DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA # 22-196 **NDA APPROVAL**

NovaDel Pharma, Inc.
25 Minneakoning Road Suite 101
Flemington, NJ 08822

Attention: David H. Bergstrom, Ph.D.
Sr. Vice President, and Chief Operating Officer

Dear Dr. Bergstrom:

Please refer to your new drug application (NDA) dated November 20, 2007, received November 21, 2007, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Zolpimist® (zolpidem tartrate), 5mg and 10 mg oral spray.

We acknowledge receipt of your submissions dated August 29, 2008, September 5, 12, 17, 18, and 23, 2008 and December 5, and 12, 2008.

This new drug application provides for the use of Zolpimist® (zolpidem tartrate), 5mg and 10 mg oral spray in the treatment of insomnia.

We have completed our review of this application, as amended and it is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text as submitted on December 19, 2008.

CHEMISTRY, MANUFACTURING AND CONTROLS

A 12-month expiration date is granted for the drug product stored at 25 °C (77 °F) with excursions permitted to 15-30 °C (59-86 °F) (USP Controlled Room Temperature).

LABELING

If not already submitted, please submit final printed carton and container labels that are identical to the labeling submitted December 19, 2008 as soon as they are available, but no more than 30 days after they are printed. Please submit these labels 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 Carton and Container Labels for approved NDA 22-196**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with final printed labeling (FPL) that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

RISK EVALUATION AND MITIGATION STRATEGIES (REMS) REQUIREMENTS

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require the submission of a REMS for an approved drug if the FDA makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)(2)). This provision took effect on March 25, 2008.

In accordance with section 505-1 of the FDCA, we have determined that a REMS is necessary for Zolpimist® (zolpidem tartrate) to ensure the benefits of the drug outweigh the risks of complex sleep-related behaviors, such as sleep-driving and sleep-eating, and severe anaphylactic and anaphylactoid reactions in patients who take sedative hypnotics.

In accordance with section 505-1 of FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Zolpimist® (zolpidem tartrate), 5mg and 10 mg oral spray 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 Zolpimist® (zolpidem tartrate), 5mg and 10 mg oral spray. FDA has determined that Zolpimist® (zolpidem tartrate), 5mg and 10 mg oral spray 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, or continue to use Zolpimist® (zolpidem tartrate), 5mg and 10 mg oral spray. FDA has also determined that Zolpimist® (zolpidem tartrate), 5mg and 10 mg oral spray is a product for which patient labeling could help prevent serious adverse events. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Zolpimist® (zolpidem tartrate), 5mg and 10 mg oral spray.

Your proposed REMS, submitted on December 05, 2008, and appended to this letter (Appendix 1), is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS included in your December 05, 2008 submission.

Your assessment of the REMS should include an evaluation of patients' understanding of the serious risks of Zolpimist.

Prominently identify REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

NDA 22-196 REMS ASSESSMENT

NEW SUPPLEMENT for NDA 22-196
PROPOSED REMS MODIFICATION
REMS ASSESSMENT (if included)

Prominently identify other REMS-related submissions with the following wording in bold capital letters at the top of the first page of the submission:

REMS - OTHER

If you do not submit electronically, please send 5 copies of submissions related to your REMS.

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, and the text for the Medication Guide (including the Instructions for Use). 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 #22-196**."

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

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.

We are waiving the pediatric study requirement for this application because there is evidence strongly suggesting that zolpidem tartrate would be ineffective and unsafe in the pediatric age group 6 to 17 years, and because studies are impossible or highly impractical in the pediatric age group 0 to <6 years. The waiver is granted based, in part, on data submitted to the Agency included in the Ambien® (zolpidem tartrate) pediatric efficacy supplement 022, where administration of oral zolpidem tartrate to attention-deficit/hyperactivity disorder (ADHD) children ages 6-17 years did not establish efficacy and showed significant safety concerns in the pediatric age group 6 to 17 years.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) 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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. 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 www.fda.gov/cder/ddmac.

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
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

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

We acknowledge your August 29, 2008, commitment to expedited reporting of "Events of Interest" based upon the following MedDRA preferred terms: Drug administered at inappropriate site, Drug administration error, Incorrect dose administered, Incorrect route of drug administration, Wrong technique in drug usage process, Intentional drug misuse, Accidental exposure, Accidental overdose, Intentional overdose, Multiple drug overdose, Multiple drug overdose accidental, Multiple drug overdose intentional, Overdose, Drug abuser, Substance abuser, Dependence, Drug dependence, Drug tolerance, Drug tolerance decreased, Drug tolerance increased.

We also acknowledge your plan to include a discussion in your quarterly periodic report and annual report based upon the Standardized MedDRA Query: "Drug Abuse, Dependence and Withdrawal." We also note that you plan to review data from the Drug Abuse Warning Network (DAWN) and the Toxic Exposure Surveillance System (TESS) report prepared by the National Poison Data System, and enter events from DAWN and TESS for the oral spray formulation or when the formulation is unknown into the safety database for individual case reporting and aggregate analysis. We acknowledge your commitment to submit this information in your quarterly periodic report and annual report.

If you have any questions, call Cathleen Michaloski, MPH, Regulatory Project Manager, at (301) 796-1123.

Sincerely,
{See appended electronic signature page}

Russell Katz, M.D.
Director, Division of Neurology Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

Enclosure: REMS, labeling

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

/s/

Russell Katz

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