DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022393/S-004

ACCELERATED APPROVAL

Celgene Corporation
Attention: Jean Nichols, Ph.D., Corporate VP
One Broadway
14th Floor
Cambridge, MA, 02142

Dear Dr. Nichols:

Please refer to your Supplemental New Drug Application (sNDA) dated December 17, 2010, received December 17, 2010 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Istodax® (romidepsin) for Injection.

We acknowledge receipt of your amendments dated January 31, February 2, March 7 and 9, April 06, 13 (2), and 20, May 2, and 27, June 7, and 16, 2011.

This "Prior Approval" supplemental new drug application proposes a new indication, for the treatment of peripheral T-cell lymphoma (PTCL) in 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 accelerated approval regulations (21 CFR 314.500), effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the patient package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at

http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

ACCELERATED APPROVAL REQUIRENTS

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies/clinical trials to verify and describe clinical benefit. We remind you of your postmarketing requirement specified in your submission dated May 27, 2011. This requirement, along with required completion dates, is listed below.

1775-1 To perform a randomized, blinded, controlled trial of previously untreated PTCL patients randomized to treatment with CHOP or to romidepsin plus CHOP, with Progression Free Survival as the primary efficacy endpoint. Final Progression Free Survival (PFS) data will be available at Trial Completion. For efficacy, the final analysis of the primary endpoint, PFS, will be performed when the trial has experienced the planned number of events. Using the same data cutoff date, an interim analysis of Overall Survival will be performed and included in the study report.

The timetable you submitted on May 27, 2011, states that you will conduct this trial according to the following timetable:

Final Protocol:	April 2012
Trial Completion:	April 2018
Final Report:	April 2019

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart H Postmarketing Requirement(s)**."

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

1775-2 Submit the results of the analysis showing either the significant reduction or elimination of the presence of residual (b) (4)

The timetable you submitted on May 27, 2011, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	December 2011
Study Completion:	March 2012
Final Report Submission:	March 2013

In accordance with your agreement in your reply dated May 27, 2011, to the FDA TC of May 16, 2011, you agree to continue to follow patients enrolled in the front-line trial of CHOP +/- romidepsin in PTCL for overall survival (OS):

1775-3 Submit the hypothesis for the final Overall Survival (OS) analysis from the required Clinical Trial (PMR), and the final OS analysis will be performed in accordance with the OS plan. The Study Completion refers to the Statistical Analysis Plan for the required Clinical PMR, it will be April 2021.

The timetable you submitted on June 16, 2011, states that you will conduct this analysis according to the following schedule:

Final Protocol Submission:	April 2019
Study Completion:	April 2021
Final Report Submission:	December 2021

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 should 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/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

Immediately submit all promotional materials (both promotional labeling and advertisements) to be used within the first 120 days after approval. Send one copy to the Division of Hematology 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
5901-B Ammendale Road
Beltsville, MD 20705-1266

In addition, as required by 21 CFR 314.550, submit all subsequent promotional materials at least 30 days before the intended time of initial distribution of labeling or initial publication of the advertisement. Send two copies of the promotional materials and the package insert to the address above.

REPORTING REQUIREMENTS

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

If you have any questions, call Lisa Skarupa, Regulatory Project Manager, at (301) 796-2219.

Sincerely,

{See appended electronic signature page}

Robert C. Kane, M.D.
Deputy Director for Safety (Acting)
Division of Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

ENCLOSURE(S): Content of Labeling

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

/s/

ROBERT C KANE
06/16/2011