

1001 G Street, N.W.
Suite 500 West
Washington, D.C. 20001
tel. 202.434.4100
fax 202.434.4646

1075 '06 JUN 29 P3:29

June 29, 2006

Writer's Direct Access
John B. Dubeck
(202) 434-4125
dubeck@khlaw.com

Via Hand Delivery

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

Re: Citizen Petition Docket No. 2005P-0498

Biovail Corporation filed the above-referenced Citizen Petition ("Petition") pursuant to 21 C.F.R. § 10.30(g) on December 20, 1995. That Petition requests the Food and Drug Administration ("FDA") to apply certain criteria in deciding whether to approve generic versions of Wellbutrin XL[®] (bupropion hydrochloride extended-release tablets). On June 7, 2006, FDA responded that it had not yet reached a decision on the issues raised in the Petition.

Biovail requests that FDA take final action on this Petition forthwith, but in no case fewer than two business days prior to finally approving any Abbreviated New Drug Application ("ANDA") for a generic version of Wellbutrin XL[®]. Biovail further requests that it be given notice of that requested action immediately upon its being taken, but in no case fewer than two business days prior to finally approving any such ANDA. If, by July 14, 2006, the Agency does not indicate that it will respond to the Petition before taking action on any relevant ANDAs, Biovail will consider itself free to pursue appropriate judicial relief.

1. FDA Can and Should Decide the Petition Now.

FDA has sufficient information in its possession with which to take final action in the near future on this Petition and it has unquestionable authority to do so.¹ Due process requires FDA to take and give Biovail notice of such action a reasonable time prior to finally approving any ANDA for Wellbutrin XL[®].

The Biovail Petition requests only that FDA, in deciding whether to approve any referenced ANDA, assure itself that the application satisfies certain safety and equivalency

¹ See, e.g., Federal Food, Drug, and Cosmetic Act Section 701, 21 U.S.C. § 371(b); 21 C.F.R. § 10.35(e).

2005P-0498

LET 2

KELLER AND HECKMAN LLP

Division of Dockets Management

June 29, 2006

Page 2

criteria. Because the Petition relates to the process for deciding whether to issue such a final ANDA approval, FDA must decide the Petition before deciding whether to finally approve the application.

Stated another way, it would be arbitrary, capricious, and an abuse of discretion for FDA to (a) decide to issue a final ANDA approval, and (b) later or simultaneously decide whether to follow the procedure that is requested by the pending Petition for making that decision on the ANDA.

It would be a similar violation of Biovail's due process rights for FDA to deny the Petition in whole or in part, but to delay the required notice to Biovail of that denial until it provides an applicant with notice of the approval of its ANDA for a generic form of Wellbutrin XL®.² Such a practice of delaying prompt notice would unlawfully impair Biovail's right to effective judicial review and, by necessary implication, it would be an *ultra vires* attempt by FDA to limit judicial oversight.

Petitioner's concern is that FDA might decide (or has already decided) to deny Biovail's Petition in whole or in part, but also might decide (or has already decided) to improperly delay giving notice of this action. This concern arises out of FDA practices with respect to similar petitions. In recent instances in which the Agency has denied such a petition, it has delayed giving notice of that denial in ways that impair effective judicial review of the denial.³ Biovail

² See, e.g., 5 U.S.C §§ 555(e), 706(1); *Sandoz v. Leavitt*, 427 F.Supp.2d 29 (DDC 1997) (applying six factor test to determine whether FDA inaction on ANDA warranted equitable relief: "(1) the time agencies take to make decisions must be governed by a rule of reason; (2) where Congress has provided a timetable or other indication of the speed with which it expects the agency to proceed in the enabling statute, that statutory scheme may supply content for this rule of reason; (3) delays that might be reasonable in the sphere of economic regulation are less tolerable when human health and welfare are at stake; (4) the court should consider the effect of expediting delayed action on agency activities of a higher or competing priority; (5) the court should also take into account the nature and extent of the interests prejudiced by delay; and (6) the court need not find any impropriety lurking behind agency lassitude in order to hold that agency action is unreasonably delayed").

