

Enclosure B

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

PUREPAC PHARMACEUTICAL CO.,

Plaintiff,

v.

TOMMY G. THOMPSON,
Secretary of Health and Human Services,

and

MARK B. McCLELLAN,
Commissioner of Food and Drugs,

Defendants,

and

IVAX PHARMACEUTICALS, INC.,

Intervenor-Defendant.

Civil Action No. CV-03-02210 (TPJ)

**INTERVENOR-DEFENDANT IVAX PHARMACEUTICALS, INC.'S
MEMORANDUM OF POINTS AND AUTHORITIES IN OPPOSITION TO
PLAINTIFF PUREPAC PHARMACEUTICAL CO.'S
MOTION FOR PRELIMINARY INJUNCTION**

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Intervenor-Defendant IVAX Pharmaceuticals, Inc. ("IVAX") submits the following memorandum of law in opposition to the motion for preliminary injunction filed by Purepac Pharmaceutical Co. ("Purepac").

I. INTRODUCTION

Purepac's legal position in this case is predicated, in its entirety, upon its fundamental refusal to accept that in enacting the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act, it was Congress – *not the FDA* – who specifically chose to impose *different* statutory notice requirements upon an amended ANDA filer (like Purepac) and an original ANDA filer (like IVAX). On this record, it is undisputed that IVAX's original ANDA submission complied with all of the statutory notice-related requirements applicable to such a submission when it was received by FDA on November 26, 2002, and was therefore "complete" for purposes of an award of marketing exclusivity as of that date. It is also undisputed on this record that Purepac *failed* to comply with the simultaneous filing/notice requirement imposed upon it by Congress until November 27, 2002, which rendered its earlier filed amendment incomplete and ineffective for purposes of an entitlement to marketing exclusivity until that day.

In enacting 21 U.S.C. § 355(j)(2)(B), and specifically clauses (i) and (iii) thereof, Congress imposed markedly different notice-giving requirements upon amended versus original ANDA applicants. Congress' command to amended ANDA filers (like Purepac) could hardly be more clear: "[i]f an application is amended to include a [Paragraph IV] certification, the notice required by clause (ii) *shall be given when the amended application is submitted.*" 21 U.S.C. § 355(j)(2)(B)(iii) (emphasis added). By stark contrast – and for good reason, as we will explain – Congress chose not to impose any such requirement upon original ANDA filers (like IVAX), but instead specifically required only that such an applicant "include in the application *a statement that the applicant will*

give the notice required by clause (ii)” at a later date. 21 U.S.C. § 355(j)(2)(B)(i) (emphasis added). Indeed, as FDA’s implementing regulations make clear, original ANDA filers (like IVAX) are not only not required to give notice when the application is submitted, they are not *permitted* to do so.

Unable to dispute that it failed to comply with the statutory notice requirements imposed upon it by *Congress*, Purepac now asks this Court to not only excuse its non-compliance, but indeed to reward it, and to ignore IVAX’s *compliance* with the statutory requirements for original ANDA submissions by setting aside what is plainly lawful and appropriate FDA action.

As a result of Purepac’s statutory non-compliance, it was well within FDA’s authority to not treat Purepac’s ANDA amendment as effective or complete for purposes of exclusivity until the date upon which such non-compliance was cured, November 27, 2002. While we will demonstrate that FDA’s decision to treat the effective date of Purepac’s filing as the day Purepac complied with its statutory notice obligations is directly supported by statutory and regulatory authority, it bears noting at the outset that this precise issue has already been decided by Judge Huvelle in *TorPharm, Inc. v. Thompson*, 260 F. Supp. 2d 69 (D.D.C. 2003). In that case, Judge Huvelle specifically held that FDA acted reasonably and lawfully in treating the effective date of an amended ANDA filing as the date the Paragraph IV notice was actually given for purposes of determining eligibility for 180-day marketing exclusivity.

