UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

BIOVAIL CORPORATION, *et al.*, Plaintiffs, v. U.S. FOOD & DRUG ADMINISTRATION, *et al.* Defendant, and TEVA PHARMACEUTICALS USA, INC. and IMPAX LABORATORIES, INC., Intervenors-Defendants.	Case No. 06-CV-3355 (RWT)

JOINT OPPOSITION OF INTERVENORS TEVA PHARMACEUTICALS USA, INC. AND IMPAX LABORATORIES, INC. TO BIOVAIL CORPORATION'S MOTION FOR A TEMPORARY RESTRAINING ORDER AND/OR PRELIMINARY INJUNCTION

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INTRODUCTION

This case represents Biovail's latest attempt to forestall generic competition and protect its monopoly in the market for 300-mg extended-release bupropion hydrochloride tablets ("bupropion"), an antidepressant that Biovail has patented and manufactures and which its business partner Smithkline Beecham Corporation ("GlaxoSmithKline") markets under the trade-name Wellbutrin XL®. But this attempt comes a day late and a dollar short: FDA has already approved the ANDA filed by proposed intervenor-defendant Impax Laboratories, Inc. ("Impax") for 300-mg bupropion, and proposed intervenor-defendant Teva Pharmaceuticals USA, Inc. ("Teva") has already begun to commercially market that product under the terms of an agreement between Teva, Impax, and Anchen Pharmaceuticals, Inc. ("Anchen"). The injunctive relief Biovail SRL seeks thus would not only irreparably harm Teva and Impax, but would come at a tremendous expense to the millions of Americans who depend on 300-mg bupropion and now have access to an affordable generic alternative. Ultimately, that relief is sought against the backdrop of an action in which Biovail SRL has ***no chance of success on the merits***.

On the merits, Biovail's principal claim is that FDA somehow abused its discretion in determining that no 30-month stay barred its final approval of Impax's generic 300-mg bupropion drug product. But Biovail has not remotely overcome the substantial deference to which FDA's interpretation of the relevant statutory framework is entitled. The key point here is straightforward: Biovail did not sue Impax for infringement based on Impax's 300-mg drug product within 45 days of Impax notifying Biovail that its 300-mg application challenged the applicability and validity of the underlying patent. And when Biovail finally did so, it filed on behalf of an entity that no longer owned the underlying patent-in-suit or the right to sue for past infringement of that patent. Biovail's claim that its 150-mg suit, brought by an improper party,

could somehow trigger a stay on Impax's 300-mg product would thoroughly undermine the statutory scheme, which depends on dosage-by-dosage applications, dosage-by-dosage certifications, dosage-by-dosage notifications, and dosage-by-dosage approvals. It thus is no wonder that FDA's longstanding regulations regarding 30-month stays not only require suit to be brought by a proper party (i.e., a patentee), but with respect to a particular dosage. FDA's interpretation of the statute and its implementing regulations are consistent with existing judicial precedent, the text and structure of the statute, and the policy choices Congress expressly delegated to FDA. FDA's decision therefore warrants substantial deference under *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984).

With respect to the equities, Biovail has not remotely demonstrated that it will suffer any irreparable injury in the absence of temporary injunctive relief barring Teva's continued marketing of Impax's generic 300-mg bupropion drug product, because Biovail's purported injuries are merely financial and monetary injuries can always be compensated with monetary damages. But even if such injuries were cognizable at this stage of the proceedings, Biovail already has suffered the only injuries it claims it will suffer in the absence of interim injunctive relief—loss of market share ***in the event a generic drug is given final FDA approval for commercial marketing***—since FDA has already granted that final approval, and Teva has now launched Impax's product into the market. As a result, the only irreparable harms that remain at issue for purposes of Biovail's TRO application are the ones that would befall Teva and Impax if this Court enjoins Teva's continued commercial marketing of Impax's approved 300-mg bupropion product. In that event, business partners Teva and Impax would be deprived of 180 days of exclusivity for sales of generic 300-mg bupropion, and "[o]nce th[at] statutory entitlement has been lost, it cannot be recaptured." *Apotex, Inc. v. FDA*, No. Civ. A. 06-627-

JDB, 2006 WL 1030151, at *17 (D.D.C. April 19, 2006), *summarily affirmed by published opinion*, 449 F.3d 1249 (D.C. Cir. 2006).

