IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

BIOVAIL CORP., *et al.*, Plaintiffs, v. U.S. FOOD AND DRUG ADMINISTRATION, *et al.*, Defendants, and ANCHEN PHARMACEUTICALS, INC., Intervenor-Defendant, and TEVA PHARMACEUTICALS USA, INC., and IMPAX LABORATORIES, INC., Proposed Intervenor-Defendants.	)	Case No. 06-CV-1487 (RMU)

INTERVENOR-DEFENDANT ANCHEN PHARMACEUTICALS, INC.'S MEMORANDUM IN OPPOSITION TO PLAINTIFF'S SECOND MOTION FOR A TEMPORARY RESTRAINING ORDER AND PRELIMINARY INJUNCTION

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INTRODUCTION

This motion is just the latest salvo in Biovail's ongoing battle to prevent competition in the WELLBUTRIN XL® market. Although claiming to be concerned about safety issues, in reality Plaintiffs Biovail Corporation (the Canadian manufacturer of WELLBUTRIN XL®) and Biovail Laboratories SRL (an offshore patent holding company) (collectively, "Biovail") are seeking to protect the financial rewards Biovail derives from a license and distribution agreement with non-party GlaxoSmithKline ("GSK"), the company that actually owns the WELLBUTRIN XL® NDA and markets the product in the United States. Biovail seeks to halt lower-priced generic competition to WELLBUTRIN XL®, which will reduce the revenue Biovail receives based on GSK's current monopoly sales of bupropion hydrochloride extended-release tablets in the United States.

Like its first motion, Biovail's Second Motion for a TRO and Preliminary Injunction falls to articulate any basis for injunctive relief. This Court has already dispensed with many of the issues Biovail currently raises. Indeed, in Biovail's first motion it claimed, just as it does now, that it would suffer irreparable harm to its reputation if FDA approved unsafe generic WELLBUTRIN XL® products. This Court properly rejected Biovail's argument as wholly speculative and lacking in evidentiary support. Despite having several months to adduce some evidence that approval of Anchen's ANDA would raise safety concerns, Biovail has failed to come forth with even a single piece of evidence to justify reexamination of this Court's original analysis.

On the same day as it filed this motion, Biovail filed another complaint and TRO motion against FDA in the District of Maryland, challenging FDA's decision to grant final approval to another ANDA applicant. The court rejected Biovail's request outright, concluding

among other things that Biovail had not shown irreparable harm from the introduction of generic competition that outweighed the tangible harms to the ANDA applicants and to FDA. (Ex. 1, Hearing Tr. at 92-93.)[1] Biovail also filed a motion for a TRO in a patent case in the Eastern District of Pennsylvania. According to the public records, this request for a TRO was also denied.

Like the others before it, Biovail's instant motion should be denied. FDA has thoroughly vetted Biovail's purported concerns about safety and has concluded, in its scientific expertise, that there is no reason to impose additional bioequivalence requirements on WELLBUTRIN XL® ANDA applicants. Biovail would have this Court supplant FDA's considered judgment based on nothing but unsupported "assumptions" and rank speculation. There is no legal basis to grant such relief. Biovail cannot show a substantial likelihood of success on the merits. Biovail cannot show irreparable harm. Biovail cannot show that the speculative harm it claims is outweighed by the real and tangible harm to ANDA applicants and FDA. And Biovail cannot show that it is in the public's interest to remove generic competition on the basis of its self-serving and unsupported speculation.

FACTS

I. Statutory Background.

This case is grounded in the Hatch-Waxman Amendments to the Federal Food Drug and Cosmetic Act ("FFDCA"). *See* Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. § 355 and 35 U.S.C. §§ 156, 271(e)). Under the FFDCA, as amended, a company seeking approval to market a drug that has not previously been approved must file with the U.S.

[1] "Ex. __" refers to Exhibits 1 - 18, attached to the Declaration of Maureen L. Rurka, which is submitted with this brief. "BV First TRO Br. __" refers to Biovail's Memorandum in Support of its First Motion for a TRO and Preliminary Injunction, filed on August 23, 2006. "Mem. Op. __" refers to this Court's Memorandum Opinion denying Biovail's August 23, 2006 Motion for a TRO. "BV Br. __" refers to the Memorandum that Biovail filed in support of the instant (Second) Motion for a TRO and Preliminary Injunction.

Food and Drug Administration ("FDA") a New Drug Application ("NDA"), which contains clinical studies showing the proposed drug product is safe and effective if used as indicated on the proposed label. 21 U.S.C. § 355(b)(1). The NDA must also include, among other things, any patent that "claims the drug for which the applicant submitted the application . . . ." *Id.* FDA lists the NDA drug, called the "listed drug" or "reference listed drug," in "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the "Orange Book," along with any patent information submitted by the NDA holder relating to the listed drug. 21 U.S.C. § 355(b)(1), -(j)(7)(A)(iii); *see also* 21 C.F.R. § 314.3 ("reference listed drug" is "the listed drug identified by FDA as the drug product upon which an applicant relies in seeking approval of its abbreviated application").

A company seeking approval to market a generic version of a listed drug may file an abbreviated new drug application ("ANDA") that relies on the safety and efficacy studies of the listed drug. 21 U.S.C. § 355(j)(1), -(j)(2). To do so, the ANDA applicant must, among other things, submit a "certification" for each patent listed in the Orange Book in connection with the brand name drug. *Id.* § 355(j)(2)(A)(vii). An ANDA applicant seeking to obtain approval prior to expiration of a listed patent must (with certain exceptions) submit a "paragraph IV" certification, which states that the patent is invalid, unenforceable and/or will not be infringed by the proposed ANDA product. *Id.* § 355(j)(2)(A)(vii)(IV); 21 C.F.R. § 314.94(a)(12)(i)(A)(4). The first ANDA applicant to file a paragraph IV certification to a patent listed in connection with the listed drug is entitled to a 180-day period of marketing exclusivity, which prevents FDA from approving any subsequent ANDAs until this exclusivity period expires. 21 U.S.C. § 355(j)(5)(B)(iv).

Importantly, each ANDA applicant must also show that its proposed ANDA product is bioequivalent to the listed drug, and that it contains the same active ingredient, conditions of use, route of administration, dosage form, strength, and (with certain exceptions) labeling as the listed drug. *See id.* § 355(j)(2)(A); 21 C.F.R. § 314.94(a). If the ANDA satisfies these statutory and regulatory requirements, the ANDA applicant is allowed to rely on the safety and efficacy studies conducted on the listed drug without replicating those studies on the ANDA product. *See In re Barr Labs., Inc.*, 930 F.2d 72, 73 (D.C. Cir. 1991) ("This expedited process [under Hatch-Waxman] permits generic drug applications to piggy-back on clinical findings that FDA has already embraced."); *Zeneca, Inc. v. Shalala*, 213 F.3d 161, 164 (4th Cir. 2000) ("The ANDA procedure 'permits generic drug applications to piggy-back on clinical findings that [the] FDA has already embraced' in the NDA and thus, the ANDA applicant need not duplicate the clinical safety studies that supported the pioneer drug's NDA.") (quoting *Barr Labs.*, 930 F.2d at 73). The ANDA product is then considered therapeutically equivalent to the listed drug and can be substituted at the pharmacy level for the listed drug. *See Approved Drug Products With Therapeutic Equivalence Evaluations* vi (26th ed. 2006) (the "Orange Book Preamble") ("FDA believes that products classified as therapeutically equivalent can be substituted with the full expectation that the substituted product will produce the same clinical effect and safety profile as the prescribed product.").[2]

In 1977, even before Congress enacted Hatch-Waxman, FDA had examined and developed detailed and extensive criteria for demonstrating bioequivalence to another drug. *See Fisons Corp. v. Shalala*, 860 F. Supp. 859, 864 (D.D.C. 1994) ("In a 1977 codification, the FDA defined bioavailability and bioequivalence in drug products."). Following enactment of Hatch-

[2] Available at www.fda.gov/cder/orange/obannual.pdf.

