DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FEB 26 2008

Rec'd 2/12/08

Deborah A. Jaskot, M.S., R.A.C.
Vice President, Regulatory Affairs
Teva Pharmaceuticals USA
1090 Horsham Road, P.O. Box 1090
North Wales, PA 19454-1090

Re: Docket No. 2007P-0316/CP1 and CR1

Dear Ms. Jaskot:

This responds to your citizen petition dated August 3, 2007 (Petition), and the revised certification to your Petition dated January 4, 2008 (Correction).[1] Your Petition requests that the Food and Drug Administration (FDA or the Agency) relist U. S. Patent Number 5,158,952 (the '952 patent) for the 0.25-milligram (mg), 0.5-mg, 1-mg, 2-mg, 3-mg, and 4-mg strengths of Risperdal (risperidone) tablets (new drug application (NDA) 20-272) in FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book). You also request that FDA confirm that Teva Pharmaceutical USA's (Teva) eligibility for 180-day exclusivity in connection with its abbreviated new drug application (ANDA) 76-228 for risperidone tablets in these strengths has not been affected by FDA's delisting of the '952 patent from the Orange Book. Your request is based on the contention that the '952 patent appeared in the printed annual edition of the Orange Book on the day that Teva submitted ANDA 76-228, which contained a certification pursuant to section 505(j)(2)(A)(vii)(IV) of the Act (paragraph IV certification) to the '952 patent, and a certification pursuant to section 505(j)(2)(A)(vii)(III) of the Act (paragraph III certification) to U. S. Patent Number 4,804,663 (the '663 patent).

We have carefully reviewed your Petition and have concluded that the '952 patent was delisted before Teva submitted ANDA 76-228 to FDA. For the reasons described in further detail in this Response, we deny your request that FDA relist the '952 patent. As Teva's ANDA did not contain a paragraph IV certification for a listed patent, and Teva did not provide the required

[1] See Docket No. 2007P-0316/CP1 and CR1. On January 4, 2008, you submitted a "revised certification pursuant to 21 U.S.C. 355(q)(1)(H)" relating to your pending citizen petition. Section 505(q) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 355(q)) was added by the Food and Drug Administration Amendments Act of 2007 (Public Law 110-85) (FDAAA) on September 27, 2007. You have alleged that your Petition, received by FDA on August 6, 2007, is subject to section 505(q)(1)(F) of the Act. It is FDA's view that the requirements, prohibitions, and benefits described in section 505(q) of the Act do not apply to requests submitted to FDA before September 27, 2007. Were it otherwise, FDA would be barred from considering your Petition, as it did not contain the required certification described in section 505(q)(1)(H) without which the Secretary "shall not consider a petition for review." A certification submitted after the petition does not make the original petition "contain" the certification. Moreover, we note that section 505(q) of the Act does not apply to a petition that relates solely to the timing of the approval of an application pursuant to current section 505(j)(5)(B)(iv) of the Act, which describes the 180-day exclusivity period accorded to certain applications (505(q)(4)(A) of the Act). As described further in this Response, although framed as a patent delisting matter, your Petition relates solely to Teva's eligibility for exclusivity and thus to the timing of the approval of ANDAs for risperidone tablets pursuant to section 505(j)(5)(B)(iv) of the Act. Because FDAAA does not apply to your Petition, we are responding to your Petition in accordance with our regulations on citizen petitions at 21 CFR 10.30.

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notice of such certification to the holder of the NDA for the reference listed drug and each owner of the listed patent, Teva would not be eligible for 180-day exclusivity pursuant to section 505(j)(5)(B)(iv) of the Act for its pending ANDA 76-228.

I. BACKGROUND

A. ANDAs and Eligibility for 180-day Exclusivity

The Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) (the Hatch-Waxman Amendments) created section 505(j) of the Act (21 U.S.C. 355(j)). The Hatch-Waxman Amendments reflect Congress' efforts to balance the need to "make available more low cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962" with new incentives for drug development in the form of marketing exclusivity and patent term extensions.[2] Section 505(j) of the Act established an abbreviated approval pathway for a drug product that is the same as a previously approved drug (the reference listed drug) with respect to active ingredient, dosage form, route of administration, strength, labeling, and conditions of use, among other characteristics. An ANDA applicant also must demonstrate that its proposed product is bioequivalent to the reference listed drug. An applicant that can meet the requirements under section 505(j) for approval may rely upon the Agency's finding of safety and effectiveness for the reference listed drug, and need not repeat the extensive nonclinical and clinical investigations required for approval of a full NDA submitted under section 505(b)(1) of the Act. The timing of approval for an ANDA is subject to the patent and marketing exclusivity protections accorded the reference listed drug.