³ See, e.g., FDA's denial of the following petitions relating to ANDAs: (1) GlaxoSmithKline's petition regarding cefuroxime axetil on Feb. 15, 2002, with approval of Ranbaxy Laboratories' generic on the same day (Docket No. 2001P-0428); (2) CollaGenex's petition regarding doxycycline hyclate on May 13, 2005 with approval of Corepharma's generic on the same day (Docket No. 2004P-0517); and (3) multiple citizen petitions regarding fluticasone propionate on Feb. 22, 2006 with approval of Roxane Laboratories' generic on the same day (Docket No. 2004P-0239).

seeks to avoid that unfair and otherwise harmful burden. As discussed more fully below, once the ANDA final approval is out the FDA door, chances of getting a court to close that door without the petitioner (Biovail in this case) suffering irreparable harm are virtually non-existent.

Biovail's above-stated concerns are heightened by the Agency's recent announcement that it would indefinitely delay its decision on the Petition beyond the 180-day initial regulatory deadline.⁴ The only basis given for this dilatory action was the following standard form sentence: "FDA has been unable to reach a decision on your petition because it raises complex issues requiring extensive review and analysis by Agency officials." Surely that cannot be the real (or at least the only) reason.⁵ We fear that undisclosed reason is that FDA wants, once again, to delay deciding the petition to minimize its risk of successful judicial review of its ANDA approval.

2. The Requested Action Would Reduce the Risk of Violating Biovail's Due Process Rights.

Procedural due process requires that agencies employ constitutionally adequate procedures so as not to deprive interested persons of property and other rights.⁶ As the holder of the patent- and approved New Drug Application-based market rights to Wellbutrin XL®, Biovail has a strong property interest that will be affected by FDA's approval of any ANDA for a competing generic version of that drug. Biovail stands to lose millions of dollars in sales and a significant portion of market share immediately upon the debut of any such generic. Because of this, Biovail is a "uniquely affected party" that is entitled to adequate process and a means to get its concerns appropriately addressed before being deprived of its property right.

Property rights of the type held by Biovail are within the zone of interest recognized in the legislative history and provisions of the Hatch-Waxman Act, the organic statute that authorizes and controls FDA's decision-making with regard to finally approving ANDAs.⁷ That

⁴ June 7, 2006, Interim Response (entered in FDA docket on June 12).

⁵ Nonetheless, given that statement, we submit that it would be arbitrary and capricious for FDA to deny the Petition without providing Biovail a delineation of such "complex issues" and the Agency's "extensive" analysis thereof. See 5 U.S.C. § 706; *Citizens to Preserve Overton Park v. Volpe*, 401 U.S. 402, 419-20 (1971); see also *Zotos International v. Kennedy*, 460 F.Supp. 268, 278-279 (D.D.C. 1978).

⁶ *Cleveland Board of Education v. Loudermill*, 470 U.S. 532, 538-42 (1985); *Mathews v. Eldridge*, 424 U.S. 319 (1976).

⁷ Pub. L. No. 98-417, § 210, 98 Stat. 1585 (1984) ("Hatch-Waxman Act"). Title II of that Act was intended to protect the property rights and interests of patent holders. H. Rep. No. 98-857, at 17 (1984), as reprinted in 1984 U.S.C.C.A.N. 2647, 2650.

Act balances the public interest in having the availability of generic drugs and the public and private interests that arise from the availability of patent rights, which promote needed innovation.

3. Sufficient Notice Is Imperative to Protect Biovail's Property Interest.

We noted above the due process impairment to effective judicial review caused by FDA's practice of giving notice of its denial of similar petitions at or after announcing the final approvals of the ANDA to which the petitions relate. The practical effect of such an improper practice is to force upon the adversely affected petitioner the unnecessary and tremendous burden of seeking a temporary restraining order ("TRO") against implementation of the final ANDA approval, while at the same time seeking to challenge FDA's denial of the petition that related to the process and criteria used for deciding that approval.