Waxman, FDA formally implemented regulations, after notice and comment, that fine-tuned the standards ANDA applicants must meet to establish bioequivalence. *See* 21 C.F.R. § 320.24(b); *Fisons*, 860 F. Supp. at 864, 865.

FDA generally considers the most accurate, sensitive and reproducible methodology for bioequivalence studies to be *in vivo* pharmacokinetic studies, which test the concentration of active ingredient in the blood or other biological fluid of a human subject as a function of time. *See* 21 C.F.R. § 320.24(b)(1)(i). Active metabolites should be measured "when appropriate." *Id.*[3]

II. Factual Background.

A. Anchen's Bupropion Hydrochloride ANDA.

In September 2004, Anchen filed an ANDA seeking FDA approval to market generic bupropion hydrochloride extended release tablets in two strengths, 150 mg and 300 mg. (Ex. 2, Selna SJ Order at 1.) The listed drug for Anchen's ANDA is WELLBUTRIN XL®, which is one of several FDA-approved bupropion products listed in the Orange Book. A Biovail company manufactures WELLBUTRIN XL® in Canada, and owns certain patents. (Amended and Supplemented Complaint ("Am. Compl."), ¶¶ 15-16; Ex. 3, Complaint for Patent Infringement ("Patent Compl."), ¶¶ 8-10.) Non-party GlaxoSmithKline or an affiliate of that company holds the NDA for WELLBUTRIN XL® and markets the product in the United States. (Am. Compl., ¶ 16.)

[3] In its citizen petition, Biovail argues that generic applicants should be required to test three active metabolites. FDA granted in part, and denied in part, Biovail's request. FDA agreed that the major metabolite, hydroxybupropion, should be measured by ANDA applicants. (Ex. 6, FDA CP letter at 10.) FDA disagreed that there was sufficient scientific evidence to draw a conclusion from testing the two other metabolites, and therefore did not require such testing. (*See id.* at 10-11.) Biovail does not challenge this aspect of FDA's decision in its moving papers.

Anchen's ANDA contains paragraph IV certifications to the patents listed in the Orange Book in connection with WELLBUTRIN XL®. As required by statute, after receiving a letter from FDA in November 2004 accepting its ANDA for filing, Anchen provided Biovail and GSK notice of its ANDA and paragraph IV certifications. (Ex. 3, Patent Compl., ¶ 12.) Anchen was the first WELLBUTRIN XL® ANDA applicant to submit paragraph IV certifications to the listed patents. As such, it was entitled to 180-day exclusivity for both its 150 mg and 300 mg ANDA products. 21 U.S.C. § 355(j)(5)(B)(iv).

Although it now claims concern for public safety, Biovail did not raise any alleged safety concerns with FDA for over a year after receiving notice of Anchen's ANDA, while FDA was conducting its review of the ANDA. Instead, Biovail sued Anchen in the Central District of California, asserting two U.S. patents. (Ex. 3, Patent Compl.) Merely by filing this lawsuit, Biovail triggered a statutory 30-month stay of FDA approval of Anchen's ANDA, absent earlier court action. *See* 21 U.S.C. § 355(j)(5)(B)(iii).

On November 14, 2005, FDA tentatively approved Anchen's ANDA. (Ex. 14, FDA Approval History for Anchen's ANDA.) This decision indicated that FDA had determined that Anchen's ANDA meets all of the statutory and regulatory requirements for approval, including demonstrating bioequivalence to WELLBUTRIN XL®. 21 C.F.R. § 314.105(c)-(d). Anchen's application would have been finally approved at that time but for the 30-month stay of final approval resulting from the Biovail patent lawsuit. *Id.* § 314.105(d); 21 U.S.C. § 355(j)(5)(B)(iii).

On December 20, 2005, Biovail filed the citizen petition that is the subject of this case. (Ex. 4, BV Citizen Petition.) In its citizen petition, Biovail asked FDA to impose a host of additional bioequivalence requirements on WELLBUTRIN XL® ANDA applicants, above and

beyond the standard bioequivalence testing FDA ordinarily requires for modified release products like WELLBUTRIN XL®. (*Id.*) Included in these additional requirements was a request for FDA to require ANDA applicants to establish bioequivalence not just to the listed drug, WELLBUTRIN XL®, but also to two drug products that are not the reference listed drug for these ANDAs, WELLBUTRIN® and WELLBUTRIN SR®. (*Id.* at 1, 5-6.)

While Biovail's citizen petition was pending (and following claim construction), Anchen filed a motion seeking summary judgment of non-infringement in the California patent case. On August 1, 2006, the court issued a decision granting Anchen's motion for summary judgment, concluding that Anchen's proposed ANDA product did not infringe the patents-in-suit. (Ex. 2, SJ Decision at 42.) That decision was to become final when the court entered a final judgment, which would terminate the 30-month stay and leave FDA free to finally approve Anchen's ANDA. 21 U.S.C. § 355(j)(5)(B)(iii)(I)(aa).

B. Biovail's First Motion For A Temporary Restraining Order.

In an effort to delay final approval of Anchen's ANDA, on August 23, 2006, Biovail filed its first action against FDA in this Court, claiming a need for extraordinary relief due to an "emergency" that Biovail alone created. (Complaint for Injunctive and Declaratory Relief and Writ of Mandamus ("Compl.").)

According to Biovail, FDA violated federal law by failing to act on Biovail's citizen petition. (Compl., ¶ 2.) Biovail further complained that FDA would deprive Biovail of its due process rights by failing to rule on Biovail's citizen petition without giving Biovail sufficient time, if FDA denied the petition, to get a court to force FDA to adopt the additional bioequivalence requirements. (*Id.* ¶ 3.) Biovail sought a TRO and preliminary injunction, asking this Court to force FDA to rule on Biovail's citizen petition and to do so at least one calendar week before finally approving any ANDAs. (*Id.*, Relief Requested.)

This Court denied Biovail's motion for a TRO. The Court concluded, among other things, that Biovail failed to show a likelihood of success on the merits and made an insufficient showing of irreparable harm. Indeed, the Court rejected as insufficient the same showing of harm that Biovail claims here. As it does again now, Biovail then claimed that it would suffer reputational harm if FDA improperly approved unsafe generic WELLBUTRIN XL® products, which, in turn, caused *grand mal* seizures. (Mem. Op. at 15-17; BV First TRO Br. at 17-18; *see also* Biovail Br. at 17-20 and n.14.) The Court concluded that Biovail "lays nothing but speculation before the court" and "[a]bsent evidence that the generic drug product pending approval will actually cause harmful health effects . . . these allegations fail to meet the requisite standard." (Mem. Op. at 16.)

> Never does [Biovail] allege that the generic drug awaiting FDA approval contains harmful variations of bupropion; it merely states that *if* the generic version is harmful and *if* the FDA applies improper procedures and approves it, and *if* the generic drug *causes* seizures, then it will affect Wellbutrin XL's reputation. These allegations of potential injury to [Biovail's] reputation are insufficient to justify the extraordinary relief of a TRO.

