DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-272 / S-033
NDA 20-588 / S-021
NDA 21-444 / S-004

Johnson & Johnson Pharmaceutical Research & Development, L.L.C.
Attention: Edward G. Brann
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

Dear Mr. Brann:

Please refer to your supplemental new drug applications dated August 14, 2003, received August 15, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Risperdal (risperidone) tablets and oral solution, and Risperdal M-TAB (risperidone) orally disintegrating tablets.

These "Changes Being Effected" supplemental new drug applications provide for revised product labeling under **WARNINGS, Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia**.

We have completed our review of these applications and they are approved, effective on the date of this letter.

As agreed in the meeting of August 13, 2003, the last sentence of the following section is amended as follows:

> **WARNINGS**
> **Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia**
> Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients (mean age 85 years; range 73-97) in trials of risperidone in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with risperidone compared to patients treated with placebo. ~~RISPERDAL® has not been shown to be safe or effective in the treatment of patients with dementia-related psychosis.~~ RISPERDAL is not approved for the treatment of patients with dementia-related psychosis.

The final printed labeling (FPL) must be identical to the above labeling (package insert submitted August 14, 2003).

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15

of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 20-272 / S-033, NDA 20-588 / S-021, and NDA 21-444 / S-004." Approval of these submissions by FDA is not required before the labeling is used.

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 Steve Hardeman, R.Ph., Senior Regulatory Project Manager, at (301) 594-5525.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug 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/

Russell Katz
9/10/03 08:42:08 AM