DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 020281/S-032
NDA 020281/S-033

SUPPLEMENT APPROVAL

Ortho-McNeil-Janssen Pharmaceuticals, Inc.
1000 Route 202 South
P.O. Box 300
Raritan, NJ 08869-0602

Attention: Melissa L. Gannon
Associate Director, Regulatory Affairs

Dear Ms. Gannon:

Please refer to your supplemental new drug applications dated June 15, 2006, received June 15, 2006 for S-032 and dated August 7, 2008, received August 7, 2008 for S-033, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for ULTRAM® (tramadol hydrochloride) tablets.

Supplement 032 was submitted in response to the September 2, 2005 letter from us requesting an update to the **WARNINGS** section of the label to provide for safe and effective use of the drug.

Supplement 033, a "Changes Being Effected" supplemental new drug application, proposes the addition of serotonin syndrome to the **WARNINGS** section of the package insert and changes to the **DESCRIPTION** and **PRECAUTIONS** section of the package insert.

We completed our review of these applications. They are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling text for the package insert. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "**SPL for approved NDA 020281/S-032, 020281/S-033**."

PROMOTIONAL MATERIALS

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in

the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the following address or by facsimile at 301-847-8444:

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 under 21 CFR 314.81(b)(3)(i), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA-2253, directly to the above address. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5600 Fishers Lane, Suite 12B05
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Kathleen Davies, Regulatory Project Manager, at (301) 796-2205.

Sincerely,

{See appended electronic signature page}

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

Enclosure – Package Insert

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20281	SUPPL-32	ORTHO MCNEIL JANSSEN PHARMACEUTICALS INC	ULTRAM (TRAMADOL HCL) TABLETS
NDA-20281	SUPPL-33	ORTHO MCNEIL JANSSEN PHARMACEUTICALS INC	ULTRAM (TRAMADOL HCL) TABLETS

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
09/09/2009