DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-029 **NDA APPROVAL**

Hisamitsu Pharmaceutical Co., Inc.
Attention: Yoshinobu Higashi
Manager of International Development
100 Campus Drive, Suite 117
Florham Park, NJ 07932

Dear Mr. Higashi:

Please refer to your new drug application (NDA) dated February 27, 2006, received February 27, 2006, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Salonpas Pain Relief Patch (10% methyl salicylate & 3% l-menthol) topical patch.

We acknowledge receipt of your submissions dated December 28, 2006, January 24, March 15, July 25, August 17, September 14, and November 16, 2007, and January 4, 11, 23 and 31, and February 11, 13, 15, 19 and 20, 2008.

The July 25, 2007 submission constituted a complete response to our December 27, 2006 action letter.

This new drug application provides for the nonprescription use of Salonpas Pain Relief Patch (10% methyl salicylate & 3% l-menthol) topical patch and Salonpas Arthritis Pain (10% methyl salicylate & 3% l-menthol) topical patch for the temporary relief of mild to moderate aches and pains of muscles and joints associated with arthritis, simple backache, strains, bruises and sprains.

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

LABELING

Submit final printed labeling as soon as it is available, but no more than 30 days after it is printed. The final printed labeling (FPL) must be identical to the enclosed labeling for Salonpas Pain Relief Patch (5- and 15-count carton and 5-count pouch labels submitted February 20, 2008) and Salonpas Arthritis Pain (5- and 15-count carton and 5-count pouch labels submitted February 15, 2008), and must be in the "Drug Facts" format (21 CFR 201.66), where applicable.

The final printed labeling should be submitted electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).*

Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Labeling for approved NDA 22-029**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

PEDIATRIC RESEARCH EQUITY ACT (PREA) POSTMARKETING STUDY COMMITMENT

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. We are waiving the pediatric study requirement for ages 0 up to 3 years because there is evidence strongly suggesting that the drug would be unsafe in this pediatric age group due to the toxicity of methyl salicylate.

We are deferring submission of your pediatric study for ages 3 to 17 years for this application because the drug is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the Food, Drug, and Cosmetic Act is a required postmarketing study commitment. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Food, Drug, and Cosmetic Act. 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, number of patients entered into each study. This commitment is listed below.

1. Deferred pediatric study under PREA for the temporary relief of mild to moderate aches and pains of muscles and joints associated with arthritis, simple backache, strains, bruises and sprains in pediatric patients ages 3 to 17.

   Final Report Submission: February 20, 2012

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**."

POSTMARKETING AGREEMENTS

We remind you of your postmarketing agreements in your submissions dated February 27, 2006 and September 12, 2006. These agreements are listed below.

1. Develop a dissolution method to replace the originally-proposed *in vitro* release method. Submit the final method and supporting data to the FDA within six (6) months of the date of this letter.

2. Evaluate the loss of drug substance during the validation campaign for commercial scale production and make appropriate adjustments to the percent overage of drug substances as necessary. Evaluate an additional five lots and make further adjustments as indicated. Submit a report detailing this work to the FDA within six (6) months of the date of this letter.

PROMOTIONAL MATERIALS

Please submit one market package of the drug product when it is available.

LETTERS TO HEALTH CARE PROFESSIONALS

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

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

STABILITY/SHELF-LIFE

An expiration dating period of 36 months when stored at 25°C with excursions permitted to 15-30°C is granted for Salonpas.

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, contact Geri Smith, Regulatory Project Manager, at geri.smith@fda.hhs.gov or (301) 796-2204.

Sincerely,
{See appended electronic signature page}

Joel Schiffenbauer, M.D.
Deputy Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

Sincerely,
{See appended electronic signature page}

Sharon Hertz, M.D.
Deputy Director
Division of Anesthesia, Analgesia and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

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

/s/

Joel Schiffenbauer
2/20/2008 03:50:08 PM

Sharon Hertz
2/20/2008 03:54:10 PM