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March 27, 2006

BY FEDERAL EXPRESS

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

Re: **Docket No. 2005P-0436:**
NDA 21-863; Ibuprofen Liquid Filled Gelatin Capsules 200 mg; Ranbaxy Laboratories Ltd.

THIRD SUPPLEMENT TO CITIZEN PETITION

Upon due consideration, our client Banner Pharmacaps Inc. is compelled to reply to the comments on Banner's above-identified Citizen Petition filed by Ranbaxy on March 23, 2006.

I. FDA's Pharmaceutical Equivalent Patent Certification Requirement Is A Valid Interpretation of Section 505(b)(2)

Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 355(b)(2), requires a 505(b)(2) NDA applicant to certify to Orange Book patents claiming a reference listed drug (RLD) upon which the applicant relies for prior safety and efficacy data. The section, however, does not explicitly address the situation where there is an additional RLD that is the pharmaceutical equivalent of the 505(b)(2) applicant's drug. As such, Section 505(b)(2) is ambiguous on this issue, and FDA has extremely broad discretion to fill the gap. *Purepac Pharmaceutical Co. v. Thompson*, 354 F.3d 877, 888-89 (D.C.Cir. 2004) (upholding FDA's interpretation that a Paragraph IV filer's certification is not effective until it sends notice, but is not void for late notice).

In *Purepac*, the U.S. Court of Appeals for the District of Columbia Circuit emphasized the long-standing recognition that "the breadth of the agency's discretion is, if anything, at its zenith when the action involved when the action assailed relates primarily not to the issue of whether conduct violates the statute or regulations, but rather to the fashioning of policies, remedies and sanctions." 354

F.2d at 889, citing *Niagara Mohawk Power Corp. v. Fed. Power Comm'n*, 379 F.2d 153, 159 (D.C.Cir. 1967).

FDA has decided to fill the instant gap by requiring a 505(b)(2) applicant like Ranbaxy to rely also upon the pharmaceutically equivalent RLD, and to certify to any patents claiming the pharmaceutically equivalent RLD. This decision is reasonable, permissible, and is entitled to great deference. *Chevron USA v. Natural Resources Defense Council*, 467 U.S. 837, 843, 104 S.Ct. 2778, 81 L.Ed. 2d (1984).

As most recently held in *Apotex Inc. v. Food and Drug Administration*, No.CIV.A. 05-0125 (JDB), 2006 WL 319042 *11 (D.D.C. Feb. 13, 2006) (sustaining FDA's "patent-by-patent" interpretation of 180-day generic exclusivity):

> The FDA has been given substantial delegated authority over a silent and ambiguous statute in this complex arena, and has chosen a method that it believes strikes the delicate balance between the competing legislative policies of incentivizing new pharmaceutical developments and encouraging lower-cost generic competition. Hence the deference to which the agency is entitled is at its apex. *See [United States v.] Mead*, 533 U.S. 218, 226-27, 121 S.Ct. 2164.

II. The Fenofibrate Decision Is Applicable Precedent

Ranbaxy's attempt to distinguish the fenofibrate decision (March 23rd comments, p.3) is meritless.

FDA's Nov. 30, 2004 fenofibrate decision fully articulated the principle, earlier embodied in the 1999 Section 505(b)(2) Guidance, that a 505(b)(2) applicant must certify to patents claiming a pharmaceutically equivalent RLD. In applying this principle to the fenobibrate facts, FDA found that it did not apply to the situation presented there, because "Reliant's section 505(b)(2) application for fenofibrate **did not seek approval for a pharmaceutical equivalent to an approved product.**" (Banner's instant Citizen Petition, Ex. I, at 10).

Here, however, Ranbaxy **does** seek approval of a pharmaceutical equivalent to Banner's previously-approved drug product, and must therefore follow the 505(b)(2) Guidance's patent certification principle affirmed in fenofibrate.

III. Conversion To An ANDA Is Mandated By Hatch-Waxman And The 505(b)(2) Guidance

Ranbaxy's assertion that it cannot be required to convert its application to an ANDA, due to lack of precedent. is unfounded.

The precedent is the statute, confirmed by FDA's 505(b)(2) Guidance. An ANDA must be filed if the drug for which approval is sought is identical to an RLD in active ingredient, strength, dosage form, route of administration and labeling. 21 U.S.C. § 355(j)(2)(A)(ii), (iii), (v); 21 C.F.R. § 314.101(d)(9). Moreover, the 505(b)(2) Guidance unequivocally states in pertinent part:

> **WHAT CAN'T BE SUBMITTED AS 505(B)(2) APPLICATIONS?**
>
> - An application that is a duplicate of a listed drug and eligible for approval under Section 505(j) (see 21 C.F.R. 314.101(d)(9)).

(Banner's instant Citizen Petition, Ex. H, at 6).

Ranbaxy's drug product is a duplicate of Banner's drug product – both are ibuprofen base, liquid-filled gelatin capsules, 200 mg, with a migraine labeling indication. As such, Ranbaxy's product is eligible for approval via an ANDA. Ranbaxy must therefore seek approval via an ANDA.

That Ranbaxy's product was initially submitted via a 505(b)(2) NDA does not alter this result. Banner's product has now received approval of a migraine indication. Prior to final approval of Ranbaxy's product, Ranbaxy's product duplicates Banner's previously-approved RLD.

In this regard, FDA routinely requires applicants to adapt to changed circumstances while their applications are pending. For example, in 2001 generic applicants for the drug omeprazole were required to amend their labeling and conduct additional bioequivalence studies, when the innovator (AstraZeneca) received supplemental NDA approval for a labeling change advising that patients with difficulty swallowing a capsule could take the product sprinkled on applesauce. No generic application received final approval until its sponsor had successfully conducted an additional bioequivalence study under sprinkle-applesauce conditions.

So too here. Ranbaxy must conduct an additional study via an ANDA demonstrating bioequivalence to Banner's previously-approved pharmaceutically

equivalent RLD.

IV. Conclusion

For the reasons set forth in the instant Petition and all supplements thereto, Banner's Citizen Petition should be granted in full.

Respectfully submitted,

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