Section 505(b)(1) of the Act requires the sponsor of an NDA to "file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture[,] use, or sale of the drug." Upon approval of an application under section 505(c) of the Act, FDA publishes the patent information provided by the drug product's sponsor in the Orange Book, which is made available to the public in several formats. FDA's role in patent listing is ministerial. As discussed in the preamble to the June 2003 final rule, FDA "will not evaluate a patent to assess whether the declaration is accurate or whether the patent has been appropriately submitted for listing. We will, however, review the declaration for completeness and to determine that the information given by the NDA applicant or holder or patent owner indicates that the patent is eligible for listing."[3]

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[2] See House Report No. 98-857, part 1, at 14 (1984), reprinted in 1984 U.S.C.C.A.N. 2647 at 2647-2648.

[3] "Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed; Final Rule" (68 FR 36676 at 36687; June 18, 2003). It should be noted that certain sections of this final rule regarding the application of 30-month stays on approval of certain ANDAs and applications submitted under section 505(b)(2) of the Act were superseded by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) (Public Law 108-173) and revoked by technical amendment (69 FR 11309; March 10, 2004).

The Orange Book is published annually and updated monthly in print. During the time period relevant to this petition, the information in the Orange Book was updated approximately on a monthly basis on the Orange Book Web page (the electronic Orange Book), which is linked from the FDA Web site. Beginning in 1998, current patent listings for approved drug products could be obtained from the electronic Orange Book in a search by *active ingredient*, *proprietary name*, *application holder*, or *application number*.

An ANDA applicant must include a patent certification described in section 505(j)(2)(A)(vii) of the Act for each patent that claims the reference listed drug or a method of using the drug for which the applicant is seeking approval and for which information is required to be filed under subsection 505(b) or 505(c) of the Act. For each patent listed in the Orange Book, the ANDA applicant must submit either a paragraph III certification (delaying approval until the date on which such patent will expire), a paragraph IV certification (certifying that such patent is invalid or will not be infringed by the manufacture, use, or sale of the drug product for which the ANDA is submitted), or, with respect to a method of use patent, a statement that the patent does not claim a use for which the ANDA applicant is seeking approval (section 505(j)(2)(A)(viii) of the Act). Submission of an ANDA for a drug product or the use of a drug product claimed in a patent is an act of patent infringement if the ANDA product is intended to be marketed before patent expiration (see 35 U.S.C. 271(e)(2)).

An applicant submitting a paragraph IV certification is required to give notice of the patent challenge to the holder of the NDA for the reference listed drug and each owner of the patent that is the subject of the certification. For an original ANDA, notice must be provided after receipt of an acknowledgment letter from the Office of Generic Drugs (OGD) advising that the application is sufficiently complete to permit a substantive review and has been received by OGD (21 CFR 314.95(b)).[4] Notice of a paragraph IV certification includes, among other things, "a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed" (section 505(j)(2)(B)(iii) of the Act) and it subjects the ANDA applicant to the risk that it will be sued for patent infringement. In addition, if the NDA holder or patent owner initiates a patent infringement action within 45 days after receiving notice of the paragraph IV certification, there will be a statutory 30-month stay of approval of the ANDA while the patent infringement litigation is pending (section 505(j)(5)(B)(ii) of the Act).

