CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203388Orig1s000

MICROBIOLOGY REVIEW(S)
Product Quality Microbiology Review

21 December 2011

NDA: 203388/N-000

Drug Product Name
Proprietary: N/A.
Non-proprietary: USAN Vismodegib.

Review Number: 1.

Dates of Submission(s) Covered by this Review

<table>
<thead>
<tr>
<th>Submit</th>
<th>Received</th>
<th>Review Request</th>
<th>Assigned to Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>08 SEP 2011</td>
<td>08 SEP 2011</td>
<td>14 SEP 2011</td>
<td>15 JUN 2011</td>
</tr>
<tr>
<td>17 OCT 2011</td>
<td>18 OCT 2011</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Applicant/Sponsor
Name: Genentech, Inc.
Address: 1 DNA Way MS#241B
South San Francisco, CA 94080-4990
Representative: Wen Liu, Ph.D.
Telephone: 650-467-1535

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

Conclusion: Recommend approval.
Product Quality Microbiology Data Sheet

   2. SUBMISSION PROVIDES FOR: Marketing authorization.
   3. MANUFACTURING SITE: 

   4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
      - Hard capsule.
      - Oral administration.
      - 150 mg.

   5. METHOD(S) OF STERILIZATION: The subject drug product is non-sterile.

   6. PHARMACOLOGICAL CATEGORY: The subject drug product is indicated for the treatment of advanced basal cell carcinoma.

B. SUPPORTING/RELATED DOCUMENTS: None.

C. REMARKS:
The subject application is submitted electronically in CTD format.

The following Microbiology Information Request was forwarded to the applicant in the 74 Day Letter:

It is understood that the microbial limits tests will be performed according to USP<61> and <62>. Provide the test methods for microbial limits testing along with data sets verifying the suitability of use of the stated microbial limits tests with the subject drug product.

The applicant provided a response to this IR on 17 October 2011. The responses are summarized and evaluated in appropriate sections of this review.

File Name: N203388N000R1.doc
Executive Summary

I. Recommendations

A. Recommendation on Approvability – NDA 203388 is recommended for approval on the basis of issues pertaining to 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

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.

B. Endorsement Block

Bryan S. Riley, Ph.D.

C. CC Block

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

/s/

JOHN W METCALFE
12/21/2011

BRYAN S RILEY
12/21/2011
I concur.
## PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number:** 203388  
**Applicant:** Genentech, Inc.  
**Letter Date:** 08 September 2011  
**Drug Name:** Vismodegib  
**NDA Type:** 505(b)(1)  
**Stamp Date:** 08 September 2011

The following are necessary to initiate a review of the NDA application:

<table>
<thead>
<tr>
<th>Content Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>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?</td>
<td>X</td>
<td></td>
<td>Module 3.2.P.</td>
</tr>
<tr>
<td>2. Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?</td>
<td>X</td>
<td></td>
<td>Module 3.2.P.3.3.</td>
</tr>
<tr>
<td>3. Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?</td>
<td>X</td>
<td></td>
<td>N/A. Product is non-sterile.</td>
</tr>
<tr>
<td>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?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?</td>
<td>X</td>
<td></td>
<td>N/A. Product is a capsule and is non-sterile.</td>
</tr>
<tr>
<td>6. Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?</td>
<td>X</td>
<td></td>
<td>Table P.5.1-1.</td>
</tr>
<tr>
<td>7. Has the applicant submitted the results of analytical method verification studies?</td>
<td>X</td>
<td></td>
<td>This will be requested but is not a reason for RTF.</td>
</tr>
<tr>
<td>8. Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?</td>
<td>X</td>
<td></td>
<td>N/A.</td>
</tr>
<tr>
<td>9. Is this NDA fileable? If not, then describe why.</td>
<td>X</td>
<td></td>
<td></td>
</tr>
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Additional Comments:

The following comment should be forwarded to the applicant in the 74 Day Letter:

*It is understood that the microbial limits tests will be performed according to USP<61> and <62>. Provide the test methods for microbial limits testing along with data sets verifying the suitability of use of the stated microbial limits tests with the subject drug product.*

John W. Metcalfe, Ph.D.  
Bryan S. Riley, Ph.D.
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/s/

 JOHN W METCALFE
 09/30/2011
 The application is filable from a product quality microbiology perspective.

 BRYAN S RILEY
 09/30/2011
 I concur.