(*Id.* at 17.) Accordingly, Biovail failed to show irreparable harm. (*Id.*)

C. Biovail's Additional Efforts To Delay Anchen's Approval.

At the same time that this Court was considering and denying Biovail's first motion for a TRO, Biovail had submitted a motion for reconsideration of summary judgment of non-infringement in the California court hearing the patent case. On August 24, 2006, that court denied the motion on the papers. In its decision, the court stated that Biovail's filing was not "a proper motion for reconsideration" and was "not well-founded." (Ex. 10, 8/24/06 Order at 1 n.1.) When the court entered final judgment on Friday, August 25, 2006, Biovail's patent lawsuit and this lawsuit seeking a TRO no longer blocked FDA approval of Anchen's ANDA. There was no longer any 30-month stay of FDA approval, Anchen's ANDA had satisfied all statutory and

regulatory requirements for approval, and Biovail's lawsuit against FDA failed in its bid for injunctive relief.

On Sunday, August 27, 2006, a Biovail outside lawyer of record in this case, John Dubeck, distributed a letter via electronic mail to Gary Buehler, head of FDA's Office of Generic Drugs (OGD) and various officials within OGD and the Office of Chief Counsel. (Ex. 13, Letter to FDA (redacted).) Biovail apparently provided Mr. Dubeck with Anchen confidential documents obtained through the patent litigation, which Mr. Dubeck used to allege purported safety "concerns" about Anchen's ANDA product.

Neither Biovail nor FDA considered this submission to be a citizen petition. The letter was simply an unsolicited blocking submission sent to FDA on a Sunday, after Biovail's two legal actions were resolved against Biovail. Biovail did not notify Anchen of this submission and it was not placed on FDA's public docket. Anchen did not learn of the submission until mid-September 2006, when FDA provided Anchen a copy of the letter.

Following this submission, Biovail sought to modify the protective order in the Central District of California patent case in order to distribute *all* of Anchen's confidential information to the Biovail lawyers in this case so that they could review the information and communicate any additional "concerns" about Anchen's ANDA product to FDA. Hon. Magistrate Judge Rosalyn M. Chapman in the Central District of California considered and soundly rejected Biovail's request to modify the protective order, observing during a hearing that Biovail's request was plainly not based on genuine concern over the safety of Anchen's ANDA product: "Maybe they think I think it's about safety, but I think it's all about money. Okay. So don't waste your time with that." (Ex. 12, Chapman Hearing Tr. at 98.)

D. Final Approval Of Bupropion Hydrochloride ANDAs.

Notwithstanding Biovail's competitive bias, FDA carefully and thoroughly examined Biovail's citizen petition requesting the imposition of additional bioequivalence testing. In a well-reasoned 18-page, single-spaced letter, FDA informed Biovail on December 14, 2006 that it granted in part and denied in part Biovail's petition. (Ex. 6, FDA CP Letter at 1-2.) Among other things, FDA explained that it would not impose an additional requirement that ANDA applicants establish bioequivalence to other bupropion products that are not the listed drug and are not referenced by the WELLBUTRIN XL® ANDAs. (*Id.* at 5-8.) FDA analyzed the statutory and regulatory requirements and concluded that there is no need to impose the additional bioequivalence requirements because the ANDA applicants do not seek a finding of therapeutic equivalence to WELLBUTRIN® or WELLBUTRIN SR®. (*Id.* at 6-7.) In addition, FDA concluded that the ANDA labeling is "the same" for purposes of 21 U.S.C. § 355(2)(A)(v) and will not pose any safety risks for the ANDA products. (Ex. 6, FDA CP Letter at 6-8.)

Also on December 14, 2006, FDA finally approved Anchen's ANDA on both its 150 and 300 mg products. (Am. Compl., ¶ 27.) Anchen commenced commercial marketing of the 300 mg product and then executed a selective waiver of its 180-day exclusivity on that product in favor of Impax Laboratories, Inc. (Chang Decl., ¶ 6; Ex. 7, Teva 12/18/06 Press Release.) This permitted approval of Impax's ANDA to sell a generic 300 mg product. Impax's strategic partner, Teva Pharmaceuticals Industries, Inc. began selling a generic 300 mg product on December 15, 2006. (*Id.*) Pursuant to an agreement with Impax and Teva, Anchen has received payments and is entitled to additional payments as long as Teva is permitted to market the Impax ANDA product. (*Id.*)

FDA's final approvals of generic products prompted a flurry of activity from Biovail. Biovail filed not one but *three* motions for TROs over a three-day span, including this

one, seeking to further stall generic competition. Apparently because this Court has already rejected Biovail's first TRO motion, Biovail sought an alternate forum to advance additional attacks on FDA. On Monday, December 18, 2006, the same day that Biovail filed this motion with this Court, Biovail filed *another* lawsuit against FDA in the District of Maryland, seeking a separate TRO. Biovail asked the Maryland court to force FDA to withdraw Impax's approval on the 300 mg product. (Ex. 8, Md. Compl., ¶ 1.) FDA had determined that Biovail failed to sue Impax for patent infringement on its 300 mg product within the 45-day period to trigger a 30-month stay of Impax's approval. Biovail challenged that decision. Other than forum shopping, there was no reason for Biovail to bring the action in Maryland rather than seeking to add those claims to this case. Biovail also filed a TRO motion in the Eastern District of Pennsylvania court that is presiding over Biovail's patent infringement suit against Impax. *See Biovail Labs., Inc. v. Impax Labs., Inc.*, No. 2:05-cv-01085-AB, Docket No. 123 (E.D. Pa.).

To date, none of Biovail's bids for injunctive relief have succeeded. The Maryland court rejected Biovail's TRO motion. The court concluded that FDA acted consistently with its long-standing rules and regulations in determining that no 30-month stay applies where the patent holder fails to sue within the 45-day period. (Ex. 1, Hearing Tr. at 93-100.) In addition, the court found that Biovail had failed to show that it would suffer irreparable harm from Impax's marketing of its product because "the harm or the vast bulk of the harm that Biovail claims has already occurred" since Teva has already begun marketing. (*Id.* at 92.) Moreover, "[i]n this case, the harm that is alleged, insofar as the court can tell, is purely economic and is a nature that if the plaintiff's [sic] prevail in their patent litigation in the U.S. District Court in Philadelphia, there is a remedy available to them in that court[.]" (*Id.* at 92.) The court further concluded that Impax and Teva would, by contrast, suffer irreparable harm

because "they have manufactured this drug, sent it out for distribution, there are expiration dates will approach [sic]. Many of these drugs may become useless and unsaleable, and that is a factor that would run in favor of the intervening defendants." (*Id.* at 93.) The court also found that FDA would suffer harm, "which is an agency charged by law with protecting the public interest with the distribution of safe drugs and also to promote through this legislation, among others, legitimate competition for the benefit of the consumer." (*Id.*) This factor too "would weigh in favor of the defendant." (*Id.*) The court concluded "that the motion for temporary restraining order and preliminary injunction should and must be denied . . . ." (*Id.* at 100.) According to the public records, the Pennsylvania court likewise rejected Biovail's motion.

Biovail is now left only with the instant motion. Rehashing arguments this Court and others have already fully heard and rejected, Biovail asks this Court to override FDA's conclusion, based on its scientific expertise, that it should not depart from its standard bioequivalence requirements for WELLBUTRIN XL® ANDAs by imposing additional requirements. This Court should reject Biovail's last effort to enjoin legitimate competition in the market for bupropion extended release tablets.