The 180-day exclusivity period described in section 505(j)(5)(B)(iv) of the Act provides an incentive for ANDA applicants to challenge listed patents that may be invalid, unenforceable, or not infringed by the drug product described in the ANDA. This patent challenge involves the filing of a paragraph IV certification to a listed patent, notification to the NDA holder and patent owner, and the opportunity for the NDA holder and patent owner to sue the ANDA applicant for patent infringement. The first applicant to submit a substantially complete ANDA containing a paragraph IV certification may be eligible for a 180-day period of marketing exclusivity during which approval of subsequent ANDAs for the same drug product that also contain a paragraph IV certification to the patent will not be granted. Any exclusivity period would run for 180 days from either the first commercial marketing of the first applicant's drug product or from a court

[4] With respect to ANDAs, FDA uses the terms *received* or *received for substantive review* to refer to the action described in the Act as filing, and these terms are used in this Response (see 21 CFR 314.101(b)).

decision finding that the patent that is the subject of the paragraph IV certification is invalid or not infringed, whichever is earlier (see section 505(j)(5)(B)(iv) of the Act), during the unexpired term of the patent.[5]

B. Patents Listed in the Orange Book for Risperdal (risperidone) Tablets

The reference listed drug for Teva's ANDA is Janssen Pharmaceutica's (Janssen) Risperdal (risperidone) tablets (NDA 20-272). The 1-mg, 2-mg, 3-mg, 4-mg, and 5-mg Risperdal tablets were approved in 1993.[6] The 0.25-mg and 0.5-mg strengths were approved in 1999. After approval, the sponsor submitted information to FDA on the '663 patent and the '952 patent for listing in the Orange Book entry for Risperdal tablets. The '663 patent expired on December 29, 2007, and pediatric exclusivity attached to that patent will expire on June 29, 2008.[7] The '952 patent will expire on October 27, 2009.

On April 4, 2001, Janssen's parent company, Johnson & Johnson, sent correspondence to the Division of Neuropharmacological Drug Products in FDA's Center for Drug Evaluation and Research (CDER) requesting removal of the '952 patent from the Orange Book listing for 1-mg, 2-mg, 3-mg, and 4-mg Risperdal tablets. On June 11, 2001, Johnson & Johnson sent correspondence via facsimile to the Division of Database Management stating that its April 4, 2001, correspondence also should have requested delisting of the '952 patent for 0.25-mg, 0.5-mg, and 5-mg Risperdal tablets, and requesting removal of the '952 patent from the Orange Book listing for these strengths. In accordance with these instructions, FDA modified its patent listing database on June 11, 2001, to remove the '952 patent from the entries for Risperdal tablets in the above-referenced strengths in response to Johnson & Johnson's requests on April 4, 2001, and June 11, 2001. The delisting of the '952 patent was reflected in the publicly available, electronic Orange Book shortly after June 29, 2001, and no later than July 20, 2001, the date of the next database update.[8] An applicant searching the publicly available, electronic Orange

[5] The version of section 505(j)(5)(B)(iv) of the Act in effect at the time of Teva's ANDA submission predates enactment of the MMA, which amended this and other provisions of the Act. Unless otherwise noted (as in footnote 1), all statutory references reflect the pre-MMA version of the Act.

[6] The 5-mg strength of Risperdal (risperidone) tablets (NDA 20-272) has been discontinued from marketing.

[7] The New Jersey federal district court's finding that the '663 patent was valid and enforceable was affirmed by the Federal Circuit on May 11, 2007 (see *Janssen Pharmaceutica N.V. v. Mylan Pharms., Inc.*, 2006 U.S. Dist LEXIS 74582 (D.N.J. 2006), *aff'd*, 2007 U.S. App. LEXIS 11686 (Fed. Cir. 2007)). The Federal Circuit's mandate issued on June 26, 2007, following denial of a petition for panel rehearing and rehearing en banc (see 2007 U.S. App. LEXIS 16041 (Fed. Cir. 2007)). Accordingly, Teva's ANDA for risperidone tablets, which contains a paragraph III certifications to the '663 patent, will not be eligible for approval prior to June 29, 2008.

[8] The Division of Database Management was responsible for updating the Orange Book. In 2001, the Division of Database Management maintained the patent information submitted by NDA holders pursuant to section 505(b) and (c) of the Act in CDER's Oracle database from which it created patent.txt files on a regular basis. Each patent database .txt file contained the public patent information available at the time of creation of the file, and was released through the electronic Orange Book shortly after it was created. The patent database .txt file created June 4, 2001, showed that the '952 patent and the '663 patent were listed for Risperdal tablets. The patent database .txt file created June 29, 2001, showed that only the '663 patent was listed for Risperdal tablets, reflecting the removal of the' 952 patent on June 11, 2001, at Johnson & Johnson's request. Although we are unable to provide the exact date on which the patent information in the June 29, 2001, .txt file became publicly available in the electronic Orange Book, FDA has determined that it was available by the time the next patent .txt file was created on July 20, 2001.

