# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 206088Orig1s000

# MICROBIOLOGY / VIROLOGY REVIEW(S)

# Product Quality Microbiology Review

**25 FEB 2014**

**NDA:** 206088

**Drug Product Name**
**Proprietary:** Otezla (proposed)
**Non-proprietary:** Apremilast tablets

**Review Number:** 1

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

| Submit | Received | Review Request | Assigned to Reviewer |
|---|---|---|---|
| 23 SEP 2013 | 23 SEP 2013 | 01 OCT 2013 | 03 OCT 2013 |
| 21 NOV 2013 | 21 NOV 2013 | 21 NOV 2013 | 21 NOV 2013 |

**Applicant/Sponsor**
**Name:** Celgene Corporation
**Address:** 86 Morris Avenue, Summit NJ 07901
**Representative:** Gerlee D. Thomas
**Telephone:** (732)-652-6582

**Name of Reviewer:** Neal J. Sweeney, Ph.D.

**Conclusion:** Recommended for Approval

# Product Quality Microbiology Data Sheet

**A. 1. TYPE OF SUBMISSION:** Type 1, NME, Original NDA

**2. SUBMISSION PROVIDES FOR:** Marketing of new drug product

**3. MANUFACTURING SITES:**
Celgene International Sarl, Route de Perreux 1, 2017 Boudry, Switzerland
(b) (4)

**4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Non-sterile oral dose Apremilast film-coated tablets, 10 mg, 20 mg, and 30 mg

**5. METHOD(S) OF STERILIZATION:** N/A (non-sterile tablets)

**6. PHARMACOLOGICAL CATEGORY:** Apremilast is a small-molecule inhibitor of phosphodiesterase 4 (PDE4), and the proposed indication is for treatment of moderate to severe plaque psoriasis in adult patients who are candidates for phototherapy or systemic therapy.

**B. SUPPORTING/RELATED DOCUMENTS:** NDA 205437

**C. REMARKS:** NDA 206088 references pending NDA 205437 for CMC information for the identical drug product (Apremilast tablets, 10 mg, 20 mg, and 30 mg). In a June 13, 2013 teleconference (for NDA 206088) FDA/CDER/Division of Dermatology and Dental Products (DDDP) agreed that Celgene could cross reference the CMC information in Module 2.3 and Module 3 to NDA 205437 submitted March 21, 2013 to the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP). Additionally, any changes made to NDA 205437 as a result of responding to CMC Information Requests during the review by DPARP will be communicated to DDDP for information only, and the 206088 Module 2.3 – Introduction will also be updated when applicable. Upon approval of both NDA 205437 and 206088, any post-approval supplements will be submitted to NDA 205437 with a notification letter to NDA 206088 at the same time.

A Product Quality Microbiology Review was requested for NDA 206088. However, a Microbiology review was not initially requested for NDA 205437, as this NDA was filed prior to the OPS/ONDQA NDA "Pilot Program". Because NDA 205437 included microbial limits (b) (4)

The applicant subsequently withdrew the (b) (4) from the drug product specifications and accordingly submitted revised release and stability specifications, as well as (b) (4) test results for both NDAs. NDA 205437 was recommended for approval from the standpoint of Product Quality Microbiology. (See NDA 205437 Product Quality Microbiology Review, dated Nov. 25, 2013.)

**filename:** N206088R1.doc

# Executive Summary

## I. Recommendations

**A. Recommendation on Approvability** - Recommended for Approval.

**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 –** Non-sterile tablet manufacturing utilizing (b) (4)

**B. Brief Description of Microbiology Deficiencies –** Based upon the information provided, no microbiology deficiencies were identified.

**C. Assessment of Risk Due to Microbiology Deficiencies –** Not applicable

**D. Contains Potential Precedent Decision(s)-** ☐ **Yes** ☒ **No**
(If yes, provide a brief description and a reference to the page where the precedent is discussed in depth)

## III. Administrative

**A. Reviewer's Signature** _____
Neal J. Sweeney, Ph.D.

**B. Endorsement Block** _____
Bryan S. Riley, Ph.D. Acting Team Leader

**C. CC Block**
N/A

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/s/

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NEAL J SWEENEY
02/26/2014

BRYAN S RILEY
02/26/2014
I concur.