**JANSSEN** · PHARMACEUTICA · · RESEARCH FOUNDATION ·

August 15, 1996

Paul Leber, M.D.,
Director, Division of Neuropharmacological Drug Products
Center for Drug Evaluation and Research, HFD-120
Office of Drug Evaluation I
Center for Drug Evaluation
U.S. Food and Drug Administration
**Attn: Document Control Room 10B-40**
5600 Fishers Lane
Rockville, Maryland 20857

**Re: NDA 20-272 and 20-588**
**RISPERDAL® (risperidone) Tablets & Oral Solution**
**Label Change: Pediatric Use Supplement**

Dear Dr. Leber:

Enclosed, for the review and evaluation of the Division of Neuropharmacological Drug Products, is Janssen's supplement to NDA 20-272 to provide for a change in the Risperdal® (risperidone) product label. This submission is intended to support the addition of a new section for "pediatric use."

This submission includes:

- Draft revised labeling;
- A copy of the current product labeling in which the suggested changes have been indicated (redline/strikeout);
- Justification for the recommended labeling, based upon 21 CFR § 201.57 (f) (9) (vii); see below;
- Specific suggested labeling for the following pediatric age groups:
  - Neonates (birth up to one month);
  - Infants (one month up to two years);
  - Children (2 years up to 12 years);
  - Adolescents (12 years up to 16 years);
- A summary of safety data for all pediatric age groups and efficacy data for the latter two;
- An overall risk-benefit assessment.



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Janssen's rationale for proposing a supplement to the currently approved product label for Risperdal under the proviso of 21 CFR § 201.57 (f) (9) (vii) is somewhat complex. Although this submission does not contain data which the Agency would normally characterize as substantial evidence, we are nevertheless aware that Risperdal is being utilized in children and adolescents (see summary). Hence we believe that the Agency's alternative labeling options [21 CFR § 201.57 (f) (9) (v-vi)] would not adequately and safely reflect this fact. Our proposed labeling considers this fact by specifically proscribing Risperdal's use in neonates and infants, and by recommending that dosing be initiated with the most conservative dosing regimen possible, i.e., 0.25 mg per day (Risperdal Oral Solution with dosing pipette), in children and adolescents. We would prefer recommending specific doses (i.e., 0.25 mg) rather than dosing by weight because we believe that it would be simpler for parents, caregivers and patients. Additionally, we also intend to study Risperdal's utility in conduct disorder in mentally retarded children (protocols submitted under IND 31,931; Serial No. 129), and will employ dosing based upon body weight in those trials. Thus, we have also considered the utility of recommending a dosing regimen in our proposed label which is based upon body weight (e.g. 0.02 - 0.06 mg/kg body weight), but recognize that we currently do not have substantial evidence to support this recommendation. Based upon these multiple considerations, Janssen invites the Division's review and assessment of our labeling supplement, and we look forward to further discussions about these matters at the Division's convenience.

Should you have any questions or comments regarding this submission, or require any further information, please contact me at your convenience (609-730-3349).

Sincerely,

Todd D. McIntyre, Ph.D.
Associate Director, Regulatory Affairs

Attachments (4)