BUC & BEARDSLEY
919 EIGHTEENTH STREET, N.W.
SUITE 600
WASHINGTON, D.C. 20006-5503

WRITER'S TELEPHONE
202-736-3600

TELEPHONE
202-736-3600
FACSIMILE
202-736-3608

February 22, 2006

Division of Dockets Management (HFA-305)
U.S. Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

Re: Response to Banner Pharmacaps Inc.
Citizen Petition Docket No. 2005P-0436

Ranbaxy Laboratories, Inc. ("Ranbaxy"), through its undersigned counsel, submits this response to the citizen petition filed by Banner Pharmacaps Inc. ("Banner"), which requests that FDA refuse to approve Ranbaxy's Section 505(b)(2) New Drug Application ("NDA") No. 21-863 for Ibuprofen Liquid Filled Gelative Capsules 200 mg unless it contains a patent certification to the patents listed in the Orange Book for Banner's ibuprofen capsules 200 mg, U.S. Patent No. 6,251,426 ("the '426 patent").

Banner's citizen petition should be denied because Ranbaxy's 505(b)(2) application does not rely on any finding of safety or effectiveness from investigations conducted on Banner's ibuprofen capsules 200 mg. Accordingly, no certification to the listed patents for Banner's ibuprofen is required to be contained in Ranbaxy's 505(b)(2) application.

Factual Background

Ranbaxy submitted a New Drug Application ("NDA") for Ibuprofen Liquid Filled Gelatin Capsules 200 mg pursuant to Section 505(b)(2) of the Food, Drug, & Cosmetic Act ("FDCA") on November 5, 2004. The proposed therapeutic indication for Ranbaxy's ibuprofen drug product is migraine relief, which is the indication approved for Wyeth's Advil® Migraine Liqui-Gels (ibuprofen liquid filled gelatin capsules 200 mg). Advil Migraine Liqui-Gels is the only ibuprofen drug product with an approved indication for migraine.

Advil Migraine Liqui-Gels contain ibuprofen as free base and potassium salt of ibuprofen. Ranbaxy's Ibuprofen Liquid Filled Gelatin Capsules contain only ibuprofen as a free acid base form. Because of the difference between the active ingredient in Ranbaxy's Ibuprofen Liquid Filled Gelatin Capsules and Advil Migraine Liqui-Gels, Ranbaxy's application could not be filed as an ANDA referencing Advil, or any other listed drug. Ranbaxy therefore submitted its application under Section 505(b)(2).

2005P-0436

C1

Ranbaxy's application relies for approval upon the investigations of safety and effectiveness conducted for Advil Migraine Liqui-Gels, for which Ranbaxy has not obtained a right of reference or use. Specifically, Ranbaxy's application relies on the nonclinical pharmacology and toxicology data and the clinical safety and efficacy data for Advil Migraine Liqui-Gels. In addition, Ranbaxy's application includes clinical bioequivalence studies conducted by Ranbaxy demonstrating that Ranbaxy's Ibuprofen Liquid Filled Gelatin Capsules 200 mg have the same pharmacokinetic profile as the Advil migraine drug product.

Because Ranbaxy's application relied in part on the investigations conducted for Advil Liqui-Gels, the application must contain the patent certification for the Advil drug product. The Orange Book lists no patents for Advil Migraine Liqui-Gels. FDA, Approved Drug Products with Therapeutic Equivalence Evaluations (2005), available at http://www.fda.gov/cder/ob/default.htm (last visited February 17, 2006). Accordingly, Ranbaxy's application contains no patent certifications.

On Feb. 18, 2005, and again in March 2005, FDA informed Ranbaxy that its application must contain a patent certification to Banner's ibuprofen capsules 200 mg because 505(b)(2) applications must contain patent certifications to all pharmaceutically equivalent drug products. The Banner drug product contains free base ibuprofen as its active ingredient and is approved for temporary relief of minor aches and pains (NDA No. 21-472). It is not approved for the treatment of migraines.

On March 4, 2005, in response to FDA's requirement, Ranbaxy submitted an amendment to its NDA containing a paragraph IV certification to U.S. Patent No. 6,251,426, the patent listed in the Orange Book as claiming Banner's ibuprofen gel capsules, and mailed notice of the certification to Banner. On April 18, 2005, Banner sued Ranbaxy under 35 U.S.C. § 271(e)(2)(A), alleging that Ranbaxy's filing of its NDA constituted patent infringement. Complaint, copy attached as Exhibit 1, at pp. 18, 24.

On May 10, 2005, Ranbaxy sent a letter asserting its objections to FDA's patent certification requirements, withdrawing the paragraph IV certification and objecting to FDA's imposition of a 30 month stay. Following discussions with FDA's Office of Chief Counsel, FDA confirmed that the agency does not require that Ranbaxy's 505(b)(2) application contain a certification to any patent listed in the Orange Book as claiming Banner's ibuprofen gel capsule 200 mg, including the '426 patent, because, among other things, Ranbaxy's 505(b)(2) application does not rely upon any investigations conducted for Banner's ibuprofen gel capsules 200 mg. Based on FDA's decision, Ranbaxy moved to dismiss Banner's patent infringement suit. The district court stayed the litigation, pending a written decision on this citizen petition.