Likewise, Biovail has not shown that the balance of hardships weighs in favor of granting injunctive relief. Whatever monetary injuries Biovail claims it may suffer, it has shown at best that "the hardships [it] may suffer if the emergency injunctive relief is denied are equal to the hardships that Teva will suffer.... Either way, some party may face significant economic disadvantage." *Teva Pharms. USA, Inc. v. FDA*, 404 F. Supp. 2d 243, 246 (D.D.C. 2005). Thus, as explained below, Teva and Impax have made an irrecoverable investment of ***millions of dollars*** to develop, stockpile, and begin distributing nearly ***seventy million doses*** of 300-mg bupropion to consumers. Those pills have a relatively short shelf-life, so entering an injunction at this stage of the proceedings jeopardizes Teva and Impax's significant investment in the development and production of this product. Moreover, temporary injunctive relief would impose substantial hardships on Teva and Impax by disrupting their current production schedules, staffing decisions, and business plans.

But whatever hardships may befall the various parties to this proceeding, those with the most at stake are the millions of Americans who depend on bupropion to relieve symptoms of their depression. Entry of a TRO or preliminary injunction would extend Biovail's monopoly hold on the market. Teva and Impax have launched their drug product and now are delivering much-needed price relief to consumers. Given the disruption that entry of an injunction would entail, this Court should deny Biovail's meritless motion for a TRO or preliminary injunction.

BACKGROUND

A. Statutory Framework

The Food, Drug, and Cosmetic Act ("FDCA" or "the statute"), as modified by the Hatch-Waxman and Medicare Modernization Acts ("HWA" and "MMA," respectively), establishes an

expedited FDA approval process for generic drugs, and creates significant incentives for manufacturers to develop affordable generic alternatives. To that end, the statute authorizes FDA to promptly approve a proposed generic drug product if its manufacturer demonstrates that the proposed drug product is bio- and therapeutically equivalent to a "listed drug" that previously has been deemed safe and effective.

In order to do so, a generic manufacturer must submit an abbreviated new drug application ("ANDA") to FDA for each proposed generic version of a listed drug. *See* 21 U.S.C. § 355(j) (2003). Because each dosage of a drug is a different listed drug for purposes of the statute, an applicant's ANDA must provide information about each dosage for which the applicant seeks approval. *See, e.g., Guidance for Industry, Listed Drugs, 30-Month Stays, and Approval of ANDAs and 505(b)(2) Applications Under Hatch-Waxman, as Amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003* at 3 (Nov. 2004) (the "MMA Guidance") (attached as Exh. 1); *180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications*, 64 Fed. Reg. 42873, 42881 (Aug. 6, 1999); *see also Apotex, Inc. v. Shalala*, 53 F. Supp. 2d 454, 461-63 (D.D.C. 1999); *United States v Baxter Health Care Inc.*, 712 F. Supp. 1352, 1358-59 (N.D. Ill. 1989). If an ANDA for a given dosage of a previously approved drug adequately demonstrates the proposed generic drug's bio- and therapeutic equivalence, the manufacturer need not repeat the safety and efficacy studies that accompanied the pioneer's new drug application ("NDA"); FDA can simply approve the ANDA applicant's generic drug product for commercial marketing. 21 U.S.C. § 355(j)(2)(A); *see also Dr. Reddy's Labs., Inc. v. Thompson*, 302 F. Supp. 2d 340, 343 (D.N.J. 2003).

An applicant's ANDA must also include a "certification" regarding each of the patents the NDA holder has listed with FDA as claiming the previously approved drug product. Again,

because each dosage of a drug product is a different listed drug under the statute, FDA has long required ANDA applicants to file a certification to each patent with respect to each dosage the applicant wishes to market. *See, e.g.*, *Ben Venue Labs., Inc. v. Novartis Pharm. Corp.*, 146 F. Supp. 2d 572, 581-82 & n.8 (D.N.J. 2001); Letter from FDA to All NDA and ANDA Holders and Applicants, Oct. 31, 1986, at 4-5 (attached as Exh. 2).