Book after July 20, 2001, would have found that only the '663 patent was listed for Risperdal tablets (see section II.A of this Response for further discussion of the availability of patent information in printed and electronic versions of the Orange Book).

C. Teva's ANDA 76-228 for Risperidone Tablets

On August 28, 2001, Teva submitted an ANDA for risperidone tablets. The Teva ANDA contained a paragraph III certification to the '663 patent and a paragraph IV certification to the '952 patent. During a filing review of the ANDA to determine whether it was sufficiently complete to permit a substantive review, OGD evaluated the ANDA in accordance with its usual practice to determine whether the ANDA contained an appropriate patent certification for each patent listed for the reference listed drug identified in the ANDA. When reviewing Teva's ANDA, the OGD project manager relied on the publicly available, electronic Orange Book for the most current patent listing information (see September 25, 2001, printout for risperidone from the electronic Orange Book, attached as Exhibit 1). In light of the absence of the '952 patent from the electronic Orange Book, an OGD project manager also contacted the Orange Book staff to clarify the discrepancy between the patent certifications provided in Teva's ANDA and the patent currently listed for Risperdal tablets. The Orange Book staff confirmed that the '952 patent had been delisted for Risperdal tablets.

OGD concluded that Teva had submitted a patent certification for a patent (the '952 patent) that was no longer listed for the reference listed drug, Risperdal tablets. On October 12, 2001, an OGD project manager contacted Philip Erickson, R.Ph., Director of Regulatory Affairs, Solid Oral Dosage Forms, for Teva Pharmaceuticals USA, and requested, among other things, that Teva submit a revised patent certification because the '952 patent had been delisted from the Orange Book. On October 22, 2001, Teva submitted a letter via facsimile withdrawing its patent certification to the '952 patent. Teva's letter stated, with reference to the revised patent certification: "U.S. Patent 5,158,952 with an expiration of October 27, 2009 ***has been officially delisted*** from the Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book), therefore only U.S. Patent 4,804,663 with an expiration of December 29, 2007 remains. Please find enclosed a patent certification revised accordingly" (emphasis added).[9] The revised patent certification, signed by D. Jaskot, Executive Director of Regulatory Affairs, Teva Pharmaceuticals USA stated: "Paragraph III Certification: The undersigned hereby certifies that to the best of our knowledge and in TEVA Pharmaceuticals USA's opinion there is one listed patent which claims the reference drug Risperdal® Tablets, 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg and 4 mg. U.S. Patent No. 4804663 Expiration December 29, 2007..."[10]

On October 24, 2001, OGD issued a standard acknowledgement letter[11] to Teva indicating that Teva's ANDA for risperidone tablets had been received for substantive review. The Teva

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[9] See Exhibit 3 to Petition: Correspondence dated October 22, 2001, from D. Jaskot (Teva) to G. Buehler (OGD) regarding ANDA 76-228 (Teva's October 22, 2001, Correspondence). A paper copy of Teva's October 22, 2001, Correspondence was received by OGD on October 23, 2001.

[10] See Attachment 2 to Teva's October 22, 2001, Correspondence.

[11] When an ANDA containing a paragraph IV certification is received for substantive review by OGD, OGD will issue a paragraph IV acknowledgment letter which describes, among other things, an ANDA applicant's obligations

ANDA, as received by OGD, did not contain a paragraph IV certification to any listed patent for Risperdal tablets, and thus there was no paragraph IV certification for which Teva would have been required to provide notice to the NDA holder for Risperdal and the owner of the '952 patent.

II. ANALYSIS

You contend that Teva is entitled to 180 days of marketing exclusivity for its pending ANDA for risperidone tablets because the '952 patent appeared in the annual edition of the Orange Book (which you describe as the "official" Orange Book) on the day that Teva submitted its ANDA containing a paragraph IV certification to the '952 patent. You also assert that FDA's delisting of the '952 patent does not affect Teva's "entitlement" to 180-day exclusivity, because FDA "failed to provide official notice of the 'delisting' for several months following the submission of Teva's ANDA" (Petition at 2). We address these arguments below.

