DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 021217/S-005

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Mallinckrodt, Inc.
675 McDonnell Boulevard
Hazelwood, MO 63042

Attention: Linda F. Noa, M.S., RAC
Senior Manager, Regulatory Affairs

Dear Ms. Noa:

Please refer to your Supplemental New Drug Application (sNDA) dated and received September 20, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for EXALGO (hydromorphone HCl) 8, 12, 16, and 32mg Extended-Release Tablets.

This Prior Approval supplemental new drug application proposes revisions to the **NONCLINICAL TOXICOLOGY**: **Carcinogenesis, Mutagenesis, Impairment of Fertility** section of the Package Insert.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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 and Medication Guide, 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 that includes labeling changes 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).

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We have received your submissions dated February 22, March 26, and September 21, 2012, containing the final reports and datasets for the following postmarketing requirements listed in the March 1, 2010, approval letter.

1568-3 Carcinogenicity study in mice
1568-4 Carcinogenicity study in rat

We have reviewed your submissions and conclude that the above requirements were fulfilled.

We remind you that there is a postmarketing requirement listed in the March 4, 2011, postapproval postmarketing requirement letter that is still open.

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 Diana L. Walker, Ph.D., Sr. Regulatory Health Project Manager, at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Bob A. Rappaport, M.D.
Director
Division of Anesthesia, Analgesia,
and Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE:
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/

BOB A RAPPAPORT
03/18/2013