ARGUMENT

"Injunctive relief is an extraordinary remedy and must be sparingly granted." *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212, 215 (D.D.C. 1996) (Urbina, J.). To prevail on a motion for a preliminary injunction, the moving party must demonstrate:

> (1) a substantial likelihood of success on the merits; (2) that irreparable injury will result in the absence of the requested relief; (3) other interested parties will not suffer substantial harm if the injunction is granted; and (4) that the public interest favors entry of a preliminary injunction.

Id. Injunctive relief "should not be granted absent a clear and convincing showing by the moving party." *Smith v. Harvey*, No. 06-1117 (RWR), 2006 WL 2025026, at *2 (D.D.C. July 17, 2006) (Ex. 18) (citing *Kahane v. Sec'y of State*, 700 F. Supp. 1162, 1165 (D.D.C. 1988)).

In this case, Biovail "faces an additional hurdle because it seeks a mandatory injunction as opposed to a prohibitive injunction." *Mylan Pharms., Inc. v. Shalala*, 81 F. Supp. 2d 30, 36 (D.D.C. 2000). Contrary to its contentions, Biovail does not merely seek to preserve the status quo with its motion. Instead, Biovail seeks to undo what has already been done. Anchen already has final approval of its ANDA. Biovail asks this Court to force FDA to withdraw Anchen's final approval and impose additional requirements on Anchen in order to regain final approval. Accordingly, Biovail "is seeking affirmative relief that would alter the status quo," rather than attempting to preserve the status quo until its objections can be considered by the court. *Mylan*, 81 F. Supp. 2d at 36. In short, Biovail seeks a mandatory injunction. *Id.*; *see also Farris v. Rice*, 453 F. Supp. 2d 76, 79 n.1 (D.D.C. 2006) (Urbina, J.) (holding that a party seeks a mandatory injunction when it seeks an order directing an agency to perform an act). In these circumstances, Biovail "must meet a higher standard than in the ordinary case: [Biovail] must show 'clearly' that [it] is entitled to relief or that extreme or very serious damage will result." *Id.* at 78 (quoting *Adair v. England*, 217 F. Supp. 2d 1, 3 n.6 (D.D.C. 2002); *Veitch v. Danzig*, 135 F. Supp. 2d 32, 35 (D.D.C. 2001)). Moreover, this Court "must review [Biovail's] request for injunctive relief with even greater circumspection than usual in determining whether the extraordinary writ of preliminary injunction is warranted." *Mylan*, 81 F. Supp. 2d at 36. (quotations and citation omitted).

I. Biovail Has Not Clearly Shown That It Is Likely To Succeed On The Merits.

As this Court has already held once in this case, "[i]t is particularly important for the movant to demonstrate a substantial likelihood of success on the merits." (Mem. Op. at 5.)

Otherwise, "there would be no justification for the court's intrusion into the ordinary processes of administration and judicial review." (*Id.* (quotations and citation omitted).) Biovail cannot "clearly" demonstrate "a substantial likelihood of success on the merits." *Farris*, 453 F. Supp. 2d at 78. To the contrary, in view of the statutory scheme and the substantial deference due FDA, Biovail clearly is *not* entitled to relief. Biovail attempts to disguise its complaint as one about Anchen's labeling, but at bottom, Biovail is simply challenging FDA's scientific decision to apply its standard bioequivalency requirements to ANDA applicants seeking to market a lower-priced, generic version of WELLBUTRIN XL®. Biovail has not shown that FDA acted arbitrarily and capriciously in refusing Biovail's request, and FDA's decision is entitled to deference. Accordingly, Biovail is not likely to succeed on the merits of its complaint.

A. FDA Reasonably Rejected Biovail's Request To Require Additional Bioequivalence Testing Of WELLBUTRIN XL® ANDA Applicants.

Biovail may only obtain the relief it seeks under the Administrative Procedures Act, 5 U.S.C. § 706, if the Court finds FDA's action "to be . . . arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law . . . ." *Id.* § 706(2)(A). This standard is difficult to meet. Under § 706(2)(A), "there is a presumption in favor of the validity of administrative action" and "the court is not empowered to substitute its judgment for that of the agency." *Bristol-Myers*, 923 F. Supp. at 216 (quoting *Ethicon, Inc. v. FDA*, 762 F. Supp. 382, 386 (D.D.C. 1991); *Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 416 (1971)). Moreover, "FDA, in particular, is often accorded special deference when its decisions are based on an evaluation of the scientific record before it." *Allergan, Inc. v. Crawford*, 398 F. Supp. 2d 13, 21 (D.D.C. 2005); *see also Bristol-Myers*, 923 F. Supp. at 216 ("FDA is to be accorded deference when it is evaluating scientific data within its technical expertise."); *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1320 (D.C. Cir. 1998) (holding that a decision resting on "the

agency's evaluations of scientific data within its area of expertise" is entitled to a "high level of deference" in court review) (quotations and citation omitted); *Henley v. FDA*, 77 F.3d 616, 620 (2d Cir. 1996) ("[A] reviewing court cannot substitute its judgment for that of the agency, particularly when that determination is propelled by the agency's scientific expertise.") (quotations and citations omitted).

As the D.C. Circuit has explained:

> [courts] review scientific judgments of the agency not as the chemist, biologist, or statistician that we are qualified neither by training nor experience to be, but as a reviewing court exercising our narrowly defined duty of holding agencies to certain minimal standards of rationality.

Troy Corp. v. Browner, 120 F.3d 277, 283 (D.C. Cir. 1997) (quotations and citation omitted); *accord Allergan*, 398 F. Supp. 2d at 22. Thus, the court should sustain FDA's decision where, as here, the agency "considered the relevant factors" and the decision "is within the bounds of reasoned decisionmaking." *Id.* (quoting *Baltimore Gas & Elec. Co. v. Natural Res. Defense Council, Inc.*, 462 U.S. 87, 105 (1983)).

Biovail implies that FDA acted arbitrarily and capriciously because it refused Biovail's baseless request to impose additional bioequivalence requirements on ANDA applicants above and beyond those required by statute and FDA regulations. (BV Br. at 15.) FDA exercised its scientific expertise and properly rejected Biovail's request to depart from its standard bioequivalence requirements. Having failed to convince FDA that there is any scientific reason to impose additional bioequivalence requirements, Biovail now asks this Court to force FDA to impose the additional bioequivalence requirements FDA has rejected as unnecessary. There is no statutory or regulatory basis for this Court to override FDA's decision in the manner Biovail requests.

The FFDCA requires ANDA applicants to show that their product is bioequivalent to "the listed drug" which, in this case, is WELLBUTRIN XL®. 21 U.S.C. § 355(j)(2)(A)(iv); *see also id.* § 355(j)(8)(B) (ANDA drug is bioequivalent to a "listed drug" if it does not significantly differ in rate and/or extent of absorption to the "listed drug"). FDA regulations are the same. *See* 21 C.F.R. § 314.94(a)(7)(i) (ANDA applicant must show bioequivalence to "the reference listed drug"); *see also Bristol-Myers*, 923 F. Supp. at 216 ("An applicant for an abbreviated approval of a generic drug must provide information to show that the new drug is the bioequivalent to the *listed drug*.") (emphasis added, quotations and citation omitted).

Consistent with the statute and regulations, FDA requires an ANDA applicant only to show that its product is bioequivalent *to the listed drug* to which the ANDA refers. Nowhere do the statute or FDA regulations require an ANDA applicant to show bioequivalence to additional drug products that are not the listed drug. Biovail therefore offers no statutory basis for its suggestion that ANDA applicants should be required to test generic products for bioequivalence to WELLBUTRIN® or WELLBUTRIN SR®.