It is not surprising that Purepac now tries to distance itself from that decision (it is not even mentioned by Purepac until the last few pages of its argument on the merits), given that it was the direct beneficiary of FDA’s decision in that case. But what is truly regrettable is Purepac’s failure to tell the Court that it is – *at this very moment* – strenuously arguing in the appeal of that decision to the D.C. Circuit that the FDA’s decision to toll the effective date of an amended ANDA Paragraph IV submission until the notice requirement was satisfied was eminently correct, reasonable, lawful

and appropriate. We submit that Purepac's willingness to simultaneously advance such diametrically opposed and inconsistent positions to different courts when it suits its interests should give the Court great cause for skepticism when considering the bona fides of Purepac's plea for consistency in the application of the statutory scheme. At a minimum, such doublespeak has no place in a court of equity.

Unable to offer any excuse or justification for its glaring failure to comply with an unambiguous statutory command, Purepac tries to divert the Court's attention from its non-compliance by trying to turn this into an equal protection case. While Purepac complains bitterly that the FDA has treated it differently than IVAX, and that the Agency's action in this case creates "a second, more arduous track for amended ANDA filers," Purepac Br. at 19, FDA can hardly be faulted for applying its "completeness" standard in a way which precisely tracks the requirements imposed by *Congress* under the two intentionally *different* statutory notice-giving provisions. Indeed, while Purepac trumpets the Supreme Court's directive in *Chevron* that "the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress," Purepac Br. at 10, Purepac turns this concept on its head by faulting FDA for not imposing the same notice-giving requirements upon amended and original filers when Congress has *mandated*, by express statutory language, that the notice-giving requirements for those filers are *different*.

Ultimately, Purepac's exhortation to the Court that "it took every step to ensure its status as first filer," Purepac Br. at 7, rings hollow when considered in the context of the administrative record. In fact, we submit that all Purepac has established by touting its heralded 20-day stretch between November 5th and November 25, 2002 – during which, it says, it filed a paragraph IV amendment to its pending ANDA *every day* thereof – is that it had *20 different opportunities* to perfect its right to exclusivity by simply complying with Congress' unambiguous statutory command

to give notice to the patent holder at the same time it amended its ANDA. Having inexplicably failed to do so, it cannot be heard now to complain that FDA acted improperly in declining to treat its amendment(s) as effective or complete before that notice was given.

With respect to irreparable harm and the balance of hardships, we assume even Purepac would concede that if IVAX is correct that FDA acted reasonably and appropriately, the grant of the injunction will impose *at least* the same irreparable harm upon IVAX that Purepac claims it would suffer if the injunction was not entered. But we also submit that, unlike IVAX – which is ready and capable of going to market right now – Purepac’s allegations of irreparable harm are at best purely speculative, because Purepac does not have even a *tentative* approval from the FDA. In other words, separate and apart from any issue regarding 180-day marketing approval, Purepac has yet to persuade FDA that its generic metformin product is suitable to be released for human consumption.

Thus, even if the Court were to grant the injunction, Purepac would be in precisely the same situation as if the injunction was not entered – unable to sell a single metformin tablet to the public. Because it is entirely speculative if or when Purepac’s ANDA will ever be approved, Purepac is unable to demonstrate that it will suffer “immediate” irreparable harm as required by the controlling law in this Circuit.

By contrast, the harm to IVAX if the injunction is entered will be immediate, non-speculative and substantial. Unlike Purepac, IVAX has demonstrated to FDA’s satisfaction that its metformin product is bioequivalent to Glucophage® XR, that it is safe and effective for consumption by diabetic patients, and that it satisfies all other regulatory requirements for final marketing approval. Unlike Purepac, IVAX has product labeled and packaged and sitting in its warehouses (and in the warehouses of its customers) waiting for release to the purchasing public. Unlike Purepac, the *only*

thing preventing IVAX's metformin product from reaching consumers is the current TRO, and an injunction if issued.

Which brings us directly to the public interest. It is difficult to imagine a case where, on these facts, the public interest tips more decidedly against the entry of an injunction. Not surprisingly, Purepac gave scant consideration to the public interest in its TRO papers, and gives it only nominally more attention in its injunction brief, arguing the non-remarkable proposition that it is in the public interest to have a federal agency act in a lawful manner. That argument, however, simply begs the merits-driven question of whether FDA acted outside of its broad discretion in implementing the regulatory scheme created by the Hatch-Waxman Amendments.

