

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

204655Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

8 NOV 2013

NDA: 204655

Drug Product Name

Proprietary: Nexium 24HR Delayed-Release Capsules Over-the-Counter 20 mg.

Non-proprietary: esomeprazole magnesium

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
30 May 2013	30 May 2013	30 May 2013	11 June 2013
27 September 2013	27 September 2013	N/A	N/A
31 October 2013	31 October 2013	N/A	N/A

Applicant/Sponsor

Name: AstraZeneca
Address: 1800 Concord Pike
PO Box 8355
Wilmington, DE 19803-8355

Representative: Judy Firor
Director Regulatory Affairs

Telephone: 302-886-2822

Name of Reviewer: Stephen E. Langille, Ph.D.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** Original submission
 - 2. SUBMISSION PROVIDES FOR:** An over the counter version of Nexium-Delayed Release Capsules.
 - 3. MANUFACTURING SITE:** AstraZeneca AB
Gartnavagen
SE-151 85 Sodertalje
Sweden
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Delayed release capsule
 - Oral
 - 20 mg
 - 5. METHOD(S) OF STERILIZATION:** Not applicable
 - 6. PHARMACOLOGICAL CATEGORY:** Treatment for frequent heartburn
- B. SUPPORTING/RELATED DOCUMENTS:** Not applicable
- C. REMARKS:** The submission was arranged in eCTD format. NDA 21-153 submitted for the prescription version of Nexium 24HR Delayed-Release Capsules did not receive a product quality microbiology review.

filename: N204655r1.doc

Executive Summary**I. Recommendations**

- A. Recommendation on Approvability** - Recommended for Approval
- 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** -
The applicant provided information regarding the conversion of a previously approved prescription version of Nexium 24HR Delayed-Release Capsules to an over-the counter version.
- B. Brief Description of Microbiology Deficiencies** -
No deficiencies were identified based upon the information provided.
- C. Assessment of Risk Due to Microbiology Deficiencies** –
Not applicable.
- D. Contains Potential Precedent Decision(s)**- Yes No

III. Administrative

- A. Reviewer's Signature** _____
Stephen E. Langille
Senior Microbiology Reviewer
- B. Endorsement Block**
Bryan Riley - Team Leader (Acting)
- C. CC Block**
N/A

7 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

STEPHEN E LANGILLE
11/08/2013

BRYAN S RILEY
11/08/2013
I concur.

PRODUCT QUALITY MICROBIOLOGY NON-STERILE DRUG PRODUCT FILING CHECKLIST

NDA Number: NDA 204-655 Applicant: AstraZeneca Letter Date: 30 May 2013

Drug Name: Nexium® 24 hr. NDA Type: Original Stamp Date: 30 May 2013

Dosage Form: Solid Oral Reviewer: Stephen E. Langille, Ph.D.

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		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?		X	
3	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?		X	
4	Has the applicant submitted the results of analytical method verification studies?		X	
5	Has the applicant submitted preservative effectiveness studies (if applicable)?		X	The drug product is (b) (4).
6	Is this NDA fileable? If not, then describe why.	X		

Additional Comments:

The applicant failed to provide a microbial limits specification or an adequate justification as to why a microbial limits specification is not necessary for this product.

Product Quality Microbiology Information Request:

Please provide the following information request to the applicant:

The justification for a waiver of microbial limits testing is not adequate.

- 1. Microbial limits testing as well as confirmation of the absence of specified microorganisms associated with the Nexium® 24 hr. delayed-release capsule should be provided. The test methods employed are to be identified and should conform to those described in USP <61> and <62>, respectively, or comparable standards. Please provide microbial limits acceptance criteria, a description of the methods and verification of the methods suitability for the finished drug product. The stability protocol should also be amended to include periodic microbial limits testing.*

2. *Alternatively, demonstrated process control including, but not limited to, the following may serve as an adequate justification for the elimination of microbial limits testing:*

- *The identification and justification of critical control points in the manufacturing process that could affect the microbial load of the drug product*
- *A description of the microbiological monitoring and acceptance criteria for the critical control points that you have identified.*
- *A description of the activities taken when microbiological acceptance criteria are not met at these control points*
- *The results of microbial limits testing performed on exhibit or stability batches of the drug product.*

Stephen E. Langille, Ph.D.

Reviewing Microbiologist

Date

John Metcalfe, Ph.D.

Microbiology Secondary Reviewer

Date

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

STEPHEN E LANGILLE
07/02/2013

JOHN W METCALFE
07/02/2013
I concur.