DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-346

Johnson & Johnson Pharmaceutical Research & Development, L.L.C.
Attention: Claude McGowan, Ph.D.
Associate Director, Regulatory Affairs
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

Dear Dr. McGowan:

Please refer to your new drug application (NDA) dated and received August 31, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Risperdal Consta (risperidone) Long-Acting Injection.

We acknowledge receipt of your submissions dated:

April 28, 2003	May 7, 2003	July 29, 2003	September 15, 2003
September 24, 2003	October 14, 2003	October 15, 2003	October 16, 2003

The submission of April 28, 2003, constituted a complete response to our June 28, 2002, action letter.

This new drug application provides for the use of Risperdal Consta (risperidone) Long-Acting Injection for the treatment of schizophrenia.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text (enclosed).

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert). Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL 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 but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-346**." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your email of October 29, 2003, and your submission of April 28, 2003. These commitments are listed below:

1. Osteodystrophy

   You have committed to further investigate the osteodystrophy observed in the 1-year i.m. depot toxicity and the 2-year i.m. depot carcinogenicity studies in rat. Additional studies to be conducted Phase 4 should address the exact nature of the bone lesion(s) and possible mechanism(s) underlying this finding.

Protocol Submission:	February 2004
Study Start:	April 2004
Final Report Submission:	April 2006

2. Process Impurity

   You have committed to conduct an *in vitro* chromosomal aberration assay in mammalian cells or an *in vitro* mouse lymphoma assay (with colony sizing) to assess the genotoxic potential of the process impurity, (b)(4)----. The study can either be conducted using a drug batch enriched in (b)(4)---- or directly testing (b)(4)----.

Protocol Submission:	February 2004
Study Start:	March 2004
Final Report Submission:	June 2004

3. Embryofetal Development Study

   You have committed to conduct an i.m. depot embryofetal development study in rats.

Protocol Submission:	Protocol has been submitted
Study Start:	Study started prior to approval
Final Report Submission:	January 2004

4. In-vitro Release Specifications

   You have committed to submit the in-vitro release data from the on-going stability tests on validation lots of all strengths within 4 months after the 24 month stability data are available.

Protocol Submission:	Protocol has been submitted
Study Start:	Study started prior to approval
Final Report Submission:	January 2004

   These data should be used to propose final dissolution specifications for this product.

Interim Dissolution Specifications

The agreed-upon interim dissolution specifications are as follows:

Test method* (medium pH 7.4)	Test point	Specification (mean)	Specification## (individual sample)
In vitro release (37^0C water bath)	Day 1 Day 15	=(b)(b) =), (b	= (b)(4) =------- -
In vitro release (45^0C water bath)	$T_{50\%}$ Day 8	(b) (4)	(b)(4) = (b)((all individual samples)
* Samples tested in triplicate; ##All individual samples should meet this criteria			

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "Postmarketing Study Protocol", " Postmarketing Study Final Report", or " Postmarketing Study Correspondence."

FDA's Pediatric Rule [at 21 CFR 314.55/21 CFR 601.27] was challenged in court. On October 17, 2002, the court ruled that FDA did not have the authority to issue the Pediatric Rule and has barred FDA from enforcing it. Although the government decided not to pursue an appeal in the courts, it will work with Congress in an effort to enact legislation requiring pharmaceutical manufacturers to conduct appropriate pediatric clinical trials. In addition, third party interveners have decided to appeal the court's decision striking down the rule. Therefore, we encourage you to submit a pediatric plan that describes development of your product in the pediatric population where it may be used. Please be aware that whether or not this pediatric plan and subsequent submission of pediatric data will be required depends upon passage of legislation or the success of the third party appeal. In any event, we hope you will decide to submit a pediatric plan and conduct the appropriate pediatric studies to provide important information on the safe and effective use of this drug in the relevant pediatric populations.

The pediatric exclusivity provisions of FDAMA as reauthorized by the Best Pharmaceuticals for Children Act are not affected by the court's ruling. Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products. You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request". FDA generally does not consider studies submitted to an NDA before issuance of a Written Request as responsive to the Written Request. Applicants should obtain a Written Request before submitting pediatric studies to an NDA.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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 Steven D. 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

Enclosure (labeling)

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

10/29/03 02:44:47 PM