CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022504Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

06 OCTOBER 2010

NDA: 22-504/N-000

Drug Product Name
Proprietary: Axiron®
Non-proprietary: Testosterone Solution 2%

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
25 January 2010	25 January 2010	09 February 2010	17 February 2010

Submission History (for amendments only): N/A

Applicant/Sponsor
Name: Acrux Pharma Pty. Ltd.
Address: 1003-113 Stanley Street
West Melbourne, Victoria 3003
AUSTRALIA

Representative: Dr. Lisa Jenkins, US Agent
Associate Director
Kendle International, Inc.
441 Vine Street, Suite 500
Cincinnati, OH 45202
Telephone: 513-444-4062

Name of Reviewer: Robert J. Mello, Ph.D.

Conclusion: The application is recommended for approval from microbiology product quality standpoint.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: New NDA

2. SUBMISSION PROVIDES FOR: Marketing Authorization

3. MANUFACTURING SITE: Orion Corporation
Orion Pharma Turku site
Tengstrominkatu 8
FI-20360 Turku
Finland

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Non-sterile solution; Topical/transdermal; testosterone 2% (w/v) (30mg, 60mg, 90mg and120mg) packaged (b) (4) with a metered dose pump.

5. METHOD(S) OF STERILIZATION: N/A; Non-sterile drug product

6. PHARMACOLOGICAL CATEGORY: Treatment of male hypogonadism

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS:

- The ONDQA Initial Quality Assessment was filed on 23 March 2010. It was recommended that a consult request for an overall evaluation by CMC Micro be issued. The request was sent on 09-Feb-2010. No specific review requests were made in the consult request.
- The submission was provided in eCTD format and is accessible through the electronic document room (EDR).

filename: N022504N000R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – Recommend Approval

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 drug product is an alcoholic solution (b) (4)

Ethanol and isopropanol (b) (4)

B. Brief Description of Microbiology Deficiencies - None

C. Assessment of Risk Due to Microbiology Deficiencies – N/A

III. Administrative

A. Reviewer's Signature: _____

Robert J. Mello, Ph.D.
Senior Microbiology Reviewer

B. Endorsement Block: _____

John W. Metcalfe, Ph.D.
Senior Microbiology Reviewer

C. CC Block

NDA 22-504

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/s/

ROBERT J MELLO
10/06/2010

JOHN W METCALFE
10/06/2010
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 22-504 **Applicant:** Acrux Pharma **Submit Date:** 1/25/2010

Drug Name: AXIRON™ (testosterone solution) 2% **NDA Type:** Original-1 **Received Date:** 1/25/2010

The following are necessary to initiate a review of the NDA application:

	Content Parameter	Yes	No	Comments
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	**X**		Section 3.2.P.2.1 and Development Report #406
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	**X**		Section 3.2.P.3.3
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	**X**		Section 3.2.P.3.5
4	Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?		**X**	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	**X**		Section 3.2.P.2.5
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	**X**		Section 3.2.P.5.1
7	Has the applicant submitted the results of analytical method verification studies?	**X**		Section 3.2.P.5.3
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	**n/a**	**n/a**	
9	Is this NDA fileable? If not, then describe why.	**X**		**Application is Fileable**

Additional Comments: This non-sterile, topical drug product is an alcoholic solution of testosterone (b) (4) Preservative effectiveness testing was performed. Release and Stability specifications include microbial limits testing per USP<61>, <62>. Bioburden testing was included in a 30-day bulk hold time study. Validation reports were included for suitability of USP<61>, <62> methods.

Robert J. Mello, Ph.D. Date
Reviewing Microbiologist

Stephen E. Langille, Ph.D. Date
Senior Review Microbiologist

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22504	ORIG-1	ACRUX PHARMA PTY LTD	TESTOSTERONE

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/s/

ROBERT J MELLO
03/04/2010

STEPHEN E LANGILLE
03/04/2010