What Purepac ignores are the real-life adverse consequences to the diabetes population if its request for an injunction is granted. If the injunction is granted, thousands of patients will continue to be forced to overspend millions of dollars for Glucophage[®] XR, while Bristol-Myers continues to reap the benefits of monopoly pricing. Enjoining the entry of a lower-priced generic metformin product now will cost the public, health care insurers, and government programs such as Medicaid literally millions and millions of dollars in overpayments which can *never* be recouped. Such a result – which could not be rectified even if the Court awarded exclusivity to Purepac today because of its lack of FDA approval to sell the drug – is obviously antithetical to the public interest. It is also inimical to the overriding purpose of the Hatch-Waxman Amendments themselves, by which “Congress sought to get generic drugs into the hands of patients at reasonable prices - *fast*.” *In re Barr Labs., Inc.*, 930 F.2d 72, 76 (D.C. Cir. 1991) (emphasis added).

Finally, we will also show that Purepac is barred from obtaining equitable relief under the doctrine of unclean hands, because it misappropriated confidential business information from IVAX

in violation of a binding confidentiality agreement, and without this information it would not have been able to apply for the temporary restraining order that it obtained on October 29, 2003.

In short, as more fully demonstrated below, Purepac has failed to meet its heavy burden of establishing any of the necessary prerequisites to the entry of injunctive relief.

II. STATUTORY AND REGULATORY BACKGROUND

The Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §§ 301 *et seq.*, establishes the requirements for seeking and obtaining approval from the United States Food and Drug Administration ("FDA") to market pharmaceutical products in the United States.

Under the FDCA, an entity seeking to market a proposed new drug (often called a "brand name" or "innovator" drug) must complete and submit to FDA a document called a New Drug Application ("NDA"). The NDA must include a variety of important information pertaining to the nature and composition of the drug, as well as the results of clinical studies establishing the proposed drug's safety and effectiveness. In addition, the NDA holder is required to submit to FDA for publication in Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the "Orange Book") all patents that claim the drug, or a method of using the drug, with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the patent-holder engaged in the manufacture, use, or sale of the drug. *See* 21 U.S.C. § 355(b)(1) & (c)(2); 21 C.F.R. § 314.53(b).

Prior to 1984, an entity seeking to market a generic version of an already approved drug was required to file a new NDA, complete with its own studies showing the drug's safety and effectiveness. In 1984, however, Congress adopted the Hatch-Waxman Amendments, which established a streamlined procedure for approval of generic drugs in order to increase competition in the drug industry and lower the cost of drugs to consumers. *See* Drug Price Competition and

Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984), codified as amended at 21 U.S.C. § 355; *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 3126 (D.C. Cir. 1998) (“The purpose of the Hatch-Waxman Amendments was . . . ‘to increase competition in the drug industry by facilitating the approval of generic copies of drugs.’”) (quoting *Mead Johnson Pharm. Group v. Bowen*, 838 F.2d 1332, 1333 (D.C. Cir. 1988)). Specifically, under the Hatch-Waxman Amendments, an entity seeking to market a generic version of an already approved drug is no longer required to file a complete NDA, but may instead file a more simplified document called an Abbreviated New Drug Application (“ANDA”) which relies on the FDA’s prior determination that the drug is safe and effective. *See* 21 U.S.C. § 355(j); *Mylan Pharms., Inc. v. Shalala*, 81 F. Supp. 2d 30, 32 (D.D.C. 2000).

In order for an ANDA to be approved, it must demonstrate, among other things, that the proposed generic drug is “bioequivalent” to the approved drug. *See* 21 U.S.C. § 355(j)(2)(A)(iv). In addition, it must contain one of four certifications with respect to each patent listed in the Orange Book. The certification at issue here – a “Paragraph IV” certification – informs the FDA that the ANDA applicant seeks to market its proposed generic product before the patent expires, because the sponsor believes the patent is invalid or will not be infringed by the proposed generic drug product. 21 U.S.C. § 355(j)(2)(A)(vii)(IV); 21 C.F.R. § 314.94(a)(12)(i)(A)(4).

Under the Hatch-Waxman Amendments, an ANDA sponsor who makes a Paragraph IV certification must also give notice of its certification to the NDA and patent holder(s). Of particular importance in this case, however, *how* and *when* that notice must be given depends upon whether the ANDA sponsor is filing an original ANDA and or amending a previously-filed ANDA to include a Paragraph IV certification to a patent which was listed in the Orange Book subsequent to the ANDA’s filing.

