CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203469Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

September 22, 2012

NDA: 203469

Drug Product Name
Proprietary: Iclusig
Non-proprietary: Ponatinib

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
7/30/2012	7/30/2012	8/13/2012	8/24/2012
10/16/2012	10/16/2012	N/A	N/A

Submission History (for amendments only): None

Applicant/Sponsor
Name: Ariad Pharmaceuticals, Inc.
Address: 26 Landsdowne St., Cambridge, MA 02139-4234
Representative: Daniel Bollag, Sr. V.P., Reg. Affairs
Telephone: 617 494 0400

Name of Reviewer: Steven P. Donald, M.S.

Conclusion: Recommended for approval.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: NDA

2. SUBMISSION PROVIDES FOR: Manufacture of an oral drug product

3. MANUFACTURING SITE:

(b) (4)

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: film-coated tablet, oral, 15 mg and 45 mg

5. METHOD(S) OF STERILIZATION: Non-sterile

6. PHARMACOLOGICAL CATEGORY: anti-neoplastic for CML or ALL

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: This is an eCTD submission. An information request was provided to the sponsor on 10/10/2012 and a response dated 10/16/2012 was received by this reviewer. See Sections 2.5 and 8.3 for information related to the information request and related response.

filename: N203469r1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability –
NDA 203469 is recommended for approval from the standpoint of product quality microbiology.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable –
N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -
The drug product is a tablet for oral administration. The tablet contents are (b) (4) before tableting.

B. Brief Description of Microbiology Deficiencies -
No deficiencies were identified based upon the information provided.

C. Assessment of Risk Due to Microbiology Deficiencies -
N/A

III. Administrative

A. Reviewer's Signature _____
Steven P. Donald, M.S.

B. Endorsement Block_____
Bryan Riley, Ph.D.
Team Leader

C. CC Block
N/A

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

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/s/

STEVEN P DONALD
10/24/2012

BRYAN S RILEY
10/24/2012
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 203469 | **Applicant: Ariad Pharmaceuticals, Inc** | **Letter Date:** 7/30/2012

Drug Name: Inclusig (ponatinib) | **NDA Type:** 505(b)(1) | **Stamp Date:** 7/30/2012

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?	x		Information is organized but microbiology information is limiting.
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	x		(b) (4) Microbiology controls not described here.
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?		x	Bacterial enumeration performed for validation batches and is acceptable; validation studies are not presented but are referenced to USP <61> and <62>
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?			N/A
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?			No microbiological specifications for drug product. The applicant proposes not to perform routine microbiological testing of the drug product; (b) (4)

	Content Parameter	Yes	No	Comments
				activity is reported; compendial excipient microbiological information is provided in CofA of each. This information helps support the proposal but additional information may be required in the NDA.
7	Has the applicant submitted the results of analytical method verification studies?		x	No microbiological methods verification information provided.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			N/A
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?			N/A
10	Is this NDA fileable? If not, then describe why.	x		

Additional Comments:
Under Justification of specifications (justification-of-specifications.pdf, pg. 14/18) It is proposed not to include microbial limits in the specifications of (b) (4) drug product. While the NDA is fileable, we will have comments on the applicant's approach to supporting this proposal. A request for additional information will be made in the review of the NDA.

Reviewing Microbiologist: Steven P. Donald, M.S. Date

Microbiology Team Leader: Bryan Riley, Ph.D. Date

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/s/

STEVEN P DONALD
09/05/2012

BRYAN S RILEY
09/05/2012
I concur.