Of the various certifications an ANDA applicant might include in their filing, the most important is a "paragraph IV" certification. Paragraph IV certifications assert that a given patent is invalid or will not be infringed by the proposed generic drug product, *see* 21 U.S.C. § 355(j)(2)(A)(vii)(IV), and therefore indicate that the applicant has either developed a viable legal challenge to the validity of a competition-blocking patent or engineered a non-infringing pathway around such a patent. By design, and in order to help clear the "patent thicket" and speed the onset of market competition, the statute rewards applicants who submit paragraph IV certifications. Congress recognized that the first generic drug company to engineer a generic pathway bears significant research and legal costs when they attack a patent directly or design their way around it. Congress also recognized that the first ANDA filer faces a significant risk that it will be sued for patent infringement. To encourage generic manufacturers to assume those risks, Congress chose to reward the first applicant to file a paragraph IV certification with eligibility for a 180-day period of marketing "exclusivity," during which it holds the right to market the generic product without competition from other generic manufacturers. *See, e.g.*, *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 879 (D.C. Cir. 2004); *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1064 (D.C. Cir. 1998); *Sandoz, Inc. v. FDA*, 439 F. Supp. 2d 26, 29 (D.D.C. 2006); *see also* 21 U.S.C. § 355(j)(5)(B)(iv) ("180-day exclusivity period"). That exclusivity period runs from the date on which the first paragraph IV ANDA applicant

commercially markets its generic drug product following final FDA approval (the "commercial marketing trigger"). *Id.* § 355(j)(5)(B)(iv)(I).

At the same time, the statute enables both patentees and putative generic entrants to obtain patent certainty through litigation. Thus, the act of filing a paragraph IV certification constitutes a "technical" act of patent infringement, *see* 35 U.S.C. § 271(e); *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 678 (1990), and ANDA applicants must promptly notify the patentee and NDA holder whenever they file such a certification. *See* 21 U.S.C. § 355(j)(2)(B). If within 45 days the patentee responds to a given paragraph IV notification by filing an infringement action based on the underlying paragraph IV certification, the statute precludes the FDA from approving the ANDA for 30 months. *See* 21 U.S.C. §§ 355(j)(2)(A)(vii), (j)(5)(B)(iii). If the patentee fails to file suit within 45 days of receiving an ANDA applicant's paragraph IV notification, the ANDA applicant may file an action against the patentee seeking a declaratory judgment of non-infringement. *See* 21 U.S.C. §§ 355(c)(3)(D)(i)(I)-(II), (j)(5)(C)(i)(I)-(II).

B. Factual Background

Biovail SRL currently owns the patent rights and manufactures extended-release bupropion, a dopamine reuptake inhibitor used to counter depression. Its business partner, GlaxoSmithKline, markets that drug in 150-mg and 300-mg dosages. Two patents are listed as claiming each dosage of extended-release bupropion in the official register of patents claiming approved pharmaceuticals (the "Orange Book"): U.S. Patent No. 6,096,341 ("the '341 patent") and U.S. Patent No. 6,143,327 ("the '327 patent"). *See* Orange Book at 81, 871, *available at* http://www.fda.gov/cder/orange/obannual.pdf (last visited December 14, 2006).

On September 21, 2004, Anchen filed the first ANDA seeking FDA approval to market generic bupropion in 150-mg and 300-mg dosages. Anchen's ANDA contained paragraph IV

certifications asserting that neither of its bupropion products would infringe either of the above-listed patents. As a result, Anchen became eligible for 180-day exclusivity for sales of generic bupropion. 21 U.S.C. §§ 355(j)(5)(B)(iv).

On November 30, 2004, Impax filed an ANDA seeking FDA approval to market generic bupropion in 150-mg dosages. *See* Impax, *ANDA for Bupropion Hydrochloride Extended-release (XL) Tablets, 150 mg* (excerpt attached as Exh. 3). Like Anchen's ANDA, Impax's ANDA contained paragraph IV certifications asserting that its version of 150-mg bupropion would not infringe either the '327 or '341 patent, or that those patents were otherwise invalid or unenforceable. *Id.* at 16-17. On December 28, 2004, Impax submitted an amendment to its ANDA that would provide for a 300-mg generic product. *See* Impax, *ANDA for Bupropion Hydrochloride Extended-release (XL) Tablets, 150 mg—Addition of 300 mg Strength* (excerpt attached as Exh. 4). That amendment included the requisite paragraph IV certifications asserting that Impax's proposed 300-mg dosage of bupropion would not infringe either the '327 or '341 patent, or that those patents were otherwise invalid or unenforceable. *Id.* at 1, 12-13.