A. Public Availability of Information Regarding Delisting of '952 Patent

As described in section I.A. of this Response, FDA makes patent information for listed drugs available to the public in several formats. In 2001, we published a printed annual edition of the Orange Book with cumulative monthly supplements, and maintained a public docket (1995S-0117) for patent term extensions and new patents listed for human drugs. We also provided an electronic Orange Book updated approximately on a monthly basis. The '952 patent was listed for Risperdal tablets in the Patent and Exclusivity Information Addendum (the Addendum) to the printed 21st annual edition of the Orange Book, which is described on the title page as current through December 31, 2000. The Addendum states that "[s]ince all parts of this publication are subject to changes, additions, or deletions, the *Addendum* must be used in conjunction with the most current Cumulative Supplement" (Orange Book, 21st ed., at AD-2). In turn, Section 1.3 of each Cumulative Supplement to the 21st annual edition of the Orange Book describes the availability of the electronic Orange Book. The Cumulative Supplements state, among other things, that

> [t]here is an Electronic Orange Book Query (EOB) at http://www.fda.gov/cder/ob. The Query provides searching of the approved drug list by active ingredient, proprietary name, applicant holder, or applicant number. Product search categories are: prescription, over-the-counter, discontinued drugs. There are links to patent and exclusivity information that may be applicable to each product. The data is updated concurrently with the publication of the annual edition or monthly cumulative supplements.[12]

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to provide the required notice to the NDA holder and each patent owner of its paragraph IV certification to a patent listed for the reference listed drug. OGD did not issue a paragraph IV acknowledgement letter to Teva because its ANDA did not contain a paragraph IV certification to a listed patent when received for substantive review by OGD,

[12] See, e.g., Orange Book Cumulative Supplement 1, January 2001, at v. Although the printed cumulative supplements to the Orange Book do not include information on patent delistings, the caveat regarding possible "changes, additions, or deletions" encourages the public to seek the most currently available information. The electronic Orange Book contained the most current information regarding patents listed for Risperdal tablets.

Moreover, the publishing history of the Orange Book, prominently displayed on the inside front cover of the printed 21st annual edition of the Orange Book, also indicates, among other things, that the Orange Book is "Updated by monthly cumulative supplements. Updated on the Internet. Address: http://www.fda.gov/cder/drug.htm."

An applicant searching the electronic Orange Book shortly after June 29, 2001, and no later than July 20, 2001, would have found that only the '663 patent was listed for Risperdal tablets. To illustrate this fact, we have loaded the June 29, 2001, patent database .txt file described in footnote 8 and the database *scripts* (the set of computer instructions to ask the database for certain data) for the electronic Orange Book that were in use in 2001.[13] The electronic Orange Book Query by active ingredient for risperidone, and the information available from each link from the search results page are attached to this Response as Exhibit 2. An applicant searching the electronic Orange Book for risperidone would have found that there was only one listed patent for NDA 20-272 for Risperdal tablets: the '663 patent. Indeed, we note that we have a printout supplied by a different ANDA applicant and dated October 30, 2001, of the electronic Orange Book entry for Risperdal tablets (NDA 20-272), which shows that the only patent listed was the '663 patent (Exhibit 3). This is the same patent information that would have been available to an applicant searching the electronic Orange Book any time after July 20, 2001. As with Teva's ANDA, OGD received for substantive review the November 2001 ANDA referencing Risperdal tablets with a patent certification only to the '663 patent.

In summary, at the time Teva submitted its ANDA, the electronic Orange Book contained the most current information regarding patents listed for Risperdal tablets. Your assertion that the delisting of the '952 patent did not become effective until publication of the 2002 annual edition of the Orange Book is without merit.