In the case of an original ANDA, the applicant must state in its ANDA that it “will give” notice to the NDA and patent holder(s) at a later date:

An applicant who makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant *will give* the notice required by clause (ii)

21 U.S.C. § 355(j)(2)(B)(i) (emphasis added). Under the FDA’s implementing regulations, that date can only be after the applicant receives from FDA “an acknowledgment letter stating that its ANDA is sufficiently complete to permit a substantive review.” 21 C.F.R. § 314.95(b).

By contrast, if an ANDA sponsor amends a pending ANDA to include a Paragraph IV certification to a newly-listed patent, the statute explicitly requires that the notice be sent “when” the amended application is submitted to FDA:

If an application is amended to include a certification described in subparagraph (A)(vii)(IV), the notice required by clause (ii) shall be given when the amended application is submitted.

21 U.S.C. § 355(j)(2)(B)(iii); *see also* 21 C.F.R. § 314.95(d) (“If an abbreviated application is amended to include the certification described in § 314.94(a)(12)(i)(A)(4), the applicant shall send the notice required by paragraph (a) of this section *at the same time* that the amendment to the abbreviated application is submitted to FDA.”) (emphasis added).

The certification and notice-giving requirements serve two important purposes. First, if within 45 days of receiving notice of a Paragraph IV certification the patent holder brings a patent infringement lawsuit against the ANDA sponsor, FDA cannot grant the ANDA final approval for a period of thirty months. *See* 21 U.S.C. § 355(j)(5)(B)(iii).^{1/} Second, and of particular importance in this case, the Hatch-Waxman Amendments also provide for a 180-day period of generic marketing

^{1/} The “thirty-month stay” provision is not relevant to the present litigation because the NDA holder did not file any lawsuits alleging infringement of the patent in question.

exclusivity to the first ANDA sponsor to submit a substantially complete application containing a Paragraph IV certification with respect to each patent listed in Orange Book applicable to the approved drug. *See* 21 U.S.C. § 355(j)(5)(B)(iv); 21 C.F.R. 314.107(c)(1).

III. FACTUAL BACKGROUND

A. Metformin ER

The drug at issue here, metformin hydrochloride extended release tablets (“metformin ER”), is designed to help improve glycemic control for adults with type 2 diabetes. Bristol-Myers Squibb Company (“BMS”) is the holder of the New Drug Application for metformin ER, which it markets under the trade name Glucophage® XR. AR at Tab 1. According to publicly available pricing information, and its own public filings, BMS charges purchasers approximately \$66 for each 100-tablet bottle of Glucophage® XR, and achieved Glucophage® XR sales of \$237 million in the first six months of 2003. Decl. of C. Hogan, ¶ 5.

B. The ‘521 Patent And The Parties’ Paragraph IV Certifications Thereto

On November 5, 2002, the United States Patent & Trademark Office (“PTO”) issued to BMS U.S. Patent No. 6,475,521 (“the ‘521 patent”), which purports to claim a novel controlled release delivery system for pharmaceuticals containing a high water solubility, such as metformin ER. Although BMS had not yet submitted the ‘521 patent to FDA for listing in the Orange Book, later that day, Purepac – which had previously submitted an ANDA for metformin ER – began sending what purported to be daily ANDA amendments containing Paragraph IV certifications against the ‘521 patent, but without providing the statutorily-required concurrent notice to the NDA and patent holder. AR at Tab 4.

On November 19, 2002, two weeks and eleven incomplete Purepac amendments later, BMS submitted the ‘521 patent to FDA for listing in the Orange Book. AR at Tab 1. BMS’s patent

submission was received by FDA on November 20, 2002. AR at Tabs 1, 11. The '521 patent listing was published in the Orange Book on November 25, 2002.^{2/}

Purepac continued submitting incomplete amendments to FDA until November 25, 2002. AR at Tab 4. Even then, however, Purepac still did not comply with the statutory requirement of concurrent notice to the NDA and patent holder. *See* AR at Tab 5.