On January 19, 2005, FDA acknowledged its receipt of Impax's ANDA. The following day, Impax dispatched a paragraph IV notification to Biovail Laboratories, Inc. ("Biovail Labs")—the Biovail entity which at that time was registered with the U.S. Patent and Trademark Office ("USPTO") as owning the bupropion patents—and GlaxoSmithKline. That notification contained a "detailed statement of ... the factual and legal bases why ... the '341 patent ... and '327 patent are invalid, unenforceable, or would not be infringed ... by the commercial manufacture, use, or sale of Impax's proposed bupropion hydrochloride extended release tablet (150 mg)." *See Impax Laboratories, Inc.'s Detailed Statement Of The Factual And Legal Bases That U.S. Patent Nos. 6,096,341 & 6,143,327 Are Invalid Or Would Not Be Infringed*, at 2

(excerpt attached as Exh. 5). It is undisputed that Biovail Labs received Impax's notification regarding the 150-mg dosage on January 24, 2005. *See* Impax, *ANDA 77-415: Bupropion Hydrochloride Extended-release (XL) Tablets, 150 mg and 300 mg—Documentation of Paragraph IV Notification and Receipt of Notice and Documentation of Litigation/Settlement Outcome* ("First FDA Notice Letter"), at 9, 11 (attached as Exh. 6).

On January 24, 2005, Impax dispatched another letter to Biovail Labs and GlaxoSmithKline. That letter indicated that "Impax has submitted an amendment to Abbreviated New Drug Application 77-415..., providing for the addition of a 300 mg tablet." It also included a paragraph IV notification containing a "detailed statement of ... the factual and legal bases why ... the '341 patent ... and '327 patent are invalid, unenforceable, or would not be infringed ... by the commercial manufacture, use, or sale of Impax's proposed bupropion hydrochloride extended release tablet (300 mg)." *See Impax Laboratories, Inc.'s Detailed Statement Of The Factual And Legal Bases That U.S. Patent Nos. 6,096,341 and 6,143,327 Are Invalid Or Would Not Be Infringed*, at 1, 2 (attached as Exh. 7). It is undisputed that Biovail Labs received that notice on January 25, 2005. First FDA Notice Letter at 10, 12.

While that process was underway, Biovail Labs was busy transferring ownership of the '327 and '341 patents through a series of off-shore transactions. On December 31, 2004, Biovail Labs transferred ownership of the '341 patent to Biovail SRL. *See* Declaration of Christopher Bovaird, *Biovail Laboratories Inc. et al. v. Abrika LLLP et al.*, No. 04-61704-CIV (S.D. Fla. filed May 2, 2005) (attached as Exh. 8). On January 27, 2005, Biovail Labs joined with another Biovail entity to form Biovail Laboratories (2005) Inc. *See* Barbados Ministry of Industry and International Business, Corporate Affairs and Intellectual Property Office, *Certificate of Amalgamation: Biovail Laboratories (2005) Inc.* (excerpt attached as Exh. 9). On January 28,

2005, Biovail Laboratories (2005) Inc. was dissolved and all of its assets were transferred to Biovail SRL. *See* Barbados Ministry of Industry and International Business, Corporate Affairs and Intellectual Property Office, *Certificate of Dissolution: Biovail Laboratories (2005) Inc.* (attached as Exh. 10). Through these transactions, Biovail SRL acquired ownership of both the '327 and '341 patents. However, Biovail SRL did not inform USPTO that it had acquired those patents until after Impax had sent its paragraph IV notices to Biovail Labs.

On March 7, 2005, Biovail Labs—not Biovail SRL—filed suit against Impax alleging that Impax's 150-mg product (but not its 300-mg product) would infringe the '341 patent. *See* First FDA Notice Letter at 14-21. On April 7, 2005, Biovail Labs amended its complaint to allege that Impax's 300-mg product also would infringe the '341 patent. *See* Impax, *ANDA 77-415: Bupropion Hydrochloride Extended-release (XL) Tablets, 150 mg and 300 mg—Documentation of Litigation/Settlement Outcome* ("Second FDA Notice Letter"), at 6-11 (attached as Exh. 11). On May 19, 2005, the parties to that litigation filed a stipulation providing "that the name of plaintiff throughout the amended complaint for patent infringement in the above-captioned action shall hereby be designated as 'Biovail Laboratories International SRL' rather than 'Biovail Laboratories, Inc.'" *See* Stipulation, *Biovail Laboratories, Inc. v. Impax Laboratories, Inc.*, No. 05-cv-1085 (E.D. Pa. filed May 20, 2005) (the "Stipulation") (attached as Exh. 12).

