DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-272/S-054
NDA 20-588/S-042
NDA 21-346/S-027
NDA 21-444/S-029

Johnson & Johnson Pharmaceutical R&D, LLC
Attention: Heddie Martynowicz, MS
Senior Director, Regulatory Affairs
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

Dear Ms. Martynowicz:

We acknowledge receipt of your supplemental new drug applications dated and received July 8, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Risperdal (risperidone) Tablets (NDA 20-272), Risperdal (risperidone) Oral Solution (NDA 20-588), Risperdal M-Tab (risperidone) Orally Disintegrating Tablets (NDA 21-444), and Risperdal Consta (risperidone) Injection (NDA 21-346).

Reference is also made to an FDA letter dated June 16, 2008 notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for antipsychotic drugs. This information pertained to the warning regarding use of antipsychotics and increased mortality in elderly patients with dementia-related psychosis.

Your supplemental applications provide for revisions to the labeling for the Risperdal product line consistent with our June 16, 2008 letter.

These supplemental new drug applications provide for the following changes to product labeling:

Under the **BOXED WARNING** section, the addition of a warning regarding increased mortality in elderly patients with dementia-related psychosis. [This new section will be added to the beginning of the label with bolded font and enclosed in a black box.]

WARNING

Increased Mortality in Elderly Patients with Dementia-Related Psychosis —
Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were

varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. Risperdal (risperidone) is not approved for the treatment of patients with dementia-related psychosis (*see* **Warnings**).

Under **WARNINGS** the language below will be implemented in bolded font in the **WARNINGS** section as the first paragraph in this section.

> **WARNINGS**
>
> **Increased Mortality in Elderly Patients with Dementia-Related Psychosis** — Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Risperdal is not approved for the treatment of patients with dementia-related psychosis (*see* **BOXED WARNING**).

We have completed our review of these supplemental applications, and they are approved, effective on the date of this letter, for use as recommended in the above 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, text for the patient 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 supplements NDAs 20-272/S-054, 20-588/S-042, 21-346/S-027, & 21-444/S-029.**"

In addition, within 21 days of the date of this letter, amend any pending applications for this NDA with content of labeling in structured product labeling (SPL) format to include the changes approved in these applications.

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.

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter and that the revised labeling be reflected in the next printing of the labeling. While you may use labeling already printed, we request that revised labeling accompany any newly shipped product within 60 days from the date of this letter.

Failure to make these changes promptly could make your product misbranded under Sections 201(n) and 502(a) of FDCA.

PROMOTIONAL MATERIALS

You must promptly revise all promotional labeling and advertising for this product to make it consistent with the labeling changes described above. These revisions should include prominent disclosure of the important new information described in the **BOXED WARNING** section that appear in the revised package labeling.

In addition, submit three copies of the introductory promotional materials that you propose to use for these products. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Psychiatry Products and two copies of both the promotional materials and the package insert(s) 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

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
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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 LCDR Sonny Saini, Pharm. D., Safety Project Manager, at (301) 796-0532.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Thomas Laughren
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