Anchen established bioequivalence to WELLBUTRIN XL®, and met all other statutory and regulatory requirements for approval. Thus, Anchen is allowed to rely on the safety and efficacy studies conducted on WELLBUTRIN XL® without replicating those studies on its ANDA product. *See Barr Labs.*, 930 F.2d at 73; *Zeneca*, 213 F.3d at 164. FDA considers Anchen's ANDA product to be therapeutically equivalent to, and substitutable for, WELLBUTRIN XL®. Orange Book Preamble at vi ("FDA believes that products classified as therapeutically equivalent can be substituted with the full expectation that the substituted product will produce the same clinical effect and safety profile as the prescribed product."). Indeed, the

Hatch-Waxman statutory scheme is grounded in this principle that bioequivalent ANDA products are therapeutically equivalent and substitutable for the listed drug. *Id.* at vii ("A major premise underlying the 1984 law is that bioequivalent drug products are therapeutically equivalent, and therefore, interchangeable.").

As FDA concluded in this case, the bioequivalence requirements set forth in the FFDCA and FDA regulations are intended to ensure that Anchen's ANDA product is therapeutically equivalent to and therefore substitutable for WELLBUTRIN XL®. (Ex. 6, FDA CP Letter at 7). The additional bioequivalence studies that Biovail conducted for WELLBUTRIN XL® were not, and cannot be, used to establish substitutability between WELLBUTRIN XL® and the other drug products, WELLBUTRIN® and WELLBUTRIN SR®. Nor are these drug products substitutable at the pharmacy based on Biovail's studies. ANDA applicants for the WELLBUTRIN XL® product likewise do not seek a designation of therapeutic equivalence to WELLBUTRIN® and WELLBUTRIN SR®. And ANDA products like Anchen's product will not be substituted at the pharmacy for WELLBUTRIN® or WELLBUTRIN SR®. Accordingly, WELLBUTRIN XL® ANDA applicants are not required to establish bioequivalence to WELLBUTRIN® or WELLBUTRIN SR®.

After thoroughly and carefully reviewing Biovail's citizen petition and analyzing the scientific issues and statutory requirements, FDA made an eminently reasonable decision that bioequivalence studies beyond those ordinarily required are not warranted for generic versions of WELLBUTRIN XL®. FDA has "historically wide discretion in defining showings of bioequivalence." *Bristol-Myers*, 923 F. Supp. at 217 (quotations and citation omitted). Courts, including this one, have repeatedly and consistently deferred to FDA's decisions, like FDA's decision here, regarding the appropriate bioequivalence requirements ANDA applicants must

meet to ensure safety and efficacy. *See Schering Corp. v. FDA*, 51 F.3d 390, 397-400 (3d Cir. 1995) (deferring to FDA's decision to allow ANDA applicants to establish bioequivalence in some circumstances without necessarily comparatively measuring drug absorption); *Bristol-Myers*, 923 F. Supp. at 216-20 (deferring to FDA's decision to waive ANDA requirement for *in vivo* bioequivalence studies of specific drug); *Fisons*, 860 F. Supp. at 863-66 (upholding FDA's regulations permitting waiver of *in vivo* bioequivalence studies); *Schering Corp. v. Sullivan*, 782 F. Supp. 645, 650 (D.D.C. 1992) ("Under the pre-existing regulatory regime, FDA had discretion to require and to accept any of a variety of showings, ranging from *in vivo* testing in humans to *in vitro* testing uncorrelated to human *in vivo* data, as sufficient to establish bioequivalence. While the 1984 amendments did make the bioequivalence requirement mandatory, there is nothing in the legislative history to indicate that Congress also intended to restrict FDA's historical discretion to decide how that requirement would be met."), *vacated as moot sub nom.*, *Schering Corp. v. Shalala*, 995 F.2d 1103 (D.C. Cir. 1993).

Biovail has offered no reason for the Court to override FDA's discretion here. Indeed, FDA is not even departing from its ordinary practice in this case, as FDA did, for instance, in *Bristol-Myers*. There, this Court upheld FDA's decision to waive *in vivo* bioequivalence testing in certain circumstances and allow an ANDA applicant to establish bioequivalence solely through *in vitro* studies. 923 F. Supp. at 216-17. Despite FDA's departure from its standard requirement that an ANDA applicant provide both *in vitro* and *in vivo* studies, this Court upheld FDA's determination, deferring to FDA's scientific expertise and "historically wide discretion" to set testing requirements for establishing bioequivalence. *Id.* at 217. Here, FDA is not departing from its standard bioequivalence requirements. Instead, it is Biovail who seeks a departure, asking this Court to require FDA to impose special requirements in addition to

FDA's standard requirements. In these circumstances, deference to FDA's scientific judgment is plainly warranted.

B. The FFDCA's Labeling Requirements Do Not Provide A Basis To Require FDA To Impose Additional Bioequivalence Requirements On ANDA Applicants.

While Biovail claims that its motion centers on a labeling issue, Biovail cannot demonstrate that Anchen's label is not the "same" for statutory or regulatory purposes as the WELLBUTRIN XL® label. It is. Moreover, Biovail makes no effort to prove that Anchen's label is, in fact, misbranded. Instead, Biovail suggests, based on unfounded assumptions and innuendo, that Anchen's label "would be inherently false and misleading," unless Anchen performs bioequivalence studies beyond those FDA normally requires for ANDA approval. (BV Br. at 15.) There are several problems with Biovail's argument, all of which require rejection of Biovail's motion.

First, Biovail is simply wrong as a factual matter when it asserts that Anchen's label is not "the same" as Biovail's for purposes of the FFDCA. (*See* BV Br. at 15.) Anchen's labeling contains the same statements as WELLBUTRIN XL® regarding bioequivalence between extended release products, and multiple dose, sustained- and immediate-release bupropion products. (*See* Ex. 9, Anchen label at 2 (under "Pharmacokinetics"), 4 (under "Major Depressive Disorder"), 6-7 (under "Seizures").) The labels are therefore the "same" as required by statute and regulations.

Second, as already discussed, there is no statutory or regulatory basis to require FDA to impose additional bioequivalence requirements on bupropion extended-release ANDA applicants to show bioequivalence to the sustained- or immediate-release products. Consistent with its standard practice, FDA has concluded that once an ANDA applicant demonstrates bioequivalence to the listed drug, as Anchen did here, the listed drug's labeling is applicable to

the ANDA product. (Ex. 6, FDA CP Letter at 7.) In other words, if the ANDA product is bioequivalent, it is expected to behave the same in the patient, including with respect to any comparisons with other products and potential side effects. Thus, the labeling claims for the listed drug are fully applicable to the ANDA product.

Indeed, the entire Hatch-Waxman scheme depends on this principle. ANDA labeling contains a myriad of statements concerning the expected behavior of the ANDA product based on safety and efficacy studies that the NDA holder conducted, but the ANDA applicant did not replicate. (*See, e.g.*, Ex. 9, Anchen label at 4-5 (discussing indicated usage for bupropion hydrochloride extended-release tablets and efficacy studies not conducted by ANDA applicant).) Congress has concluded that the ANDA applicant is entitled to rely on the safety and efficacy tests conducted on the listed drug, including relying on the listed drug's claims regarding safety and efficacy. *See* 21 U.S.C. § 355(j)(2)(A) (setting forth ANDA requirements); *Barr Labs.*, 930 F.2d at 73; *Zeneca*, 213 F.3d at 164. If Biovail were correct that such statements in the labeling constitute misbranding – that an ANDA applicant must conduct any study discussed in the listed drug's label in order for the label to be accurate – the entire Hatch-Waxman statutory scheme would fall apart. FDA rightly rejected Biovail's attempt to impose on ANDA applicants obstacles to approval that Congress intended to remove.

