconference, this reviewer asked Dr. Richardson whether he knows if the API is antimicrobial or not. Dr. Richardson replied that he did not know the answer to this question, and that since the drug product formulation contains lactose, it is possible that it would support bacterial growth. Dr. Richardson agreed that it was prudent to perform the study adding that such knowledge would be useful for both answering this question posed by The Agency, as well as in addressing future questions from physicians and pharmacists who read the label storage conditions. Following is a summary of the study design discussed during the teleconference:

- Inoculate reconstituted product with low numbers (<100 CFU) of test microbes.
- Use a panel of microbes which is similar to that described in USP <51>.
- Incubate the test vials at 25°C (the stated hold temperature of the reconstituted product).
- Periodically remove samples for determination of microbial counts. Continue through the stated hold period of 24 hours.

The applicant representative understood the rationale for performing the study, as well as the design of the study, and pledged to contact the agency once the data are accumulated.

An amendment (16 June 2006) to the application was filed containing the results of a validation study as described above, supporting the hold time of 24 hours at room temperature for the reconstituted drug product. The review of this validation is found on pages 17-19 in Section G (Labeling) of this document.

**APPEARS THIS WAY
ON ORIGINAL**

File Name: N050807R1.doc

Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** – NDA 50-807 is recommended for approval based on product quality microbiology.
- 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 subject drug product is

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

III. Administrative

- A. **Reviewer's Signature** _____
John W. Metcalfe, Ph.D.
- B. **Endorsement Block**
Bryan Riley, Ph.D.
- C. **CC Block**
In DFS

15 Page(s) Withheld

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

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

**This is a representation of an electronic record that was signed electronically and
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/s/

John Metcalfe
6/26/2006 01:11:36 PM
MICROBIOLOGIST

Bryan Riley
6/26/2006 01:16:05 PM
MICROBIOLOGIST