On December 14, 2006, FDA granted final approval to Anchen's 300-mg bupropion product, and Anchen triggered its 180-day exclusivity period by commercially marketing its 300-mg generic bupropion product. *See* Anchen, *Request for Expedited Selective Waiver of 180-Day Market Exclusivity Subsequent to a Triggering Event* at 2-3 (the "Selective Waiver Letter") (attached as Exh. 13). Pursuant to the terms of an agreement between Anchen, Teva and Impax,

Anchen then "selectively waived" its exclusivity for 300-mg generic bupropion sales to Teva and Impax. *Id.* Together, those actions permitted FDA to grant final approval to Impax's 300-mg bupropion product, and FDA did so on December 15, 2006. *See* FDA Letter Decision (attached as Exh. 14).[1] In granting Impax's ANDA, FDA affirmed that "the drug is safe and effective for use" and is "bioequivalent" and "therapeutically equivalent" to Wellbutrin XL®. *Id.* at 1-2. It likewise observed that while Biovail had filed suit against Impax within 45 days of receiving Impax's 150-mg paragraph IV notification, Biovail had failed to file suit based on Impax's 300-mg certification within the 45 -ay period. *Id.* at 2. Based on the record before the agency, FDA therefore determined that the 30-month stay was inapplicable. *Id.*

As soon as FDA approved Impax's ANDA, Impax began delivering its 300-mg bupropion drug products to Teva for immediate commercial marketing under the terms of the parties' strategic alliance agreement, and within hours, Teva began commercially marketing Impax's 300-mg bupropion to its major customers. *See* Declaration of David Marshall ("Marshall Declaration") at ¶ 9. By December 16, 2006, Teva had distributed some 60 million tablets of Impax's 300-mg bupropion drug product to its customers. *Id.* Those tablets are already being dispensed to patients. *Id.*

LEGAL STANDARD FOR INJUNCTIVE RELIEF

The purpose of a preliminary injunction "is to protect the status quo and prevent irreparable harm during the pendency of a lawsuit." *Sun Microsystems, Inc. v. Microsoft Corp.*, 333 F. 3d 517, 525 (4th Cir. 2003). To demonstrate an entitlement to temporary injunctive relief

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1 For nearly a decade, FDA has honored selective waiver agreements between generic pharmaceutical manufacturers, *e.g.* FDA Letter Decision Denying Citizen Petition No. 2004P-0227, July 2, 2004, at 4-5, and for just as long, courts have upheld them. *See, e.g., Boehringer Ingelheim Corp. v. Shalala*, 993 F. Supp. 1, 2 (D.D.C. 1997). Biovail does not challenge any aspect of the selective waiver at issue here.

a plaintiff must show that (1) there is a substantial likelihood of success on the merits; (2) the plaintiff would suffer irreparable injury if the requested injunction is denied; (3) an injunction will not substantially injure the opposing party or other third parties; and (4) the public interest will be furthered by the issuance of the injunction. *See, e.g.*, *United States Dep't of Labor v. Wolf Run Mining Co.*, 452 F.3d 275, 280 (4th Cir. 2006). There is a "flexible interplay among all the factors considered [and they] are intertwined and each affects in degree all the others." *Blackwelder Furniture Co. v. Statesville, Inc.*, 550 F.2d 189, 196 (4th Cir. 1997).

ARGUMENT

I. BIOVAIL SRL HAS NO CHANCE OF SUCCESS ON THE MERITS.

Biovail has not remotely sustained its heavy burden of demonstrating that it is likely to prevail on the merits of its claim that FDA abused its discretion in declining to stay its final approval of Impax's ANDA for 30 months. Biovail's claim fails first because Biovail did not file an infringement action against Impax based on Impax's 300-mg paragraph IV certification within 45 days of receiving Impax's 300-mg paragraph IV notification, and second because the only Biovail entity that did sue Impax for patent infringement during the 45-day window (Biovail Labs, and then only with respect to Impax's 150-mg certification) was one that did not own the right to sue on the patent Impax allegedly infringed—and which thus lacked standing to pursue the action, much less trigger a 30-month stay.

A. Biovail Did Not Sue Impax For Infringement Based On Impax's 300-mg Paragraph IV Certification Within The 45-Day Triggering Period For That Product.