Meanwhile, on November 25, 2002, IVAX filed original ANDA 76-545, seeking approval to market generic metformin ER in the United States, which was received by FDA on November 26, 2002. AR at Tab 7. Among other things, IVAX's ANDA contained a Paragraph IV certification with respect to the '521 patent, certifying that the patent is invalid, unenforceable, or will not be infringed by IVAX's manufacture, use, or sale of metformin ER. AR at Tab 7. It also included the statement required by 21 U.S.C. § 355(j)(2)(B)(i) and 21 C.F.R. § 314.94(a)(12)(i), that it "w[ould] give" notice of the Paragraph IV certification to the NDA and patent holder(s) at a later date. As a result, IVAX's ANDA was complete for exclusivity purposes as of November 26, 2002, the date it was received by FDA.^{3/}

It was not until the following day, November 27, 2002, that Purepac finally sent the statutorily-required notice to BMS, AR at Tab 5, giving its application a "completeness" date for exclusivity purposes of November 27, 2002. AR at Tab 11.

^{2/} FDA regards November 20, 2002 as the date on which BMS listed the '521 patent, AR at Tab 11, notwithstanding that the listing was not publicly-disclosed until five days later.

^{3/} This was later confirmed in FDA's January 14, 2003 letter to IVAX – received on January 21, 2003 – acknowledging the filing of IVAX's ANDA 76-545 and informing IVAX that the ANDA had been deemed sufficiently complete for review. AR at Tab 8. Shortly thereafter, on February 3, 2003, IVAX sent a notice letter to BMS informing it of the Paragraph IV certification with respect to the '521 patent and the basis therefor. AR at Tab 10.

C. IVAX's Preparation For Final Approval

Because only a single day separated the publication of the '521 patent listing in the Orange Book and the filing of IVAX's ANDA for metformin ER, IVAX reasonably believed from the outset (which belief was later confirmed by FDA) that it was the first ANDA applicant for metformin ER to have submitted a substantially complete ANDA with a Paragraph IV certification against the '521 patent, and, thus, would be eligible upon final approval for 180 days of generic market exclusivity. Accordingly, during the first quarter of 2003, IVAX began the laborious and expensive process of preparing for a commercial launch of its generic metformin ER product. Decl. of C. Hogan, ¶ 8.

This process included, among other things, the creation of a launch team responsible for performing various functions, coordinating the purchase and installation of new manufacturing equipment, coordinating the purchase of raw materials and supplies, setting up various internal systems, preparing marketing and sales staff, the hiring of numerous manufacturing and packaging personnel, the scheduling of manufacturing capacity, and large-scale production and packaging of approximately 100 million meformin ER tablets, which commenced in July of 2003. Decl. of C. Hogan, ¶ 9.

Needless to say, this process was treated as a high priority and required an enormous effort on the part of dozens of IVAX personnel, as well as a tremendous expenditure of resources. The cost of preparing for the commercial launch of IVAX's metformin ER product was in excess of \$20 million. Decl. of C. Hogan, ¶ 10.

D. FDA's Grant Of Final Approval To IVAX And Award Of 180-Day Exclusivity

On October 28, 2003, FDA informed IVAX by facsimile that its ANDA for metformin ER had received final approval and that IVAX was eligible for 180 days of market exclusivity. AR at

Tab 12. The FDA's letter also directed IVAX to “begin commercial marketing of this drug product in a prompt manner.” *Id.*

In reaching its determination as to IVAX's entitlement to the 180-day exclusivity period, FDA adhered to several longstanding interpretations of the applicable statutory and regulatory provisions. First, consistent with the plain language of 21 U.S.C. § 355(j)(2)(B)(i) and its established practice of treating the receipt date of an original ANDA containing a Paragraph IV certification and the prescribed “will give notice” statement as the applicable priority date for exclusivity purposes, FDA properly determined that IVAX's ANDA was complete for exclusivity purposes as of November 26, 2002. AR at Tab 11. Second, following the rationale it had previously applied with respect to gabapentin, which was endorsed by Purepac itself in that case and approved by Judge Huvelle in *Torpharm, Inc. v. Thompson*, 260 F. Supp. 2d 69 (D.D.C. 2003), FDA regarded Purepac's ANDA amendment as incomplete for exclusivity purposes until the date on which it gave the statutorily-mandated notice to BMS; in this case, November 27, 2002. AR at Tab 11.