B. Patent Certification Obligations for Receipt of ANDAs

You contend that Teva was required to provide a certification to the '952 patent in its submission of an ANDA for risperidone tablets on August 28, 2001, because "where a patent remains listed for a particular drug in the official Orange Book, a generic applicant has no choice but to believe that the NDA holder is continuing to assert that patent as claiming the listed drug" (Petition at 1 to 2, and 4). However, by July 20, 2001, it was publicly known from the electronic Orange Book that the NDA holder was not continuing to assert the '952 patent as claiming Risperdal tablets. As the '952 patent was no longer listed for the reference listed drug when Teva's ANDA 76-228 was submitted, a certification to the '952 patent was neither necessary nor permitted.

The Agency's regulations at 21 CFR 314.94(a)(12)(i), implementing section 505(j)(2)(A)(vii) of the Act, require that an ANDA contain a certification with respect to each patent that "claims the reference listed drug or that claims a use of such listed drug for which the applicant is seeking approval under section 505(j) of the act and for which information is required to be filed under section 505(b) and (c) of the act and [21 CFR] 314.53." Patent information for approved drug products changes with some frequency as a result of requests by NDA holders to list newly issued patents or delist patents for their products in accordance with their statutory obligations

[13] FDA's database protocols and scripts have changed over time.

under section 505(b) and (c) of the Act. As a result, OGD's filing review of ANDAs routinely includes a determination of whether the patent certifications contained in the ANDA correspond to the patents actually listed for the reference listed drug, as assessed by the most current patent information the Agency has received. OGD does not rely solely on the applicant's representation that the ANDA contains the required patent certifications; OGD conducts an independent review of the patent information for the reference listed drug that FDA has received from the NDA holder.[14] The '952 patent was delisted for Risperdal tablets before any applicant, including Teva, submitted an ANDA referencing that drug. Accordingly, Teva was required to remove its certification to the '952 patent before its ANDA would be formally received by the Agency.

C. Hatch-Waxman Incentives for Developing Generic Drugs

With reference to the decision by the Circuit Court of Appeals for the District of Columbia in *Ranbaxy Laboratories Ltd. v. Leavitt*,[15] you assert that "adoption of a rule that would divest the first generic applicant of its exclusivity after that applicant has assumed the very risks 180-day exclusivity is designed to reward – the expense of formulating a non-infringing product and preparing a legal defense to a potential action for patent infringement, and then the submission of an infringing paragraph IV certification to the Agency – would fundamentally 'change the incentive structure adopted by Congress,' in clear violation of the plain text and structure of the Hatch-Waxman Act" (Petition at 2, citing 469 F.3d at 125-26). We recognize that, based on the *Ranbaxy* decision, once an ANDA applicant has submitted a paragraph IV certification to a listed patent, FDA may not remove the patent from the Orange Book until that applicant's 180-day exclusivity has expired (or the patent has expired). However, the factual predicate upon which the *Ranbaxy* decision was based is absent from Teva's risperidone ANDA. In *Ranbaxy*, the patents had been listed for Zocor (simvastatin) at the time Ranbaxy and Ivax Pharmaceuticals, Inc. (Ivax) (subsequently acquired by Teva) submitted their paragraph IV certifications and, after OGD had received their ANDAs, Ranbaxy and Ivax each provided the required notice of their paragraph IV certifications to Merck & Co., Inc., the NDA holder and patent owner, thereby subjecting themselves to the risk of patent infringement litigation. The NDA holder's request to delist the patents for simvastatin came almost 2 years ***after*** the Ranbaxy ANDA was submitted and almost 3 years ***after*** the Ivax ANDA was submitted.[16] In contrast, Johnson & Johnson requested that the '952 patent for Risperdal be delisted 2 to 4 months ***before*** Teva's ANDA for risperidone was submitted. Moreover, the fact of patent delisting was available in the electronic Orange Book at least 1 month before Teva submitted its application.

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[14] Section 505(j)(2)(c)(vii) requires that an ANDA contain a certification with respect to each patent claiming the drug or use of the listed drug for which the applicant seeks approval "and for which information is required to be filed under [505(b) or (c)]." Therefore, to determine what certifications an ANDA must contain, FDA will refer to the most recent patent information submitted by the NDA holder. For example, if a new patent has been timely submitted to FDA for the reference listed drug and an ANDA does not contain a certification to the patent, OGD will contact the ANDA applicant and require that the applicant submit an appropriate patent certification. It is FDA's long-standing practice to require a certification to a patent recently submitted to FDA (if submitted within the time frame established by section 505(c) of the Act) even if the patent has not yet appeared in the Orange Book in any format.