Third, Biovail has not adduced a shred of evidence to conclude that Anchen's product would, in fact, be unsafe as labeled. Instead, Biovail asks this Court to "assume" that there is a "4% chance" that a single tablet of WELLBUTRIN XL® is "not truly equivalent" with sustained-release or immediate-release forms of bupropion, and further "assume" that there is a "4% chance" that Anchen's ANDA product is "not truly equivalent with WELLBUTRIN XL®." (BV Br. at 16.) Why this Court is supposed to accept Biovail's "assumptions" as true is not at all

apparent. Biovail offers no evidence to support its assumptions. Biovail did not even offer an analysis of the statistical probability of such tablets existing. Nor has Biovail offered any evidence of the risk that such tablets, if they existed, would, in fact, present *any* increased risk of seizure or the statistical likelihood of that risk.

Fourth, Biovail completely mischaracterizes the supposed risk, even if this Court accepted Biovail's assumptions as true. In the "Warnings, Seizure" section of the label that discusses the potential seizure risk, Anchen's label only states, like the WELLBUTRIN XL® label, that the seizure incidence with extended-release bupropion hydrochloride tablets "while not formally evaluated in clinical trials, *may be similar* to that presented below for the immediate release and sustained release formulations of bupropion." (Ex. 9, Anchen label at 7 (emphasis added).) This statement of potential risk is qualified – even for the WELLBUTRIN XL® product – because FDA did not require Biovail and GSK to formally evaluate in clinical trials the actual risk of seizures for the WELLBUTRIN XL® product. At most, the statement on the label is precautionary language that physicians should consider when deciding whether to switch a user of the old WELLBUTRIN® products to the WELLBUTRIN XL® products. Physicians should consider that the seizure risk may be similar to the risk described for the other dosage forms. Nowhere does the label state that the seizure risk is exactly the same among the different products. And Biovail has offered no scientific basis to "assume" that a "4 percent" plus "4 percent" difference in bioequivalence between the various products will result in an increased seizure risk. Nor has Biovail offered a reason to think that a prescribing physician would believe, based on this or any other statement in the label, that Anchen's ANDA product is therapeutically equivalent to WELLBUTRIN® or WELLBUTRIN SR® with regard to the seizure risk.

Fifth, Biovail has offered no evidence whatsoever that FDA's scientific judgment violates any statutes or regulations. Biovail suggests that FDA is not following its own rules and regulations because, according to Biovail, Anchen's product might not be bioequivalent to WELLBUTRIN® or WELLBUTRIN SR®. (*See* BV Br. at 15-16.) But, again, Anchen does not seek a finding of therapeutic equivalence, nor is its product approved as therapeutically equivalent to WELLBUTRIN® or WELLBUTRIN SR®. It will not be substituted at the pharmacy level for either of those products. Thus, Biovail's suggestion that FDA is not following its own rules and regulations is simply a red herring.[4]

Finally, and most fundamentally, FDA has fully examined these purported risks as well as Anchen's labeling. Biovail does not contend otherwise. And FDA has concluded that Anchen's labeling contains adequate warnings of the potential side effects of its ANDA product. Biovail asks this Court to override FDA's scientific analysis and judgment based on sheer speculation and unsupported assumptions, and offers no legal basis for this Court to do so. In this respect, this case is remarkably similar to the Second Circuit's decision in *Henley*. In *Henley*, a third party filed a citizen petition asking FDA to include a warning on labeling for oral contraceptives that they mighty cause cancer. *See Henley*, 77 F.3d at 620-21. FDA examined the published studies on the topic and concluded that cancer warnings were not warranted. *Id.* The court concluded that "FDA possesses the requisite know-how to conduct such analysis, by sifting through the scientific evidence to determine the most accurate and up-to-date information regarding a particular drug, and how those data affect human usage." *Id.* at 621. The court accordingly deferred to FDA's expert decision and declined to find the label misleading or

[4] For this same reason, Biovail's argument that FDA frequently requires the ANDA applicant to conduct additional bioequivalence studies in the fed state when the listed drug has been studied in the fed state is a non-starter. FDA requires fed studies to show bioequivalence *to the listed drug*, not to an non-reference-listed drug as Biovail wants to require here.

misbranded. *Id.* As with FDA's bioequivalence determinations, this Court should defer to FDA's determinations concerning the appropriate labeling for drug products as well. *Id.*; *see also Zeneca*, 213 F.3d at 166-69 (deferring to FDA's determinations concerning appropriate labeling for ANDA product).

In sum, Biovail has offered no legal or factual basis for this Court to overturn FDA's reasoned decision concerning the bioequivalence testing requirements for ANDA applicants seeking approval to market a lower-priced version of WELLBUTRIN XL®. Biovail cannot show any likelihood of success on the merits of its complaint, let alone a substantial one. For this reason alone, this Court should deny its motion.

II. Biovail Has Not Shown Irreparable Harm.

Biovail argues that it will sustain irreparable harm if injunctive relief is not granted because: (1) it "has a significant property interest in Wellbutrin XL" and will suffer an economic injury from generic competition (BV Br. at 17, 18-19), and (2) the reputation of WELLBUTRIN XL® might be harmed if generic versions create a higher risk of seizures, and this might cause Biovail to lose customers and good will (*id.* at 17, 20 n.14.) Neither claim has merit and Biovail's arguments have already been rejected by this Court, as well as the Maryland District Court.

A. Biovail's Claims That It Will Suffer Economic Injury Do Not Establish Irreparable Harm.

Biovail's claim that it will suffer an economic injury as the result of generic competition does not constitute irreparable harm. As this Court recognized in denying Biovail's prior motion for injunctive relief, "[i]t is well established that economic loss is insufficient to demonstrate irreparable injury," and "the fact that [Biovail] will face competition in the market and may lose profits if the [FDA] approves generic Wellbutrin XL is insufficient to establish

irreparable harm." (Mem. Op. at 15, 16.) *See also Abbott Labs. v. Andrx Pharms., Inc.*, 452 F.3d 1331, 1347 (Fed. Cir. 2006) (fact that generic competition will impact sales of brand drug does not establish irreparable harm); *Eli Lilly & Co. v. Am. Cyanamid Co.*, 82 F.3d 1568, 1578 (Fed. Cir. 1996) (no irreparable harm from entry of generic drug because money damages would compensate the patent owner).

