CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202057Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

23 May 2012

NDA: 202057/N-000.

Drug Product Name
Proprietary: Vascepa.
Non-proprietary: Icosapent ethyl.

Review Number: 1.

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
25 SEP 2011	26 SEP 2011	07 OCT 2011	13 OCT 2011
30 JAN 2012	31 JAN 2012	N/A	N/A
06 FEB 2012	06 FEB 2012	N/A	N/A

Applicant/Sponsor
Name: Amarin Pharmaceuticals Ireland Limited.

Address: (US Agent)
12 Roosevelt Ave.
Mystic, CT 06355
Representative: Peggy J. Berry
Telephone: 302-563-4575

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

Conclusion: Recommend approval.

Product Quality Microbiology Data Sheet

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

2. SUBMISSION PROVIDES FOR: Market authorization.

3. MANUFACTURING SITE:

Drug Product:

Banner Pharmacaps Europe BV De Posthoornstraat 7 5048 AS Tilburg The Netherlands	&	Catalent Pharma Solutions, LLC 2725 Scherer Dr. St. Petersburg, FL 33716

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:

- Capsule.
- Oral.
- 1000 mg.

5. METHOD(S) OF STERILIZATION: The drug product is not sterile.

6. PHARMACOLOGICAL CATEGORY: The drug product is indicated for the reduction of triglycerides in patients with very high triglycerides.

B. SUPPORTING/RELATED DOCUMENTS: None.

C. REMARKS:

The subject NDA is submitted electronically in CTD format.

The following Microbiology Information Request was included in a Filing Communication letter to the applicant on 08 December 2011:

> *Submit the test methods and data sets verifying the suitability of the use of the stated microbial limits test with the drug product.*

The applicant amended the NDA with a response to this information request on 30 January 2012.

A second Microbiology Information Request was forwarded to the applicant by the OND Project Manager on 02 February 2012 by electronic mail. Following is the information request:

> *A microbiology review of NDA 202057 is in progress. Reference is made to the 30 January 2012 Response to 74-Day Filing Letter and Question #9 which requests test methods and data sets verifying the*

suitability of use of the microbial limits tests with the subject drug product.

Report No. TTP-ANN-M0013 states, "…method suitability and microbial enumeration testing were performed on one lot of AMR101 Capsules, lot number 262477A (Placebo) according to …". In addition the report states, "microbial enumeration testing was also performed on lot number 263672A (strength: 1 g)" (Section I. of Report No. TTP-ANN-M0013).

What is meant by the term "placebo" with regard to lot number 262477A? The report is not clear as to whether this lot number has the same formulation as lot number 263672A and product to be marketed. The purpose of these microbial limit test verification studies is to demonstrate that the product to be marketed does not interfere with the test methods.

- *Provide confirmation that lots 262477A and 263672A are identical with regard to product formulation.*
- *If lot 262477A is not representative of product to be marketed, then submit additional data sets from studies verifying the suitability of use of the microbial limits tests with the subject drug product to be marketed.*

The applicant amended the NDA with a response to this information request on 06 February 2012. The response is summarized and reviewed in appropriate sections of this review.

File Name: N202057R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – NDA 202057/N-000 is recommended for approval on the basis 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 – Capsules are filled with the drug substance.

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.
Senior Microbiology Reviewer
CDER/OPS/NDMS

B. Endorsement Block_____

Stephen E. Langille
Senior Microbiology Reviewer
CDER/OPS/NDMS

C. CC Block

N/A

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/s/

JOHN W METCALFE
05/23/2012

STEPHEN E LANGILLE
05/23/2012

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 202057. **Applicant:** Amarin Pharmaceuticals. **Letter Date:** 25 September 2011.

Drug Name: Vascepa. **NDA Type:** 505(b)(1). **Stamp Date:** 26 September 2011.

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		Module 3. The drug product is a capsule for oral admin.
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		Module 3.2.P.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	The applicant states that process validation will be performed prior to commercialization (Module 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	Not applicable for this non-sterile drug product.
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Table 3.2.P.5.1-1.
7	Has the applicant submitted the results of analytical method verification studies?		X	Verification data sets for microbial limits testing will be requested.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			This reviewer has no knowledge of pre-submission discussions.
9	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The applicant should provide the following information: *Test methods and data sets verifying the suitability of use of the stated microbial limits tests with the subject drug product.*

John W. Metcalfe, Ph.D. 09 November 2011
Senior Microbiology Reviewer, CDER/OPS/NDMS.

Bryan S. Riley, Ph.D. 09 November 2011
Senior Microbiology Reviewer, CDER/OPS/NDMS.

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/s/

JOHN W METCALFE
11/09/2011

BRYAN S RILEY
11/09/2011
I concur.