[15] 469 F.3d 120 (D.C. Cir. 2006).

[16] See *Ranbaxy Laboratories Ltd. v. Leavitt*, 459 F.Supp.2d 1 (D.D.C. 2006).

Given that an NDA holder's request to delist a patent is implicitly an acknowledgment that the standard for patent listing set forth in section 505(b) and (c) of the Act – that a "claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture[,] use, or sale of the drug" – could no longer be met, Teva's purported paragraph IV certification to a delisted patent assumed none of the risks that 180-day exclusivity is designed to reward. By the time Teva submitted its ANDA, Johnson & Johnson had effectively informed FDA (and, with publication in the electronic Orange Book, the generic drug industry) that a claim of infringement of the '952 patent could not reasonably be brought against an ANDA applicant referencing Risperdal tablets. Because Teva withdrew its paragraph IV certification and never notified the NDA holder and patent owner that it believed the '952 patent to be invalid, unenforceable, or not infringed, Teva has not been subject to any risk of patent infringement litigation.[17]

The "reward Congress guaranteed in the Hatch-Waxman Act" (Petition at 5) is the opportunity for an ANDA applicant to compete with other ANDA applicants for the first substantially complete ANDA containing a paragraph IV certification to a listed patent for the reference listed drug. The uncertainties associated with this "guarantee" are encountered by all ANDA applicants – i.e., another applicant may be the "first applicant," thereby blocking a competitor from marketing for 180 days following its approval; the patent may be held to be valid and enforceable (as was the '663 patent listed for Risperdal); the patent that is the subject of a paragraph IV certification may expire before the applicant can obtain approval of its ANDA; or a patent may be delisted before submission of an ANDA (as was the '952 patent).

III. CONCLUSION

We have concluded that the '952 patent was delisted before Teva submitted to FDA ANDA 76-228 with a paragraph IV certification to the patent. Accordingly, we deny your request that FDA relist the '952 patent. Because the '952 patent was properly delisted and Teva's ANDA could not contain a paragraph IV certification for that patent, Teva is not eligible for 180-day exclusivity for ANDA 76-228.

Sincerely,

Janet Woodcock, M.D.
Acting Director
Center for Drug Evaluation and Research

[17] To the extent that Teva complains that it has gone to the expense of formulating a non-infringing product, this expense is borne by any ANDA applicant that seeks to market its proposed generic product before expiration of a valid and enforceable patent, irrespective of whether the patent is listed in the Orange Book. Indeed, in the preamble to our 1994 final rule on patent and exclusivity provisions, we noted: "FDA, however, believes it would be prudent for [ANDA] applicants to conduct patent searches if possible. A patent search could reveal the existence of an unlisted, but valid, patent and thus prevent an unnecessary expenditure of resources by applicants and FDA on a product that might not be marketable" (see "Abbreviated New Drug Application Regulations; Patent and Exclusivity Provisions, Part II; Final Rule" (59 FR 50338 at 50346; October 3, 1994).

Patent and Exclusivity Search Results from query on 020272 001.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Use Code
020272	001	4804663	DEC 29,2007	U-90

Exclusivity Data

There is no unexpired exclusivity for this product.

Thank you for searching the Electronic Orange Book

Patent and Exclusivity Terms

Return to Electronic Orange Book Home Page

Electronic Orange Book Query

Query by Active Ingredient:
risperidone (Type in part or all of name)

Select the list you would like to search:

- (•) Rx (Prescription Drug Products)
- ( ) OTC (Over-the-Counter Drug Products)
- ( ) Disc (Discontinued Drug Products)

[redacted]

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Active Ingredient Search Results from "Rx" table for query on "risperidone."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
020588		Yes	RISPERIDONE	Solution; Oral	1MG/ML	RISPERDAL	JANSSEN
020272		No	RISPERIDONE	Tablet; Oral	0.25MG	RISPERDAL	JANSSEN
020272		No	RISPERIDONE	Tablet; Oral	0.5MG	RISPERDAL	JANSSEN
020272		Yes	RISPERIDONE	Tablet; Oral	1MG	RISPERDAL	JANSSEN
020272		No	RISPERIDONE	Tablet; Oral	2MG	RISPERDAL	JANSSEN
020272		No	RISPERIDONE	Tablet; Oral	3MG	RISPERDAL	JANSSEN
020272		No	RISPERIDONE	Tablet; Oral	4MG	RISPERDAL	JANSSEN

Thank you for searching the Electronic Orange Book

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Search results from the "Rx" table for query on "020272."