Irreparable harm would occur to a petitioner such as Biovail if it did not seek or achieve a TRO and preliminary injunction virtually immediately after FDA's final approval of the ANDA in question. The certainty of such harm is well known to FDA and has been recognized by federal courts granting injunctive relief against FDA:

[Plaintiff] cites industry publications to demonstrate that generic Prozac achieved 59% market penetration of total prescriptions for one dosage strength and 70% of new prescriptions for another dosage strength within one month of launch. Within two weeks of availability of a generic version of Astra's drug Zestril, Merck-Medico mail order pharmacy apparently achieved 91% generic conversion. Megestrol is said to have achieved 75% market share within six months.⁸

As the court recognized in that case:

It is not at all difficult to foresee that [Plaintiff]'s market position would collapse as soon as one or more generic drugs became available. [Plaintiff] would lose its head start in the market and its continued viability would be at issue. It could never recoup from FDA any losses that would occur These are the kinds of circumstances in which irreparable harm has been found.⁹

⁸ *CollaGenex Pharms., Inc. v. Thompson*, 2003 WL 21697344 at *10 (D.D.C. Aug. 26, 2003) (unreported opinion granting preliminary injunction).

⁹ *Id.*

4. Sound Public Policy Grounds Support the Action Requested.

FDA must fulfill its statutory and regulatory responsibilities with respect to the safety and effectiveness of drug products. It should exercise extreme care in its approval of generic drugs to avoid potential harm to the public and the pharmaceutical industry.

The approval of purported generic drugs that are not shown to be bioequivalent to the innovator drug is unlawful. Any such action could put unsuspecting patients at risk while damaging the integrity of the generic drug industry. Moreover, the harm that could be caused by an FDA mistake here would cause a significant reduction in the public's confidence in FDA. Sound public policy clearly supports requiring FDA to comply with its statutory and regulatory requirements.

5. Public Health and Other Public Interests Outweigh the Effects of the Requested Stay.

Biovail recognizes the important role that generic drugs can play in making proper healthcare available to patients and in controlling the growth of healthcare costs. Biovail is not seeking to prohibit or delay the eventual approval of properly-supported generic versions of Wellbutrin XL®, nor is it seeking to unnecessarily burden FDA or ANDA submitters. Any delay caused by the need for additional data would be outweighed by the need to ensure that FDA follows the appropriate procedures and applies the proper approval criteria. FDA's primary obligation is to protect the public health; drug cost considerations should not override the Agency's duty to assure the safety and effectiveness of the drugs it finally approves. And, of course, it goes without saying that all stakeholders – the Agency, drug manufacturers, and the public at large – are harmed when unconstitutional and otherwise improper procedures are used for deciding whether to issue such approvals.

In practical terms, granting Biovail's Petition in whole or part in the near future may very well satisfy Biovail's concerns. Denying it in whole or in part in the near future may result in judicial review, but such review would be prior to the ultimate decision on an ANDA that would result in the marketplace being flooded by products that might not be as safe or effective as Wellbutrin XL®.

CONCLUSION

For the reasons stated here and in its Petition, Biovail respectfully requests that FDA take final action on this Petition forthwith, but in no case fewer than two business days prior to finally approving any ANDA for a generic version of Wellbutrin XL® and that Biovail should be given notice of that requested action immediately upon its being taken, but in no case fewer than two business days prior to finally approving any such ANDA.

KELLER AND HECKMAN LLP

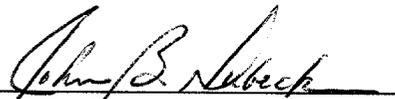
Division of Dockets Management

June 29, 2006

Page 6

If, by July 14, 2006, the Agency does not indicate that it will respond to Biovail's Citizen Petition before taking action on any relevant ANDAs, Biovail will consider itself free to pursue appropriate judicial relief.

Respectfully submitted,



John B. Dubeck

Richard J. Leighton

Frederick A. Stearns

Counsel to Biovail Corporation