In relevant part, the statute's 30-month stay provision provides:

> If the applicant made a [paragraph IV] certification..., the approval shall be made effective immediately unless, ***before the expiration of 45 days after the date on which the [paragraph IV notification] is received, an action is brought for infringement of the patent that is the subject of the certification***.... If such an action is brought before the expiration of such days, the approval shall be made

> effective upon the expiration of the thirty-month period beginning on the date of the receipt of the [paragraph IV notification].

21 U.S.C. § 355(j)(5)(B)(3) (emphasis added); *id.* § 355(c)(3)(C) (same). The analysis here is straightforward: Biovail received Impax's paragraph IV notification regarding its 300-mg paragraph IV certifications on January 24, 2005, but did not sue Impax for infringement based on Impax's 300-mg paragraph IV certification until it amended its complaint to add such a claim on April 7, 2005—some 73 days later. *See* Second FDA Notice Letter at 6-11. Because Biovail did not assert that Impax's 300-mg product would infringe the '341 patent within 45 days of receiving Impax's notification of its 300-mg paragraph IV certification, no 30-month stay precluded FDA from granting final approval to Impax's 300-mg drug product.

Biovail's only answer is that within 45 days of receiving Impax's ***300-mg*** paragraph IV notification with respect to the '341 patent, Biovail Labs had filed suit against Impax based on Impax's ***150-mg*** paragraph IV patent certification to that same patent. Biovail Br. at 6. Biovail thus argues that Biovail Labs's ***150-mg*** lawsuit somehow triggered the 30-month stay with respect to Impax's ***300-mg*** bupropion drug product, because both products involve the same patent. *Id.*

That construction of the statute (under which a suit based on one drug product could stay approval of another drug product simply because they share a common patent) would unleash absurd results. In many cases, multiple drug products—including products produced by different companies—claim a single patent. For instance, both Paxil (a GlaxoSmithKline product) and Zoloft (a Pfizer product) claim U.S. Patent No. 5,789,449. *See* Orange Book at 950-53 (Paxil products), 967 (Zoloft product), *available at* http://www.fda.gov/cder/orange/obannual.pdf (last visited December 14, 2006). But it would be absurd to suggest that the filing of a patent infringement suit against one manufacturer for one drug product should or could trigger a 30-

month stay with respect to another company's different drug product simply because both have submitted a paragraph IV certification to the same patent. The result is no less absurd where the two products are manufactured by the same company. Indeed, as FDA has long recognized, even "[d]ifferent strengths of the same drug may be formulated differently for a variety of reasons, and varying formulations of the different strengths may provide separate and distinct bases for patent protection or for patent challenges." *See* Memorandum in Support of Defendants' Motion to Dismiss and in Opposition to Plaintiff's Motion for Injunction, at 19, quoted in *Apotex*, 53 F. Supp. 2d at 461 (quotation and internal alteration omitted). As a result, the only plausible interpretation of the 30-month stay provision recognizes that suit must be filed with respect to ***a particular drug product***, and that the trigger for any such stay is keyed to the receipt of a paragraph IV notification regarding a paragraph IV certification ***for that particular drug product***.

The key point, then, is simple: As FDA has long explained and just recently reiterated, ***different dosages are different drugs*** for purposes of the statutory scheme. *See, e.g.*, MMA Guidance at 3 ("[E]ach strength of an approved drug is a separate listed drug."); *180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications*, 64 Fed. Reg. at 42881 ("[E]ach strength of a drug product is itself a listed drug."). That interpretation of the statute is unimpeachable. ***First***, Congress has expressly authorized FDA to define the statutory term "listed drug," 21 U.S.C. § 355(j)(2)(D)(iii) ("Within 60 days after December 8, 2003, the Secretary shall issue guidance defining the term 'listed drug' for purposes of this subparagraph."), and deference to an agency's statutory interpretation is at its greatest when the agency is acting pursuant to an express delegation of interpretative authority. *Chevron*, 467 U.S. at 843-44 ("If Congress has explicitly left a gap for the agency to fill, there is an express

delegation of authority to the agency to elucidate a specific provision of the statute by regulation. Such legislative regulations are given controlling weight unless they are ***arbitrary, capricious, or manifestly contrary to the statute***.") (emphasis added).