Discussion

It its citizen petition, Banner relies on part of a 1999 Draft Guidance for Industry, "Applications Covered by Section 505(b)(2)," which indicates that 505(b)(2) applications should include, in addition to the certifications required by the statute, patent certifications for any listed drug that is the pharmaceutical equivalent of the drug referenced in the 505(b)(2) application.

Banner also relies on FDA's discussion of the Draft Guidance in FDA's response to a citizen petition filed on behalf of Abbott Laboratories regarding fenofibrate. However, Banner's citizen petition fails to account for the statutory provisions, which do not require a certification to patents listed by sponsors of pharmaceutically equivalents drugs. In addition, FDA's 1999 Draft Guidance, upon which Banner's argument is based, is a draft document, never finalized, which does not operate to bind FDA or the public. Finally, the position announced in the Draft Guidance cannot have been intended to apply in circumstances such as these, where the pharmaceutical equivalent is not approved for the indication sought by the 505(b)(2) applicant and no applicable patent is circumvented by the 505(b)(2) application.

Ranbaxy's 505(b)(2) Application Complies with the Statute and Regulations

The FDCA provides that an application submitted for a drug for which any of the investigations of safety and effectiveness relied upon by the applicant for approval were not conducted for the applicant and for which the applicant has not obtained a right of reference or use must include:

> a certification . . . with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under [subsection 505(b)] and for which information is required to be filed under [Section 505(b)(1)] or [Section 505(c)].

Food, Drug, and Cosmetic Act, Section 505(b)(2)(A). In this case, the only prior findings of safety and effectiveness on which Ranbaxy relies are investigations conducted on Advil Migraine Liqui-Gels. Thus, the "drug for which such investigations were conducted" is Advil Migraine Liqui-Gels. Ranbaxy does not rely on any investigations conducted for the Banner drug product. Accordingly, under the clear language of the statute, the Ranbaxy NDA must include a certification only for those patents listed in the Orange Book as claiming Advil Migraine Liqui-Gels. Ranbaxy fulfilled the statutory requirement by certifying to FDA that no patents claim the drug.

Ranbaxy's patent certification also comports with the agency's regulations. Under the regulations, a 505(b)(2) application is required to contain a patent certification:

> with respect to each patent issued by the United States Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims a drug (the drug product or drug substance that is a component of the drug product) on which investigations that are relied upon by the applicant for approval of its application were conducted or that claims an approved use for such drug and for which information is required to be filed under section 505(b) and (c) of the act and § 314.53.

21 C.F.R. § 314.50(i)(1)(i)(A). See also 21 C.F.R. § 314.54(a)(1)(iii) (directing applicants to identify the listed drug on which the application relies). The investigations relied upon by Ranbaxy were conducted for Advil Migraine Liqui-Gels, for which no patent information is listed in the Orange Book.

The preamble to FDA's regulation confirms that Ranbaxy's 505(b)(2) application contains all required certifications. In the preamble, FDA explained that "an applicant submitting a 505(b)(2) application must make certifications with respect to patents claiming any listed drug on which investigations that are relied upon by the applicant for approval of its application were conducted or claiming a use for such listed drug." Proposed Rule, Abbreviated New Drug Application Regulations, 54 Fed. Reg. 28,872, 28,875 (July 10, 1989); Final Rule, Abbreviated New Drug Application Regulations; Patent and Exclusivity Provisions, 59 Fed. Reg. 50,338 (Oct. 3, 1994) (certification required for patents claiming listed drug). The term "listed drug" in turn means simply a new drug product that has an effective approval. 21 C.F.R. § 314.3(b). The relevant listed drug on which Ranbaxy relied is Wyeth's Advil Migraine Liqui-Gels. Banner's ibuprofen capsules is a different listed drug, the application for which does not contain investigations on which Ranbaxy relies.

Whether assessed by the clear statutory language, the express provisions of the regulations, or both, Ranbaxy's 505(b)(2) application clearly satisfies all applicable patent certification requirements. No patent certifications to the Banner drug product are required.

The 1999 Draft Guidance Does Not Require Certification to Banner's Drug Product.

FDA's draft guidance appears to indicate that 505(b)(2) applications should include patent certifications to pharmaceutical equivalents of the drug for which the 505(b)(2) approval is sought. FDA has explained that the provision is intended to prevent applicants for a generic version of a drug from avoiding the ANDA patent certification obligations by using the 505(b)(2) pathway. Response to Citizen Petition of Abbott Laboratories and Laboratories Fournier SA, Docket Nos. 2004P-0386/CP1 and RC1 (November 30, 2004), p. 9 ("Abbott Petition"). At the same time, FDA has emphasized the link between the 505(b)(2) applicant's reliance on data and the patents to which it must certify. Id. at 6-8. ("The language of section 505(b)(2) of the Act explicitly links the drug relied on for approval to the drug for which patent certifications must be made;" "FDA's implementing regulations reinforce this relationship between reliance and certification;" "Patent certification obligations thus are linked to identification of the listed drug or drugs on which the application relies . . ."). Reconciling the command of the statute and regulations, FDA's statements linking reliance and certification, and FDA's guidance, suggests that FDA intends to require certification to the patents of a pharmaceutical equivalent where the 505(b)(2) applicant might otherwise choose to rely on one among several listed drugs and avoid certifications by choosing the listed drug with patent certification-related considerations in mind. Whether or not FDA's interpretation correctly reflects the statute, the situation here is not the kind that FDA sought to prevent. Ranbaxy did not choose from among several possible listed drugs or base its decision on patent-related

considerations. Ranbaxy needed to rely on the Wyeth NDA because only that NDA contained the finding of safety and efficacy regarding the migraine indication. The Banner application, in contrast, offered no data on which Ranbaxy could usefully rely.

