CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202324Orig1s000

MICROBIOLOGY REVIEW(S)
Product Quality Microbiology Review

06 January 2012

NDA: 202-324/N000

Drug Product Name
Proprietary: INLYTA
Non-proprietary: Axitinib

Review Number: 2

Dates of Submission(s) Covered by this Review

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<th>Received</th>
<th>Review Request</th>
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Submission History (for amendments only) –

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<td>14 April 2011</td>
<td>1</td>
<td>12 December 2011</td>
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 Applicant/Sponsor
Name: Pfizer, Inc.
Address: 10646 Science enter Drive
         San Diego CA 92121
Representative: Alison Russell, Worldwide Regulatory Strategy
Telephone: (858) 622-3234

Name of Reviewer: Denise A. Miller

Conclusion: Approve
Product Quality Microbiology Data Sheet

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

2. SUBMISSION PROVIDES FOR: The manufacture of a tablet drug product.

3. MANUFACTURING SITE:

Pfizer Manufacturing Deutschland GmbH
Betriebsstatte Freiburg
Mooswaldallee 1
79090 Freiburg Germany

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
   ➢ Tablet
   ➢ Oral, Immediate Release
   ➢ 1 and 5 mg/tablet

5. METHOD(S) OF STERILIZATION: not sterile

6. PHARMACOLOGICAL CATEGORY: tyrosine kinase inhibitor used for the treatment for advanced renal cell carcinoma

B. SUPPORTING/RELATED DOCUMENTS: NA

C. REMARKS:
   1) Application is in e-CTD format.

filename: N202324N000R2.doc
Executive Summary

I. Recommendations

A. Recommendation on Approvability – The recommendation is to approve this submission 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 – Formulated powders are film coated and packaged. This is a non-sterile drug product.

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, NDMS

B. Endorsement Block ______________________________
   Stephen E. Langille
   Senior Microbiologist, NDMS

C. CC Block
   N/A
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/s/

DENISE A MILLER
01/09/2012

STEPHEN E LANGILLE
01/09/2012
Product Quality Microbiology Review

12 December 2011

NDA: 202-324/N000

Drug Product Name
Proprietary: INLYTA
Non-proprietary: Axitinib

Review Number: 1

Dates of Submission(s) Covered by this Review

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Submission History (for amendments only) – NA

Applicant/Sponsor
Name: Pfizer, Inc.
Address: 10646 Science enter Drive
San Diego CA 92121
Representative: Alison Russell, Worldwide Regulatory Strategy
Telephone: (858) 622-3234

Name of Reviewer: Denise A. Miller

Conclusion: Approvable pending resolution of quality microbiological deficiencies listed on page 9.
Product Quality Microbiology Data Sheet

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

2. SUBMISSION PROVIDES FOR: The manufacture of a tablet drug product.

3. MANUFACTURING SITE:

   Pfizer Manufacturing Deutschland GmbH
   Betriebsstatte Freiburg
   Mooswaldallee 1
   79090 Freiburg Germany

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
   - Tablet
   - Oral, Immediate Release
   - 1 and 5 mg/tablet

5. METHOD(S) OF STERILIZATION: not sterile

6. PHARMACOLOGICAL CATEGORY: tyrosine kinase inhibitor used for the treatment for advanced renal cell carcinoma

B. SUPPORTING/RELATED DOCUMENTS: NA

C. REMARKS:
   1) Application is in e-CTD format.
   2) Consult requested evaluation of Pfizer’s request exclude microbial limit testing as a release test. The testing was also excluded in the stability program.
   3) Information request #1 was sent on 26 September 2011. A response was received on 28 October 2011.

filename: N202324N000R1.doc
Executive Summary

I. Recommendations

A. Recommendation on Approvability - This submission is approvable pending resolution of microbiological deficiencies.

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 – Formulated powders are film coated and packaged. This is a non-sterile drug product.

B. Brief Description of Microbiology Deficiencies – Lack of microbial testing on the final product for either release or stability was not sufficiently justified.

C. Assessment of Risk Due to Microbiology Deficiencies – There is a small risk to the patient to ingest contaminated product as a result of the deficiencies.

III. Administrative

A. Reviewer's Signature _____________________________
   Denise A. Miller
   Microbiologist, NDMS

B. Endorsement Block ______________________________
   Bryan S. Riley,
   Senior Microbiologist, NDMS

C. CC Block
   N/A

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/s/

DENISE A MILLER
12/12/2011

BRYAN S RILEY
12/13/2011
I concur.
**CMC MICROBIOLOGY AND STERILITY ASSURANCE**

**REVIEW REQUEST**

**TO (Division/Office):** New Drug Microbiology Staff  
*Email to:* CDER OPS IO MICRO  
*Mail to:* WO Bldg 51, Room 4193

**FROM:** Don Henry  
*PROJECT MANAGER (if other than sender):*

**REQUEST DATE** 5/17/2011  
**IND NO.**  
**NDA NO.** 202324  
**TYPE OF DOCUMENT** Original NDA submission  
**DATE OF DOCUMENT** 4/14/2011

**NAMES OF DRUG** axitinib  
**PRIORITY CONSIDERATION** standard  
**PDUFA DATE** February 14, 2012  
**DESIRED COMPLETION DATE** September 14, 2011

**NAME OF APPLICANT OR SPONSOR:** Pfizer

**GENERAL PROVISIONS IN APPLICATION**

- ☐ 30-DAY SAFETY REVIEW NEEDED  
- ☐ NDA FILING REVIEW NEEDED BY: ____________  
- ☐ BUNDLED  
- ☑ DOCUMENT IN EDR  
- ☐ CBE-0 SUPPLEMENT  
- ☐ CBE-30 SUPPLEMENT  
- ☐ CHANGE IN DOSAGE, STRENGTH / POTENCY

**COMMENTS / SPECIAL INSTRUCTIONS:**

This is a NME. For this solid oral tablet, the sponsor has provided justification for not including the microbial limits testing as part of the specification.

**SIGNATURE OF REQUESTER**  
Don L. Henry

**REVIEW REQUEST DELIVERED BY (Check one):**

- ☐ DARRTS  
- ☐ EDR  
- ☐ E-MAIL  
- ☐ MAIL  
- ☐ HAND

**DOCUMENTS FOR REVIEW DELIVERED BY (Check one):**

- ☐ EDR  
- ☐ E-MAIL  
- ☐ MAIL  
- ☐ HAND

Reference ID: 2948110
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/s/

DON L HENRY
05/17/2011