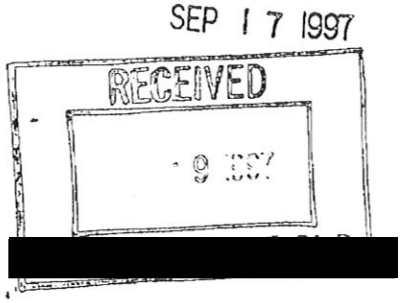
DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-272 / SLR-006
NDA 20-588 / SLR-001

Janssen Research Foundation
Attention: [redacted]
1125 Trenton-Harbourton Road
Post Office Box 200
Titusville, NJ 08560-0200



Dear [redacted]

Please refer to your supplemental new drug applications dated August 15, 1996, received August 21, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Risperdal (risperidone) 1mg, 2mg, 3mg, 4mg tablets and Risperdal (risperidone) 1mg/mL oral solution.

These supplemental applications provide for a change in the labeling with the addition of a new section for pediatric use.

We have completed our review and find the information presented is inadequate, and the supplemental applications are not approvable under section 505(d) of the Act and 21 CFR 314.125(b).

Your supplement proposes the expansion of Risperdal use into pediatric patients, however, you never state for what child or adolescent psychiatric disorders Risperdal would be intended. Indeed, you acknowledge that you have not provided substantial evidence from adequate and well-controlled trials to support any pediatric indications nor developed a rationale to extend the results of studies conducted in adults to children. Your rationale for proposing this supplement appears to be simply that, since Risperdal is being used in pediatric patients, this use should be acknowledged in some way in labeling.

We note that labeling changes proposed are nonspecific:

1. Under the Pharmacokinetic subsection of Clinical Pharmacology, you propose acknowledging that no systematically collected PK data are available, but you refer nevertheless to the Dosage and Administration section.

2. Under the Pediatric Use subsection of Precautions, you refer to "limited evidence regarding the safety and effectiveness of risperidone in the pediatric population," and again refer to the Dosage and Administration section.

3. Finally, in the Dosage and Administration section, you again suggest that there is limited evidence of safety and effectiveness from "small clinical studies, literature reports, and spontaneously reported adverse events." As noted, you never state in this language what indications are supported by these data. Regarding safety, you simply suggest that the safety profile for Risperdal appears to be similar in pediatric patients to that observed in adults. Nevertheless, you advise caution, i.e., avoidance of prescribing in neonates and infants, and cautious titration, beginning with 0.25 mg/day in children and adolescents.

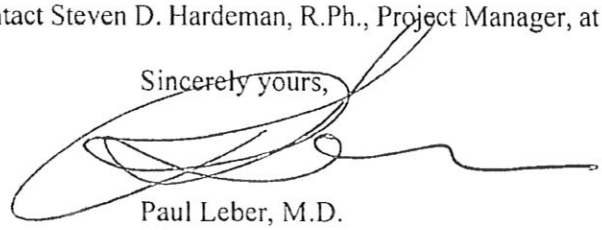
You have provided very little information to support these proposed labeling changes. You acknowledge that the supplements provide no i nterpretable efficacy data. The safety data submitted were also very limited, including data for n=14 pediatric patients exposed to Risperdal in Janssen-sponsored studies, n=29 pediatric patients exposed to Risperdal in studies reported in the published literature, and n=186 spontaneous reports involving pediatric patients exposed to Risperdal. None of these data were suggestive of any unusual or unexpected adverse events occurring specifically in association with the use of Risperdal in the pediatric age group.

Accordingly, we must conclude that there is inadequate support for the changes sought. As noted, you have not identified any pediatric indications for which you believe Risperdal could be approved and you have provided no data from adequate and well controlled trials to support any such approvals. There were no specific safety findings of sufficient concern among the meager safety data submitted to justify adding any information to labeling about the safety experience with this drug in the pediatric age group. To permit the inclusion of the proposed vague references to the safety and effectiveness of Risperdal in pediatric patients and the nonspecific cautionary advice about how to prescribe Risperdal for the unspecified target indications would serve only to promote the use of this drug in pediatric patients without any justification. Consequently, this supplement is not approved.

Within 10 days after the date of this letter, you are required to amend the supplemental applications, notify us of your intent to file amendments, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw these supplemental applications. Any amendments should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

If you have any questions, please contact Steven D. Hardeman, R.Ph., Project Manager, at (301) 594-5533.

Sincerely yours,



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