Second, FDA's interpretation is consistent with other provisions of the statutory scheme, which ***exempt*** ANDA amendments "seek[ing] approval of a ***different strength***" from the statute's general bar against amendments "seek[ing] approval of a drug referring to a ***different listed drug***." *Id.* § 355(j)(2)(D)(i)-(ii) (emphases added). That exemption would have been superfluous if different dosages of a drug product were not different listed drugs, and it is axiomatic that statutes should be construed to avoid rendering any "'clause, sentence, or word ... superfluous, void, or insignificant.'" *Duncan v. Walker*, 533 U.S. 167, 174 (2001) (quoting *Market Co. v. Hoffman*, 101 U.S. 112, 115 (1879)).

Third, FDA's interpretation is consistent with existing case law regarding exclusivity. Indeed, it is now well-settled that a manufacturer is entitled to an exclusivity period for each dosage of a given drug. *Apotex*, 53 F. Supp. 2d at 463 ("The Hatch-Waxman Amendments provide that ANDAs must reference a particular listed drug product, and the Act requires the generic version of each drug to have the same strength as the listed drug. The Court is persuaded by the FDA's reasoning that allowing separate exclusivity for various strengths encourages prompt entry onto the market of the greatest number of drug strengths in an attempt to obtain maximum protection from other generic drug competitors.") (internal quotations and alterations omitted). That holding and its underlying reasoning were summarily affirmed by the D.C. Circuit, *Apotex, Inc. v. Shalala*, No. 99-5231, 1999 WL 956686 (D.C. Cir. Oct. 8, 1999), and Biovail's apparent belief that different dosages of the same drug are the same drug simply cannot be squared with this settled understanding of the statute's exclusivity scheme.

Finally, FDA's interpretation comports with common sense. After all, the term "overdose" is not a misnomer, and as Congress has recognized, drugs that might be safe and effective in one dosage are not necessarily safe or effective in another. *See, e.g., id.* § 355(j)(2)(c) (providing that FDA may deny an applicant permission even to submit an ANDA "for a new drug which has a different ... strength ... from that of a listed drug" where it finds that further "investigations must be conducted to show the safety and effectiveness of the drug").

Thus, because each dosage of a drug is a different listed drug for purposes of the statute, each dosage requires its own paragraph IV certification(s) and corresponding paragraph IV notification(s) to the registered patentee and/or NDA holder. That, too, has been settled law for more than twenty years. *See, e.g., Ben Venue Labs., Inc. v. Novartis Pharm. Corp.*, 146 F. Supp. 2d 572, 581-82 & n.8 (D.N.J. 2001) ("[W]hen an applicant seeks to amend their ANDA to include a new dosage formulation, the FDA will require that a supplemental Paragraph IV Certification be filed with the agency and appropriate notice given the patentee. The new Paragraph IV Certification can then provide the basis for a new infringement suit. Novartis has submitted to the Court an open letter from the FDA to all NDA and ANDA holders and applicants, dated October 31, 1986. In that letter, the FDA indicates that an ANDA filer who makes 1) formulation changes, 2) changes in conditions of use, or 3) strength changes should file a supplemental Paragraph IV Certification."); 21 U.S.C. § 355(j)(2)(A)(vii) (requiring every ANDA to include "a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims ***the listed drug***"); 21 U.S.C. § 355(j)(2)(B)(ii)-(iv) (requiring that "[a]n applicant that makes a [paragraph IV] certification ... give notice ... stat[ing *inter alia*] that an application that contains data from bioavailability or

bioequivalence studies has been submitted under this subsection ***for the drug with respect to which the certification is made***").

Finally, because the 45-day window for filing a stay-triggering patent infringement lawsuit runs from the date of a given paragraph IV notification, 21 U.S.C. §§ 355(j)(5)(B)(3), 355(c)(3)(C), and because (as set forth above) paragraph IV notifications are necessarily dosage-specific, it follows that a patentee cannot trigger a 30-month stay with respect to one dosage of a drug product by filing a lawsuit alleging that another dosage of that drug product infringes the underlying patent or patents. Instead, before the 30-month stay can be applied, the patentee must file an infringement action with respect to a particular dosage of a drug within 45 days of receiving the paragraph IV notification regarding that dosage. Biovail simply did not do so in this case.

