SYNOPSIS (CONTINUED)

NAME OF SPONSOR/COMPANY: Johnson & Johnson Pharmaceutical Research & Development, L.L.C. NAME OF FINISHED PRODUCT: RISPERDAL® NAME OF ACTIVE INGREDIENT(S): Risperidone (R064766)	INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER Volume: Page:	(FOR NATIONAL AUTHORITY USE ONLY)
Duration of Treatment: This study was planned to continue for a period of at least 12 months but not more than 24 months and would end whenever risperidone LAI was commercially available in the U.S. The protocol was amended to allow subjects to continue for more than 24 months, when it seemed unlikely that commercial availability would occur in the first 24 months of the study.		
Criteria for Evaluation: Pharmacokinetics: Not applicable Efficacy: Efficacy was measured by the Positive and Negative Syndrome Scale (PANSS) and by Clinical Global Impression (CGI) - severity. Safety: Safety parameters included adverse events, clinical laboratory tests, vital signs, ECG, physical examinations, and height and body weight. Pharmacokinetic/Pharmacodynamic Relationships: Not applicable		

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SAFETY RESULTS: No major safety concerns were observed in this long-term extension study that lasted approximately 2 years. A total of 87 of 100 subjects reported treatment-emergent adverse events. Headache was the most frequently occurring treatment-emergent event (25.0%) followed by psychosis (21.0%). The overall incidence of EPS-related adverse events with onset during CR003274 was 22.0%. No adverse event of tardive dyskinesia was reported. Serious adverse events occurred in 25.0% of subjects. Most serious adverse events were of a psychiatric nature and were most likely due to the underlying disease condition.

Ten subjects prematurely discontinued study treatment associated with a treatment-emergent adverse event; 2 of the 10 subjects discontinued treatment due to a treatment-emergent adverse event and a non-treatment-emergent adverse event (weight increase and hyperkinesia). One additional subject discontinued due to an adverse event (hyperprolactinemia) with onset during the prior study. The majority of treatment-emergent adverse events were of mild or moderate intensity as determined by the investigators.

One subject died during treatment with risperidone LAI; the death was due to cardiac arrest and pulmonary arrest secondary to severe COPD, pulmonary hypertension and arteriosclerotic heart disease. The investigator assessed the adverse events leading to death as unrelated to study medication.

Overall, 64.0% of subjects discontinued study treatment. The most frequent reason for discontinuation was withdrawal of consent (21 [21.0%] of 100 subjects) followed by adverse event and insufficient response in 11 (11.0%) subjects each. There was no apparent relationship between the dose of risperidone LAI and withdrawal of consent.

There was no pattern of laboratory findings, ECG data, or vital signs that were of concern in this study. Subjects with abnormally high glucose values had only transient increases that resolved without treatment. Most abnormally high values for liver enzymes (ALT, AST, and GGT) were transient and returned to normal levels by end point.

An increase in mean body weight (1.7 kg) and mean BMI (0.6 kg/m^2) was observed from previous baseline to end point. An increase from extension baseline to end point was seen in mean body weight of 1.3 kg and mean BMI of 0.4 kg/m^2. In this extension study, little or no further increase in weight occurred after the first 12 months.

PHARMACOKINETIC/PHARMACODYNAMIC RELATIONSHIPS: not applicable

CONCLUSION: Risperidone LAI (25, 37.5, and 50 mg) intramuscular injection, given every 2 weeks, was safe, well tolerated, and effective in maintenance treatment of subjects with schizophrenia

Date of the report: 4 March 2005