E. IVAX's Preparation For Launch Of Metformin ER

In accordance with FDA's directive that IVAX “begin commercial marketing of this drug product in a prompt manner,” AR at Tab 12, IVAX began the process of transporting its metformin ER product to customers the same day it received final approval. Decl. of C. Hogan, ¶ 12. During the first 24 hours, IVAX transported over 15 million metformin ER tablets (153,160 bottles, 100 tablets each) to certain commercial distributors and pharmacy chains, yielding a potential sales value of over \$6 million. *Id.* ¶ 13. In addition, by the afternoon of October 29, 2003, IVAX already had open customer orders for more than 640,000 additional bottles of its metformin ER product. *Id.* ¶ 14. The sales value of those anticipated shipments was over \$25 million. *Id.*

F. The October 29, 2003 TRO

On October 29, 2003, despite its admitted failure to comply with a clear statutory mandate, and using confidential information pertaining to IVAX's ANDA which it had obtained pursuant to a confidentiality agreement with IVAX,^{4/} Purepac invoked the equitable powers of this Court seeking a temporary restraining order compelling FDA to delay the effective date of IVAX's final approval for metformin ER and abstain from granting any other final approvals for metformin ER pending its challenge to IVAX's entitlement to the 180-day exclusivity period. After a brief hearing later that day, this Court granted the requested TRO, subject to a \$100,000 bond.

Once the TRO was issued, IVAX promptly ceased any shipment of its metformin ER product to commercial customers and began the laborious process of contacting those customers who had already received shipments to apprise them of the situation and instruct them not to sell any of the product received. Decl. of C. Hogan, ¶ 15. Many – if not most – customers reacted with expressions of anger and frustration with IVAX; however, all agreed to cooperate. *Id.* Specifically, with the exception of one customer who simply refused its shipments of IVAX metformin ER product, all customers agreed to quarantine any and all IVAX metformin ER product received until further notice. *Id.*

Eckerd's national Pharmacy Administration, for instance, circulated an email to all Eckerd Pharmacies stating that:

Your store has recently received Ivax's Metformin ER 500 mg Tablets. Since the shipment of this product under a FDA approved ANDA letter, a temporary restraining order on distribution has been

^{4/} Information about ANDA submissions, Paragraph IV submission dates, and notice dates is not publicly available at the time of final ANDA approval. In this instance, however, Purepac and IVAX had previously shared such information for limited purposes in the course of business negotiations conducted pursuant to a Confidentiality Agreement. *See* Decl. of M. Browder, ¶¶ 15-19.

placed on this ANDA. This legal action requires that the product is not released to patients until the legal challenge is resolved. Please place the product in your store's C-II cabinet to secure the product from dispensing. . . .

Decl. Of C. Hogan, ¶ 16 & Ex. 2.

G. The Status Of Purepac's ANDA

Although Purepac filed its original ANDA well before IVAX, Purepac has yet to receive even tentative approval.^{5/} In other words, it has yet to persuade FDA that its metformin ER formulation is safe, effective, and otherwise suitable to be released for human consumption. Thus, exclusivity considerations aside, it is unknown when – if ever – Purepac will be able to receive final marketing approval and market a generic product for the benefit of American consumers; raising the specter that the entire market for generic versions of Glucophage®XR could be blocked indefinitely. *See Purepac Pharm. Co. v. Friedman*, 162 F.3d 1201, 1205 (D.C. Cir. 1998).

IV. PUREPAC'S MOTION FOR PRELIMINARY INJUNCTION SHOULD BE DENIED

“A court considering a plaintiff's request for a preliminary injunction must examine whether: (1) there is a substantial likelihood plaintiff will succeed on the merits; (2) plaintiff will be irreparably injured if an injunction is not granted; (3) an injunction will substantially injure the other party; and (4) the public interest will be furthered by the injunction.” *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1317-18 (D.C. Cir. 1998); *Mylan Pharms., Inc. v. Shalala*, 81 F. Supp. 2d 30, 36 (D.D.C. 2000); *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212, 215 D.D.C. 1996); *Mead Johnson Pharm. Group v. Bowen*, 655 F. Supp. 53, 54 (D.D.C. 1986). “These factors interrelate on a sliding scale and must be balanced against each other.” *Serono Labs.*, 158 F.3d at 1318.

