# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 203756Orig1s000

# MICROBIOLOGY REVIEW(S)

# Product Quality Microbiology Review

**10 October 2012**

**NDA:** 203-756/N000

**Drug Product Name**
**Proprietary:** Cometriq
**Non-proprietary:** cabozantinib (S)-malate

**Review Number:** 1

**Dates of Submission(s) Covered by this Review**

| Submit | Received | Review Request | Assigned to Reviewer |
|---|---|---|---|
| 08 March 2012 | 09 March 2012 | 30 May 2012 | 31 May 2012 |

**Submission History (for amendments only) –** NA

**Applicant/Sponsor**
**Name:** Exelixis, Inc.
**Address:** 210 East Grand Ave.
San Francisco, CA 94083
**Representative:** Kirk Rosemark, RAC
VP, Regulatory Affairs
**Telephone:** (650) 837-7038

**Name of Reviewer:** Denise A. Miller

**Conclusion:** Approve

# Product Quality Microbiology Data Sheet

**A. 1. TYPE OF SUBMISSION:** Original Drug Application

**2. SUBMISSION PROVIDES FOR:** This is an original application for the commercial manufacture of the oral drug product.

**3. MANUFACTURING SITE:**

(b) (4)

[redacted]

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

- Dosage Form: Capsules packaged in either a blister package system in three card configurations; a 140mg, 100mg and a 60 mg dosage card. The 20 mg capsule is also provided in a bottle packaging system.
- Route of Administration: Oral
- Strength/Potency: 20 mg and 80 mg/capsule

**5. METHOD(S) OF STERILIZATION:** NA

**6. PHARMACOLOGICAL CATEGORY:** Anti-cancer treatment for unresectable, locally advanced, or metastatic medullary thyroid cancer.

**B. SUPPORTING/RELATED DOCUMENTS:** NA

**C. REMARKS:**
This NDA was a rolling submission for which the CMC portion was received on 28 May 2012.

**filename:** N203756N000R1.doc

# Executive Summary

## I. Recommendations

**A. Recommendation on Approvability** - Recommend to approve from a quality microbiology standpoint.

**B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** - NA

## II. Summary of Microbiology Assessments

**A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology –** This is a non-sterile solid oral product. (b) (4)

**B. Brief Description of Microbiology Deficiencies** - None

**C. Assessment of Risk Due to Microbiology Deficiencies** - NA

## III. Administrative

**A. Reviewer's Signature** _____

Denise A. Miller,
Microbiologist, OPS/NDMS

**B. Endorsement Block** _____

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

**C. CC Block**

N/A

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/s/

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DENISE A MILLER
10/11/2012

STEPHEN E LANGILLE
10/16/2012

# PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number: 203-756** **Applicant: Exelixis, Inc** **Letter Date:** 08 March 2012

**Drug Name: cabozantinib (XL184)** **NDA Type: 505 (b)(1)** **Stamp Date:** 09 March 2012

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? | √ | | |
| 2 | Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product? | √ | | |
| 3 | Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product? | √ | | |
| 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? | | √ | |
| 5 | Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies? | NA | | |
| 6 | Has the applicant submitted microbiological specifications for the drug product and a description of the test methods? | √ | | |
| 7 | Has the applicant submitted the results of analytical method verification studies? | √ | | |
| 8 | Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions? | NA | | |
| 9 | Is this NDA fileable? If not, then describe why. | √ | | |

Additional Comments: This in a non-sterile oral drug product.
This application is a rolling submission in which the final portion was submitted on 29 May 2012.

Denise A. Miller
Microbiologist, OPS/NDMS Date

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

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/s/

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DENISE A MILLER
06/27/2012

STEPHEN E LANGILLE
06/27/2012