DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-880/S-001

Celgene Corporation
86 Morris Avenue
Summit, New Jersey 07901

Attention: Gretchen Toolan
Director, Regulatory Affairs

Dear Ms. Toolan:

Please refer to your supplemental new drug application (NDA) dated December 29, 2005, received December 30, 2005, submitted under section 505 (b) of the Federal Food, Drug, and Cosmetic Act for Revlimid® (lenalidomide) capsules 5 mg, 10 mg, 15 mg and 25 mg.

We acknowledge receipt of your submissions dated January 4, 13, 18, 27 and 31, 2006; February 24, 2006; March 10, 14, 22, and 23, 2006; April 6, 7, 18, 21, and 24, 2006; May 2, 5, 9, 10, 15, 19, 22, 24, 26 and 31, 2006; June 2, 9, 22 and 23, 2006.

This supplemental new drug application, considered for approval under 21 CFR 314.520 (Subpart H), provides for the use of Revlimid® 15 mg and 25 mg capsules in combination with dexamethasone for the treatment of multiple myeloma patients who have received at least one prior therapy.

We have completed our review of this supplemental application, as amended. It is approved under the provisions of 21 CFR 314.520 (Subpart H), effective on the date of this letter, for use as recommended in the agreed upon labeling text, required patient labeling, and the components of the RevAssist^{SM} Risk Minimization Action Plan (RiskMAP).

We also remind you of your post marketing study commitments specified in your submission dated June 26, 2006. These commitments, along with any completion dates agreed upon, are listed below.

A. Conduct an epidemiologic study to address the questions detailed below:

1. What is the failure rate for each of the different types of thromboembolic prophylaxis (e.g. antiplatelet or anticoagulant therapy) for multiple myeloma patients treated with a lenalidomide-containing regimen?

2. What is the failure rate for each type of Deep Vein Thrombosis (DVT) treatment (dose-adjusted heparin, low molecular weight heparin, coumadin) for those patients with multiple myeloma and a DVT who continue to receive ongoing treatment with lenalidomide?

3. What is the failure rate for each type of post-DVT thromboembolic prophylaxis for those patients with multiple myeloma and a DVT who continue to receive ongoing treatment with lenalidomide?

This prospective epidemiologic study will enroll select patients identified in the RevAssist[SM] program, and collect the necessary additional data on these patients to further evaluate occurrences of thrombosis and anticoagulant use. The final details of the design will be as agreed upon between the Agency and Celgene.

Protocol Submission:	by December 2006
Study Start:	by June 2007
Final Report Submission:	by December 2012

B. Provide updated time to progression (TTP) and survival data for studies MM-009 and MM-010 when 194 death events have occurred in each study.

Protocol Submission:
MM-009 original protocol submitted November 26, 2002 Serial No. 92.
Amendment No. 2 submitted April 29, 2005 Serial No. 550

MM-010 original protocol submitted December 10, 2002, Serial No. 96.
Amendment No. 2 submitted May 12, 2005, Serial No. 557.

Study Start:

MM-009	September 22, 2003
MM-010	February 11, 2003

Final Report Submission: by December 2008

C. Provide a proposal to assess for QTc prolongation.

Proposal Submission: by December 2006

D. Conduct a bioequivalence study comparing the 25 mg capsule (test) to 5 X 5 mg capsules (reference).

Protocol Submission:	by December 2006
Study Start:	by March 2007
Final Report Submission:	by December 2007

We also remind you of your required post marketing study commitments specified in your submission dated December 21, 2005 for Revlimid® for use in myelodysplastic syndromes (MDS), approved on December 27, 2005. These commitments, along with any completion dates agreed upon, are listed below.

1. The embryo-fetal toxicity assessment of Revlimid® has not been adequately addressed. You have agreed to provide adequate information for this assessment in appropriate models designed to fully assesses the possible toxicity of Revlimid®. You indicated you plan to conduct these studies in two different species that are appropriate to assess the full range of thalidomide embryo-fetal effects. As discussed, the rat is not an acceptable model. If the study with lenalidomide in the first species shows clear evidence of teratogenesis, than a confirmatory study will not be necessary. Although not generally considered “definitive” test systems for pharmaceutical products, additional studies of an

exploratory nature on the embryo-fetal effects of lenalidomide (e.g., frog embryo assay; FETAX assay), may be useful.

Protocol Submission:	06/06
Study Start:	09/06
Final Report Submission:	12/07

2. You have agreed to submit the study report and data from the ongoing study, CC-5013-MDS-004, a randomized, double-blind, placebo-controlled, multicenter, 3-arm study of the efficacy and safety of 2 doses of lenalidomide (5 mg daily versus 10 mg day 21 days of a 28 day cycle) versus placebo in red blood cell (RBC) transfusion-dependent patients with low-or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenetic abnormality when completed.

Protocol Submission:	03/05
Study Start:	08/05
Final Report Submission:	12/08

3. Following Revlimid® dosing, approximately 2/3 of lenalidomide is excreted as unchanged drug in urine. In multiple myeloma patients with mild renal impairment, exposure (plasma AUC) was 56% higher than in similar patients with normal renal function who received the same dose. Based on these data, you have agreed to conduct a study to determine the pharmacokinetics of lenalidomide in subjects with renal impairment. To assist with the study design, please refer to the FDA Guidance, "Pharmacokinetics in Patients with Impaired Renal Function."

Protocol Submission:	11/04
Study Start:	03/06
Final Report Submission:	12/07

4. Regarding the Evaluation/Surveillance Plan:

   You have agreed to submit a Pregnancy Exposure follow-up plan which will document your plan to follow-up pregnancy exposures to their outcome. This plan may be submitted as a post-marketing commitment.

   Plan submission: 06/01/06

   You have agreed to submit an Evaluation Plan of RevAssist^{SM} to FDA within 3 to 6 months of approval. Please include, at a minimum, plans to study the Pharmacy Audit Plan, Outcomes of Pregnancy Exposures, and the Knowledge Surveys of physicians, nurses, and patients.

   Plan submission: 06/01/06

5. You have agreed to submit all exposed pregnancies within 15 days of receipt as 15 day expedited reports.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you must include a status summary of each commitment

in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments should be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

Pursuant to 21 CFR Part 208, FDA has determined that Revlimid® poses a serious and significant public health concern requiring distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Revlimid®. FDA has determined that Revlimid® is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use Revlimid®. In addition, patient labeling could help prevent serious adverse events related to use of the product. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Revlimid®.

The final printed labeling (FPL) must be identical to the enclosed labeling (package insert, Medication Guide and immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-880**." Approval of this submission by FDA is not required before the labeling is used.

Submit content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt and verification, we will transmit that version to the National Library of Medicine for posting on the DailyMed website.

As part of the approval under Subpart H, we acknowledge that you submitted to the Agency your promotional materials (both promotional labeling and advertisements) that are to be used within the first 120 days after approval. In addition, as required by 21 CFR 314.550, after the initial 120 day period following this approval, you must submit all subsequent promotional labeling as well as advertisements at least 30 days before the intended time of initial distribution of the labeling or initial publication of the advertisement. Send one copy to the Division of Drug Oncology Products and two copies of the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

We remind you that you must comply with the reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm

If you have any questions, call Carl Huntley, Regulatory Project Manager, at (301) 796-1372.

Sincerely,

{See appended electronic signature page}

Robert Justice, M.D.
Division Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Office of New Drugs
Center for Drug Evaluation and Research
Food and Drug Administration

Enclosure -Label

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

/s/

Robert Justice

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