CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202231Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

26 April 2011

NDA: 202231/N-000

Drug Product Name
Proprietary: N/A
Non-proprietary: Levothyroxine Sodium for Injection

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
31 August 2010	31 August 2010	06 September 2010	09 September 2010
18 February 2011	18 February 2011	-	-

Submission History (for amendments only)

Applicant/Sponsor
Name: APP Pharmaceuticals, LLC.
Address: 1501 E. Woodfield Road
Suite 300 E
Schaumburg, IL 60173-5837
Representative: Brent Yurschak
Regulatory Scientist
Telephone: 847-330-3896

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: 505(b)(2)

2. SUBMISSION PROVIDES FOR: Marketing Authorization

3. MANUFACTURING SITE: APP Pharmaceuticals, LLC.
2020 N. Ruby Street
Melrose Park, IL 60160

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Sterile Lyophilized powder for injection; Intravenous (b) (4) 100µg/vial in a 6.5ml rubber stoppered vial, 200µg/vial and 500µg/vial both in a 10ml rubber stoppered vial.

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: Replacement therapy for reduced or absent thyroid function of any etiology.

B. SUPPORTING/RELATED DOCUMENTS:

- Letter of Authorization, dated 23 June 2010, to reference the (b) (4) DMF (b) (4) (May 28, 2010 update (b) (4)
- Microbiology Review #8 of DMF (b) (4) dated 06 July 2010 (OGD review).

C. REMARKS:

- An ONDQA Initial Quality Assessment was performed by the Chemistry CMC Lead and entered into DARRTS on 10/14/2010. A consult was requested from Microbiology for a review of sterility assurance issues.
- The NDA is an electronic submission in eCTD format. It is accessible for review via the Global Submit pathway

filename: N202231N000R1.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 (b) (4)

[redacted]

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 202231

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/s/

ROBERT J MELLO
04/28/2011

JOHN W METCALFE
04/28/2011
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 202231 **Applicant: APP Pharmaceuticals, LLC** **Submit Date: 30 August 2010**

Drug Name: Levothyroxine Sodium for Injection, 100mcg/vial, 200mcg/vial and 500mcg/vial **NDA Type: 505(b)(2)** **Receipt Date: 30 August 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		Provided in Section 3.2.P.3.3
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		Provided in Section 3.2.P.3.3.1
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		Provided in Section 3.2.P.3.3.1. Filter validation studies in Section 3.2.P.3.5.2
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		Container-closure integrity studies provided in Section 3.2.P.2.3
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Provided in Section 3.2.P.5.1
7	Has the applicant submitted the results of analytical method verification studies?	X		Provided in Section 3.2.P.2.4
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	-	-	Not Applicable
9	Is this NDA fileable? If not, then describe why.	X		**Submission is Fileable**

Additional Comments: The drug product is a light sensitive product.

Robert J. Mello, Ph.D. (Senior Microbiology Reviewer) Date

John W. Metcalfe, Ph. D. (Senior Microbiology Reviewer) Date

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/s/

ROBERT J MELLO
09/20/2010

JOHN W METCALFE
09/20/2010
I concur.