Irreparable injury is a "very high standard." *Bristol-Myers*, 923 F. Supp. at 220. Injuries are not "irreparable" unless they are "certain, great, actual, and imminent." *Sandoz, Inc. v. FDA*, 439 F. Supp. 2d 26, 32 (D.D.C. 2006); *accord Sociedad Anomia Viña Santa Rita v. Dep't of Treasury*, 193 F. Supp. 2d 6, 14 (D.D.C. 2001). Accordingly, "financial harm alone cannot constitute irreparable injury unless it threatens the very existence of the movant's business." *Sociedad*, 193 F. Supp. 2d at 14; *see also Mylan*, 81 F. Supp. 2d at 42 ("[P]otential loss in revenue does not amount to irreparable harm under the standards set forth in this Circuit."); *Sandoz*, 439 F. Supp. 2d at 32 (same).[5]

To establish irreparable harm, Biovail relies on speculative projections by analysts regarding the harm that may be caused by generic entry. (*See, e.g.*, Howling Decl. ¶¶ 16-22.) But Biovail does not allege – much less demonstrate – that such alleged economic harm would threaten Biovail's existence**.** To the contrary, Biovail has repeatedly acknowledged in other contexts that any harm from the launch of a generic Bupropion XL will *not* be debilitating or irreparable. For example, on August 10, 2006, Biovail's CEO, Douglas Squires, was quoted as stating that the entry of a generic version of WELLBUTRIN XL® "*is not a mortal or life-*

[5] Biovail erroneously asserts that purely economic losses constitute irreparable harm when such losses are non-recoverable. (*See* BV Br. at 17-18.) That is not the law. To demonstrate irreparable harm based on purely economic loss, a plaintiff "must show that it will suffer harm that is more than simply irretrievable." *Sandoz*, 429 F. Supp. 2d at 32 (citation omitted). Specifically, "a plaintiff must establish that the potential economic harm is so severe as to cause extreme hardship to the business or threaten its very existence." *Id.* (citation and internal quotation omitted).

threatening situation for us" and that it has $571 million in cash on hand. (Ex. 15, B. Erman, "Biovail shifts gears to thwart generics," The Ottawa Citizen (August 11, 2006) (emphasis added).) Squires described Biovail's plans to replace any lost revenue and to use cash on hand to accelerate other opportunities. (*Id.*) Thus, Biovail's public statements over the last several months belie any suggestion that competition from generic bupropion will threaten Biovail's existence.

Moreover, the Maryland court rejected Biovail's exact same claims of harm in its other case against FDA. There, too, Biovail claimed that it would be harmed by generic entry, but the court did not accept this argument. Instead, the court concluded that the harm to Biovail was not irreparable but "purely economic" and that "the vast bulk of the harm has already occurred" because Teva is already marketing a product. (Ex. 1, Hearing Tr. at 92-93.) Biovail offers no reason for this Court to reach a different conclusion.

B. Biovail Has Failed To Establish Any Link Between Its Economic Injury And The Claimed Harm.

In addition, there is an insufficient link between Biovail's alleged irreparable financial injury and the safety issues raised in its citizen petition. Even if this Court grants Biovail's motion and ultimately reverses FDA's denial of Biovail's citizen petition, Biovail will eventually face financial loss from generic competition. Every competitor faces an economic loss upon the entry additional competitive products. Such a loss cannot constitute irreparable injury absent a sufficient connection to the substance of the underlying agency decision.

In an effort to suggest a link, Biovail again speculates that it will suffer an irreparable injury to the reputation of WELLBUTRIN XL® if unsafe generics hit the market. (BV at 17, 20 n.14.) In denying Biovail's prior motion for injunctive relief, this Court correctly rejected this argument because Biovail presented no evidence that generic bupropion

hydrochloride extended release tablets will cause health problems. (*See* Mem. Op. at 16-17 (citing *Bristol-Myers*, 923 F. Supp. at 221).) Nor has Biovail corrected this deficiency by submitting any such evidence in support of its current motion.

Biovail relies on the Declaration of Dr. Peter Silverstone, but that Declaration alleges only that there is a "significant risk" that patients will be harmed by taking the proposed generic drug when equivalence between the generic and brand drugs "is not properly determined, and does not exist." (BV Br. at 20 n.14, (citing Silverstone Decl, ¶ 9).) Silverstone, however, does not allege – much less demonstrate – that Anchen's ANDA product is not equivalent to WELLBUTRIN XL®, or that or that it is harmful in any way. Instead, just as it did in support of its prior motion, Biovail "lays nothing but speculation before the court," asserting that *if* the generic drug is harmful and *if* it causes seizures, then it will affect WELLBUTRIN XL®'s reputation. (Mem. Op. at 16, 17.) As this Court has already concluded, such speculative allegations "are insufficient to justify the extraordinary relief of a TRO." (*Id*. at 17.)[6] *See also Bristol-Myers*, 923 F. Supp. at 220 (rejecting drug manufacturer's claim of irreparable injury based on the "possible injury to [its] reputation that could result if a health risk ensues from the approval of" a generic drug, and finding that the claim was "based solely upon conjecture").[7]

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[6] This fact distinguishes this case from the cases cited in Biovail's Memorandum. (*See* BV Br. at 17-18 (citing *Morgan Stanley DW, Inc. v. Rothe*, 150 F. Supp. 2d 67, 77 (D.D.C. 2001); *Express One Int'l, Inc. v. U.S. Postal Serv.*, 814 F. Supp. 87, 91 (D.D.C. 1992); *Honeywell, Inc. v. Consumer Prod. Safety Comm'n*, 582 F. Supp. 1072, 1078 (D.D.C. 1984); *CollaGenex Pharm., Inc. v. Thompson*, No. Civ. A. 03-1405 (RMC), 2003 WL 21697344, at *10 (D.D.C. Aug. 26, 2003) (Ex. 17).) In *Morgan Stanley*, *Express One*, *and Honeywell*, unlike here, the plaintiff made a strong showing that the defendant's improper conduct would directly harm the plaintiff's reputation or would cause the plaintiff to lose customer goodwill or important business relationships. In *CollaGenex*, the plaintiff drug manufacturer demonstrated that the FDA's potentially improper classification of its drug would deprive the plaintiff of its statutory right to exclusivity.

[7] It also is not clear what "reputational interest" Biovail actually has in the WELLBUTRIN XL® product. GlaxoSmithKline owns the NDA, the U.S. product distribution rights, and the WELLBUTRIN XL® trademark. GSK is not a party to this action. Further, as indicated on the WELLBUTRIN XL® label, the actual seizure incidence of WELLBUTRIN XL® has not been "formally evaluated in clinical trials." Therefore the claim that Biovail has established a safety profile or reputation for the WELLBUTRIN XL® is wholly unsupported by this record.

Biovail does not offer evidence that Anchen's ANDA product is harmful because no such evidence exists. A search of the Electronic Orange Book available at FDA's website indicates that approximately thirty (30) bupropion hydrochloride tablet products have been approved by FDA over the years. (Ex. 11.) Biovail does not question FDA's competency in having reviewed these prior products, and there is no record basis to conclude that the FDA has failed to conduct a proper review of all safety issues with respect to the generic applications at issue, or that Anchen's ANDA product will have a safety profile different than WELLBUTRIN XL®.

C. Biovail's Alleged Harm Is Self-Inflicted.

Finally, to the extent any financial harm to Biovail is "irreparable," it is Biovail's own fault. Biovail delayed in filing its citizen petition, creating the alleged calamity of which it now complains. Biovail knew there were pending WELLBUTRIN XL® ANDAs for more than a year before it filed its citizen petition. The timing of the citizen petition (a few weeks after Anchen received tentative approval) and the initiation of its initial motion for injunctive relief (a few weeks after it lost its infringement case on summary judgment) manifests Biovail's attempted "manipulation of the judicial process." *See Sandoz*, 439 F. Supp. 2d at 31. After its TRO was denied, Biovail did nothing further in this case for almost four months, until it started the TRO process over again. As this Court has recognized, such delay "further undermines any showing of irreparable injury." (Mem. Op. at 18 (citing *Sandoz*, 439 F. Supp 2d at 31, and *Mylan*, 81 F. Supp. 2d at 36).)[8]

[8] Biovail asserts that the FDA failed to "respond[] promptly" to Biovail's citizen petition, and that the FDA "should not be permitted to use its own dilatory conduct to defeat meaningful judicial review." (BV Br. at 21 n.15.) This is wrong. First, the FDA took the time it needed to resolve complex issues raised in Biovail's petition, and Biovail presents nothing to suggest that the FDA unreasonably or improperly delayed the process. Second, Biovail still has a full and "meaningful" opportunity to appeal the FDA's denial of its citizen petition and approval of Anchen's ANDA. (Mem. Op. at 17 (noting that Biovail cannot show "why the economic harm that may occur" after the FDA's decision "is sufficient to render the review of the decision meaningless").) *See also Pfizer, Inc. v. Shalala*, 182 F.3d 975, 979 (D.C. Cir. 1999) (recognizing that a drug manufacturer can obtain "meaningful judicial review" of the FDA's approval of an ANDA "after the final approval is issued").

