LAW OFFICES
HYMAN, PHELPS & MCNAMARA, P.C.
700 THIRTEENTH STREET, N.W.
SUITE 1200
WASHINGTON, D.C. 20005-5929
(202) 737-5600
FACSIMILE
(202) 737-9329
www.hpm.com

KURT R. KARST

Direct Dial (202) 737-7544
KKarst@hpm.com

June 25, 2013

BY HAND DELIVERY

Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

CITIZEN PETITION

Hyman, Phelps & McNamara, P.C., on behalf of a client, submits this petition in accordance with 21 C.F.R. § 10.25 and § 10.30, and pursuant to Sections 505(j) and 505(w) of the Federal Food, Drug, and Cosmetic Act ("FDC Act") and 21 C.F.R. § 314.161 to request that the Commissioner of the Food and Drug Administration ("FDA") determine whether a listed drug has been voluntarily withdrawn for reasons of safety or effectiveness.

A. Action Requested

The undersigned requests that the Commissioner make a determination that the 12 mg strength of Ortho-McNeil-Janssen Pharmaceuticals, Inc.'s ("Janssen's") INVEGA (paliperidone) Extended-release Tablets, approved under New Drug Application ("NDA") No. 021999, was not discontinued for safety or effectiveness reasons.

B. Statement of Grounds

Paliperidone, the major active metabolite of risperidone, is a centrally active dopamine Type 2 (D_2) antagonist and with predominant serotonin Type 2 ($5HT_{2A}$) activity. Paliperidone is also active as an antagonist at α1 and α2 adrenergic receptors and H_1 histaminergic receptors. FDA approved paliperidone as INVEGA under NDA No. 021999 on December 19, 2006 in 3 mg, 6 mg, 9 mg, and 12 mg extended-release tablet strengths for the treatment of schizophrenia. A 1.5 mg strength was subsequently approved on August 26, 2008 (NDA No. 021999/S-005).

FDA approved a second marketing application – NDA No. 022043 – for INVEGA Extended-release Tablets, 3 mg, 6 mg, 9 mg, and 12 mg, on April 27, 2007 for the maintenance treatment of schizophrenia. This NDA is not separately listed in FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"). It was presumably submitted and approved separately for FDA administrative purposes, and is bundled within the approval of NDA No. 021999.

FDA has approved multiple additional supplements under NDA No. 021999, including supplements approved on July 31, 2009 providing for use of INVEGA for the treatment of schizoaffective disorder as monotherapy and as an adjunct to mood stabilizers and/or antidepressants (NDA No. 021999/S-013 & S-014), and a supplement approved on April 6, 2011 for the treatment of schizophrenia in adolescents 12-17 years of age (NDA No. 021999/S-024).

On or about December 19, 2006, the same day FDA approved NDA No. 021999, Janssen discontinued marketing the 12 mg strength of INVEGA. See FDA, Approval Letter, NDA No. 021999, at 1 (Dec. 19, 2006) ("We note that, at this time, you do not intend to market the 12 mg tablet strength. Therefore, we have not included this strength in the enclosed labeling."). Indeed, there is no evidence that the 12 mg strength of INVEGA was ever marketed, despite the original and subsequent supplemental NDA approvals including the 12 mg strength. The 12 mg strength of NVEGA is currently listed in the Discontinued Drug Product List section of the "Orange Book."

Under applicable regulations, drug product approvals are removed from the Orange Book if FDA withdraws or suspends approval of the drug product's application for reasons of safety or effectiveness, or if FDA determines that the listed drug was withdrawn or withheld from sale for reasons of safety or effectiveness. See 21 C.F.R. § 314.162. FDA's regulations also provide that the Agency must make a determination as to whether a listed drug is withdrawn from sale for reasons of safety or effectiveness before approving a generic version of that listed drug under an Abbreviated New Drug Application ("ANDA") that refers to that listed drug. See id. § 314.161(a)(1). FDA has previously determined that, for purposes of § 314.161 and § 314.162, the discontinuation of marketing of a product is equivalent to withdrawing the drug from sale.

FDA may approve an ANDA for a discontinued listed drug upon a determination that the listed drug was not withdrawn for reasons of safety or effectiveness. No documentation or other information is known to exist that establishes that the 12 mg strength of INVEGA was discontinued by Janssen for reasons of safety or effectiveness.

Accordingly, it appears that the 12 mg strength of INVEGA was not withdrawn for reasons of safety or effectiveness and that ANDAs for generic INVEGA, Extended-release Tablets, 12 mg, are eligible for approval upon completion of the ANDA review process.

C. Environmental Impact

Petitioner claims a categorical exclusion under 21 C.F.R. § 25.31.

D. Economic Impact Statement

Petitioner will, upon request by the Commissioner, submit economic impact information, in accordance with 21 C.F.R. § 10.30(b).

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this Petition includes all information and views on which the Petition relies, and that it includes representative data and information known to the Petitioner that are unfavorable to the Petition.

Sincerely,

Kurt R. Karst

KRK/eam