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APPLICATION NUMBER:

203794Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

7 AUGUST 2012

NDA: 203794/N-000

Drug Product Name
Proprietary: NUCYNTA
Non-proprietary: Tapentadol Hydrochloride

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
15 December 2011	15 December 2011	6 January 2012	13 January 2012
7 May 2012	7 May 2012	N/A	N/A
13 June 2012	13 June 2012	N/A	N/A

Submission History (for amendments only): N/A

Applicant/Sponsor
Name: Janssen Pharmaceuticals, Inc.
Address: 1125 Trenton-Harbourton Road, P.O. Box 200
Titusville, NJ 08560-0200
Representative: Peggy Ferrone
Telephone: 908-704-5116

Name of Reviewer: Bryan S. Riley, Ph.D.

Conclusion: Recommend Approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: 505(b)(1) NDA

2. SUBMISSION PROVIDES FOR: A new oral solution drug product

3. MANUFACTURING SITE: (b) (4)

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Non-sterile, aqueous solution for oral administration in a HDPE bottle, 100mL in a 120 mL bottle or 200 mL in a 235 mL bottle, 20 mg/mL.

5. METHOD(S) OF STERILIZATION: N/A

6. PHARMACOLOGICAL CATEGORY: Analgesic

B. SUPPORTING/RELATED DOCUMENTS: N/A

C. REMARKS: This was an eCTD submission. Information requests were sent to the applicant via email on 20 April 2012 and 6 June 2012. The text of the Product Quality Microbiology questions is provided below:

20 April 2012 IR

1. The drug product microbiological specifications should clearly identify the acceptance criteria both for enumeration and specific microorganisms. Merely stating that the drug product meets Current USP <1111> is not sufficient.

2. Provide test methods and acceptance criteria to demonstrate the product is free of the objectionable microorganisms of the *Burkholderia cepacia* complex. We recommend that potential sources are examined and sampled as process controls, and these may include raw materials and the manufacturing environment. A risk assessment for this species in the product and raw materials is recommended to develop sampling procedures and acceptance criteria. Your test method should be validated and a discussion of those methods should be provided. Test methods validation should address multiple strains of the species and cells that are acclimated to the environments (e.g., warm or cold water) that may be tested.

3. Your proposal to perform skip lot testing for the Microbial Limits test is unacceptable because it does not comply with 21 CFR 211.165(a) and (b). Microbial limits testing should be performed on each lot of drug product at release. After obtaining sufficient data to demonstrate control of drug product bioburden, you may submit a prior approval supplement proposing to omit finished product microbial limits testing for batch release.

After approval of omitting microbial limits testing at release, microbial limits testing should continue to be performed at the initial time point (at a minimum) on stability samples.

6 June 2012 IR
Your proposal to perform skip lot testing for the Microbial Limits test is unacceptable because it does not comply with 21 CFR 211.165(a) and (b). An attribute listed in the drug product specifications must be assessed for each lot of drug product at release by performing the appropriate test procedure. Therefore, the proposal to use skip lot testing for microbial limits should be withdrawn from your application.

However, after obtaining sufficient manufacturing experience and acceptable microbial limits testing data to demonstrate control of drug product bioburden, you may submit a prior approval supplement proposing to omit finished product microbial limits testing for batch release. After approval of omitting microbial limits testing from the release specification, microbial limits testing should continue to be performed at the initial time point (at a minimum) on stability samples.

> The applicant responded with amendments dated 7 May 2012 and 13 June 2012. The review of the amendments is included in section 3.2.P.5.

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Executive Summary

I. Recommendations

A. Recommendation on Approvability – This submission is recommended for approval on the basis of 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 drug product is a non-sterile oral liquid. Although the drug product does not contain a specific preservative, it meets the acceptance criteria for USP Chapter <51>. The drug product is tested for microbial limits at release.

B. Brief Description of Microbiology Deficiencies – N/A

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

III. Administrative

A. Reviewer's Signature _____

Bryan S. Riley, Ph.D.
Senior Review Microbiologist, OPS/NDMS

B. Endorsement Block _____

Stephen E. Langille, Ph.D.
Senior Review Microbiologist, OPS/NDMS

C. CC Block

N/A

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