Banner seeks to obscure the critical distinction between the drug for which Ranbaxy seeks approval and its drug product by claiming that both Ranbaxy's product and Banner's product are pain relievers. To be sure, it can be said of both products that they relieve pain, but they are not approved for the same indication. Banner's product, unlike Wyeth's, is not approved for a migraine indication. Ranbaxy, therefore, cannot obtain a migraine indication by submitting an ANDA to the Banner product. Moreover, it is undisputable that Ranbaxy's 505(b)(2) application contains the same patent certifications that would be required for an ANDA referencing the Wyeth product.

FDA Cannot Enforce the Draft Guidance in Derogation of the Statute

To be consistent with the statute, the draft guidance's requirement cannot apply in situations where the pharmaceutical equivalent is not approved for the indication sought and where neither the effect nor the intent of the application is to circumvent a patent. If the draft guidance were read to require that Ranbaxy certify to the Banner patent, it would be inconsistent with the statute and regulations.

FDA cannot lawfully impose a patent certification requirement that is inconsistent with the statute. See, e.g., Nutritional Health Alliance v. FDA, 318 F.3d 92,104 (2d Cir. 2003); Mova Pharm. Co. v. Shalala, 140 F.3d 1060, 1076 (D.C. Cir. 1998) (holding FDA may not exceed statutory authority in imposing additional requirement that is inconsistent with statutory text and structure of Hatch Waxman); Granutec, Inc. v. Shalala, 1998 U.S. App. LEXIS 6685 (4th Cir. Apr. 3,1998); Nutraceutical Corp. v. Crawford, No. 2:04CV049TC (D. Utah, Order April 13, 2005) (holding FDA may not apply different evidentiary burden to dietary supplements than that identified in DSHEA). Section 505(b)(2) of the FDCA identifies those drugs as to which patent certifications are required; it is those drugs on whose investigation the application relies.

Moreover, FDA's 1999 Draft Guidance has never been adopted even as a final guidance, let alone as a regulation. There is no legal basis for Banner's contention that FDA must apply the 1999 Guidance to require patent certifications that the statute does not require.

Requiring Ranbaxy to Certify to Banner's Patent Would Undermine Hatch Waxman Policy Objectives

Requiring patent certifications to the Banner drug product would undermine, rather than advance, the very policy objectives FDA sought to advance. FDA has recognized in many contexts that Hatch Waxman reflects an attempt to balance two competing interests: promoting competition and encouraging research and innovation. See, e.g., Response to Citizen Petition of Pfizer, Inc. et al., Docket Nos. 2001P/0323/CP1 and C5, 2002 P-0447/CP1 and 2003P-0408/CP1 (Oct. 14, 2003). It accomplishes that objective in part by providing patent protection only when an innovator's data are relied upon. The language of Section 505(b)(2) therefore requires a

505(b)(2) applicant to certify to patents listed for any drug product on which the applicant relies for a finding safety and effectiveness, but not to patents for drug products on which the applicant does not seek to rely.

This approach ensures that patent certification obligations for 505(b)(2) applications and for ANDAs are parallel. Response to Abbott Petition at 10. Requiring a 505(b)(2) applicant to certify to patents claiming drugs on which the 505(b)(2) applicant has not relied would alter the Hatch Waxman balance, providing patent protection even when the innovator has not been potentially disadvantaged by someone else's use of its data. The absence of a certification does not mean, of course, that an owner of patents on a different drug has no recourse. If the patent owner believes that the drug infringes its patent, it may always sue for patent infringement, regardless of whether an application contains a certification to the patent. Severing the connection between the use of data and patent protection would leave no principled way to decide which drugs will receive patent protection and which do not.

In addition, imposing requirements that 505(b)(2) applicants certify to additional patents would be a significant deterrent to developing innovative drugs for approval under Section 505(b)(2) and could slow down the approval of those that are developed, thus increasing barriers to entry of potentially competing drug products. Innovative drugs should be allowed to reach the market without unnecessary constraints.

In sum, there is no policy rationale for requiring 505(b)(2) applicants to certify to patents for drug products on whose findings of safety and effectiveness they do not seek to rely. Even if any legitimate policy objective could be served by FDA's requirement, however, the statutory language in Section 505(b)(2)(A) and the clear Congressional intent evidenced by the language preclude FDA from imposing any additional patent certification requirements.

Very truly yours,

Kate C. Beardsley
Carmen M. Shepard