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	1MG
Application Number:	020272
Product Number:	001
Approval Date:	Dec 29, 1993
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: Click Here

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	2MG
Application Number:	020272
Product Number:	002
Approval Date:	Dec 29, 1993
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: Click Here

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	3MG
Application Number:	020272
Product Number:	003
Approval Date:	Dec 29, 1993
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: Click Here

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN

Strength:	4MG
Application Number:	020272
Product Number:	004
Approval Date:	Dec 29, 1993
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: Click Here

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	0.5MG
Application Number:	020272
Product Number:	007
Approval Date:	Jan 27, 1999
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: Click Here

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	0.25MG
Application Number:	020272
Product Number:	008
Approval Date:	May 10, 1999
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: Click Here

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Patent and Exclusivity Search Results from query on 020272 001.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Use Code
020272	001	4804663	DEC 29,2007	U-90

Exclusivity Data

There is no unexpired exclusivity for this product.

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Patent and Exclusivity Terms

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Patent and Exclusivity Search Results from query on 020272 002.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Use Code
020272	002	4804663	DEC 29,2007	U-90

Exclusivity Data

There is no unexpired exclusivity for this product.

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Patent and Exclusivity Terms

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Patent and Exclusivity Search Results from query on 020272 003.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Use Code
020272	003	4804663	DEC 29,2007	U-90

Exclusivity Data

There is no unexpired exclusivity for this product.

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Patent and Exclusivity Terms

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Patent and Exclusivity Search Results from query on 020272 004.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Use Code
020272	004	4804663	DEC 29,2007	U-90

Exclusivity Data

There is no unexpired exclusivity for this product.

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Patent and Exclusivity Terms

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Patent and Exclusivity Search Results from query on 020272 007.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Use Code
020272	007	4804663	DEC 29,2007	U-90

Exclusivity Data

There is no unexpired exclusivity for this product.

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Patent and Exclusivity Terms

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Patent and Exclusivity Search Results from query on 020272 008.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Use Code
020272	008	4804663	DEC 29,2007	U-90

Exclusivity Data

There is no unexpired exclusivity for this product.

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Patent and Exclusivity Terms

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Approved Drug Products
with
Therapeutic Equivalence Evaluations

Current through July 2001

Preface

FAQ

Search by Active Ingredient Search by Applicant Holder

Search by Proprietary Name Search by Application Number

The products in this list have been approved under section 505 of the Federal Food, Drug, and Cosmetic Act.

Drug questions email: DRUGINFO@CDER.FDA.GOV

U.S Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Information Technology
Division of Data Management and Services

Updated: October 19, 2001

Active Ingredient Detail Record Search

Search results from the "Rx" table for query on "020272."

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	1MG
Application Number:	020272
Product Number:	001
Approval Date:	DEC 29, 1993
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	Click Here

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	2MG
Application Number:	020272
Product Number:	002
Approval Date:	DEC 29, 1993
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	Click Here

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	3MG
Application Number:	020272
Product Number:	003
Approval Date:	DEC 29, 1993
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	Click Here

Active Ingredient Detail Record Search

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	4MG
Application Number:	020272
Product Number:	004
Approval Date:	DEC 29, 1993
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	Click Here

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	0.5MG
Application Number:	020272
Product Number:	007
Approval Date:	JAN 27, 1999
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	Click Here

Active Ingredient:	RISPERIDONE
Dosage Form;Route:	Tablet; Oral
Proprietary Name:	RISPERDAL
Applicant:	JANSSEN
Strength:	0.25MG
Application Number:	020272
Product Number:	008
Approval Date:	MAY 10, 1999
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	Click Here

Patent and Exclusivity Search Results from query on 020272 001.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Use Code
020272	001	4804663	DEC	U-90

Exclusivity Data

There is no unexpired exclusivity for this product.

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