Biovail raised the same arguments and allegations of potential irreparable harm in its prior motion for injunctive relief, which this court denied. At that time, this Court carefully considered each of Biovail's claims and rejected them. Biovail chose not to appeal this Court's denial of its initial motion for a TRO, and it did not attempt to pursue or renew its request for a preliminary injunction. Biovail has presented no new evidence in support of its claim of irreparable harm. Accordingly, this Court should reject Biovail's improper attempt to resurrect claims that this Court has correctly rejected.

III. The Harm Caused To Others Greatly Outweighs Biovail's Alleged Interest In Protecting Its Monopoly.

Any injury to Biovail "must be weighed against . . . the extent to which an injunction will substantially injure [another] party[.]" *Mylan*, 81 F. Supp. 2d at 44. Contrary to Biovail's assertion, if this Court grants Biovail's Motion, Anchen will suffer far more harm than a mere "brief delay in recovering its investment while the status quo is preserved so the Court can address Biovail's claims on their merits." (BV Br. at 21.) As noted above, Biovail is not merely seeking to preserve the status quo. To the contrary, it is attempting to alter the status quo by requiring FDA to withdraw its final approval of Anchen's ANDA and force Anchen to conduct additional studies.

Now that the FDA has finally approved Anchen's ANDA, Anchen has an immediate and unqualified statutory right to manufacture and market a generic version of WELLBUTRIN XL® and to exclude all other generic manufacturers from manufacturing and marketing competing generic products for 180 days. Anchen is a start-up company and its bupropion extended release ANDA product is its first and only approved ANDA product. (Chang Decl., ¶ 9.) An injunction would harm Anchen in terms of lost revenues and lost

opportunities. As a start-up company, the loss of these revenues would deprive Anchen of the capital necessary to fund other products and expand its operations. (*Id.* ¶ 12.)

The requested injunction itself would also cost Anchen money and indefinite delay, none of which Anchen would recover. Anchen would be forced to conduct costly, time-consuming and unnecessary studies to prove what is already known – that its ANDA product is safe and effective as labeled. Anchen would then have to wait indefinitely for FDA to conduct a review of these additional studies. This process could take months; it could take years, with no apparent benefit other than to preserve Biovail's monopoly. *See generally Teva Pharms., USA, Inc. v. FDA*, 182 F.3d 1003, 1011 n.8 (D.C. Cir. 1999) (concluding that generic drug makers "face continued harm [when they are] denied access to the market").

In the meantime, Anchen might forfeit its statutory right to exclusivity if it fails to market its 150 mg product within 75 days of either the FDA's approval of its ANDA or a final decision of invalidity or non-infringement, whichever is later. *See* 21 U.S.C. § 355(j)(5)(d)(1)(I). Accordingly, if this Court grants Biovail's motion, Anchen could lose millions of dollars in the short term, and might permanently and irreparably forfeit its right to exclusivity. "Once the statutory entitlement has been lost, it cannot be recaptured." *Sandoz,* 439 F. Supp. 2d at 32 (citation and quotation omitted); *see also Apotex, Inc. v. FDA*, No. 06-0627, 2006 WL 1030151, at *17 (D.D.C. Apr. 19, 2006) (Ex. 16) (recognizing the loss of a statutory entitlement as an irreparable harm); *Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060, 1067 n.6 (D.C. Cir. 1998) (loss of exclusivity period is loss of "officially sanctioned head start").

Moreover, Anchen could lose the benefit of its bargain with Teva and Impax on the 300 mg product because their 180-day exclusivity period, which has already begun, would almost certainly run before any of the ANDA applicants could regain final approval. (*See* Chang

Decl., ¶¶ 6, 7.) Anchen could lose rights to additional payments under its agreement with Teva and Impax if the 180-day exclusivity period is lost on the 300 mg product. (*Id.*)

Anchen, of course, is not the only party that would be harmed by an injunction. The injunctive relief Biovail seeks would cause substantial and immediate harm to other parties, such as Teva and Impax. (*See* Ex. 1, Hearing Tr. at 93.) And, as the Maryland court concluded, it would cause harm to FDA. (*Id.*) In addition, Biovail seeks to enjoin the FDA from approving any pending ANDAs for generic versions of WELLBUTRIN XL®. As this Court has recognized, such an injunction would harm all potential generic competitors with pending ANDAs. (Mem. Op. at 18-19.) As it did in response to Biovail's first TRO motion, this Court should reject Biovail's improper attempt to use this proceeding to enlarge the 30-month stay provided by statute and further delay generic competition.

IV. The Public Interest Would Be Harmed If Injunctive Relief Is Allowed.

There can be no doubt that the public would be irreparably harmed if this Court issues the requested injunction. An injunction will deprive the public of a lower cost generic version of WELLBUTRIN XL®. Generic competition lowers medical costs and thereby provides more patients with access to potentially life-saving medications. Every day that Biovail delays the sale of FDA-approved generic WELLBUTRIN XL® costs the public millions of dollars that cannot be recompensed. *See Bristol-Myers*, 923 F. Supp. at 221-22; *Sandoz*, 2006 WL 1897728, at *5.

Further, if Biovail is successful in using this tactic to delay generic competition (even for a day), it is a certain bet that the courts and the FDA will be flooded with additional, meritless claims filed simply for the purpose of complicating and delaying generic competition across the board. Such delays run contrary to the entire purpose of the Hatch-Waxman

Amendments to the FFDCA because, as the D.C. Circuit has recognized, Congress' goal in enacting that critical legislation was "to get generic drugs into the hands of patients at reasonable prices – fast." *Barr Labs.*, 930 F.2d at 76.

Biovail baldly asserts that "[t]he public interest in cheaper drugs is, of course, outweighed by the significant public health risks in allowing a potentially unsafe and mislabeled product to enter the marketplace." (BV Br. at 22.) However, as noted above, Biovail has presented no evidence that generic WELLBUTRIN XL® is unsafe in any respect. Indeed, Biovail has not even *alleged* that to be the case. Nor has Biovail alleged or demonstrated that generic WELLBUTRIN XL® is misbranded. Instead, Biovail merely alleges (without any factual support) that the FDA's expert determination of bioequivalency and its approval of Anchen's ANDA *might* create an increased risk of certain health problems or misbranding. Confronted with these identical allegations in Biovail's previous motion for injunctive relief, this Court concluded that "the public interest is best served by denying" Biovail's motion, because Biovail "has not established, or even alleged, that [Anchen's] ANDA represents a drug that is unsafe." (Mem. Op. at 19.) The same conclusion is warranted here.

CONCLUSION

For the foregoing reasons, Biovail's motion is completely lacking in any legal basis, and devoid of the facts and equity necessary to obtain mandatory injunctive relief. The Court should summarily deny the request on the papers.

Dated: December 29, 2006

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CERTIFICATE OF SERVICE

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