Despite all of this, Biovail maintains that its suit was nonetheless sufficient to trigger the stay because its complaint "sought relief as against the entire ANDA," and thus that notwithstanding Biovail's failure to reference the 300-mg product at any point in its pleadings, that prayer for generalized relief should have triggered the stay as to any product for which Impax might seek approval under its ANDA. Biovail Br. at 6. But for the same reasons set forth above, that argument does not pass the straight-face test. The 30-month stay provision requires the aggrieved party to file a complaint alleging "infringement of the patent that is the subject of ***the certification***." 21 U.S.C. § 355(j)(5)(B)(3) (emphasis added); *id.* § 355(c)(3)(C) (same). Congress thus clearly contemplated that the stay-triggering infringement action would be linked to a particular certification, and because the only certification Biovail referenced in its complaint was Impax's certification with respect to its 150-mg product, *see* Complaint at ¶¶ 1, 12, it cannot be enough to simply seek vaguely defined relief that might apply to another drug product

under the same ANDA—including one for which the applicant might not even have filed a paragraph IV certification at all.

At bottom, then, the statute's dosage-by-dosage certification and notification requirements, and its express link between 30-month stays and dosage-specific notifications, compel the rejection of Biovail SRL's attempt to piggyback Biovail Labs's 300-mg lawsuit onto its earlier response to Impax's 150-mg notification. On this point, Biovail SRL has no chance of eventual success on the merits, and its claim that the FDA abused its discretion should be denied.

B. In The Alternative, Biovail's Failure To Bring File Suit On Behalf Of A Proper Party Precludes Application Of The 30-Month Stay.

Even if patent litigation with respect to one drug ***could*** trigger a 30-month stay with respect to another drug simply because they might implicate a common patent, Biovail still would not be able to prevail on the merits of its 30-month stay claim. After all, at the time the Biovail entity which filed suit against Impax, ***Biovail Labs***, did so in response to Impax's alleged 150-mg infringement, that entity had transferred ownership of all of its assets (including the patent-in-suit and the right to sue on that patent) to ***Biovail SRL***, and thus lacked the standing necessary to trigger a 30-month stay.

Once again, the argument here is straightforward. The 30-month stay provision is phrased in the passive voice, and thus does not specify who must bring suit in order to trigger a stay. *See* 21 U.S.C. § 355(j)(5)(B)(iii) ("[A]pproval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, ***an action is brought*** for infringement...."). But FDA long ago exercised its regulatory discretion to fill that statutory gap by requiring a stay-triggering suit to be brought by "the patent owner or its representative or the exclusive licensee." *See* 21 C.F.R. § 314.107(b)(3). This regulation has never been challenged, and it represents an eminently reasonable

construction of the statute. After all, the 30-month stay provision is keyed to "the date on which the [paragraph IV] notice ... is received," 21 U.S.C. § 355(j)(5)(B)(iii), and the point of the statute's notice provision is to ensure that the registered "owner of the patent that is the subject of the certification [or] the holder of the approved application ... for the drug that is claimed by the patent" can preserve its interests in the patent by filing an infringement action. 21 U.S.C. § 355(j)(2)(B)(iii).

It thus makes little sense to think that a suit brought by someone who does not own the right to sue for infringement of the challenged patent could trigger a 30-month stay. By definition, such entities lack any interest in that patent, and indeed, it is well-settled that such entities lack standing to sue for infringement in the first instance. *See, e.g.*, *Mas-Hamilton Group v. LaGard, Inc.*, 156 F.3d 1206, 1210 (Fed. Cir. 1998); *Ortho Pharm. Corp. v. Genetics Inst., Inc.*, 52 F.3d 1026, 1030 (Fed. Cir. 1995). As a matter of law and logic, then, ***Biovail Labs's*** infringement action against Impax's 150-mg dosage could not have triggered a 30-month stay with respect to Impax's 300-mg dosage—even if it were in theory possible to dissemble the statute's dosage-by-dosage certification and notification requirements and deem the filing of an infringement suit on one dosage sufficient to trigger a 30-month stay regarding another dosage.

It is no answer that Biovail and Impax eventually stipulated "that the name of plaintiff throughout ***the amended complaint*** for patent infringement in the [underlying patent infringement] action shall hereby be designated as 'Biovail Laboratories International SRL' rather than 'Biovail Laboratories, Inc,'" Stipulation at 1 (emphasis added), and that that "party substitution" somehow "relates back" to ***the original filing***. ***First***, the stipulation, by its own terms, applied only to the ***amended complaint*** (not the ***original filing***), so it cannot on its own terms relate back to the time of the initial filing. ***Second***, and even assuming that the name-