^{5/}According to FDA's website and public announcements by other companies, at least four other generic drug manufacturers have received tentative ANDA approval for metformin ER. *See* <http://www.fda.gov/cder/approval/index.htm>.

In this case, Purepac also “faces an additional hurdle because it seeks a mandatory injunction as opposed to a prohibitive injunction.” *Mylan Pharms.*, 81 F. Supp. 2d at 36. Namely, it bears an even heavier burden than the typical movant. *Id.* (“In this Circuit, ‘the power to issue a preliminary injunction, especially a mandatory one, should be sparingly exercised.’”) (quoting *Dorfman v. Boozer*, 414 F.2d 1168, 1173 (D.C. Cir. 1969)).

Here, these factors all weigh heavily toward denial of Purepac’s motion for preliminary injunction, as discussed in detail below.

A. Purepac Is Unlikely To Succeed On The Merits.

Purepac predicates its entitlement to exclusivity on the demonstrably incorrect proposition that the controlling date for determining “first to file” status is the date it filed a Paragraph IV amendment, even though Purepac's submission failed to comply with the statutory requirement that notice be given simultaneously with the amendment. Because Purepac’s amendment was legally incomplete and ineffective at the time it was filed, and did not satisfy the completeness requirements *until* Purepac complied with its statutory obligations to send simultaneous notice, FDA was correct in deciding that Purepac's priority date for purposes of entitlement to 180 days of marketing exclusivity was November 27, 2002, the day it belatedly complied with its statutory obligations. And because IVAX did comply with all of its statutory and regulatory obligations at the time its original ANDA was received by FDA on November 26, 2002, its application was legally complete under the controlling statutes and regulations, and FDA properly concluded that IVAX was entitled to that earlier priority date and, as a result, exclusivity.

1. APA Review

Under the Administrative Procedure Act (“APA”), a reviewing court may set aside agency action only if it is found to be arbitrary, capricious, an abuse of discretion, or otherwise not in

accordance with law. See 5 U.S.C. § 706. In other words, “there is a presumption in favor of the validity of administrative action.” *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212, 216 (D.D.C. 1996); *Ethicon, Inc. v. FDA*, 762 F. Supp. 382, 386 (D.D.C. 1991). And “the scope of review is ‘narrow.’” *Sentara-Hampton General Hosp. v. Sullivan*, 980 F.2d 749, 755 (D.C. Cir. 1992); *Bristol-Myers*, 923 F. Supp. at 216; *Ethicon, Inc. v. FDA*, 762 F. Supp. 382, 386 (D.D.C. 1991).

The analysis of the validity of an agency’s interpretation of a statute is governed by *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). As explained by the D.C. Circuit in *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1319 (D.C. Cir. 1998):

Under *Chevron*, we first ask “whether Congress has directly spoken to the precise question at issue,” in which case we “give effect to the unambiguously expressed intent of Congress.” . . . But if Congress has been silent or ambiguous about the meaning of the specific question at issue, we defer to the agency’s interpretation so long as it is “based on a permissible construction of the statute.”

Id.; *Mylan Pharms., Inc. v. Shalala*, 81 F. Supp. 2d 30, 37 (D.D.C. 2000).

In determining whether Congress has unambiguously expressed its intent, courts use “traditional tools of statutory construction.” *Serono Labs.*, 158 F.3d at 843; *Mylan Pharms.*, 81 F. Supp. 2d at 37 (“In ascertaining whether the plain language of the statute is dispositive, ‘the court must look to the particular statutory language at issue, as well as the language and design of the statute as a whole.’”) (quoting *K Mart Corp. v. Cartier*, 486 U.S. 281, 291 (1988)).

If *Chevron* “step two” is reached, courts then ask whether the agency employed a “permissible construction of the statute,” which has been construed to mean “a ‘reasonable’ one.” *Serono Labs.*, 158 F.3d at 843; *Mylan Pharms.*, 81 F. Supp. 2d at 37. In the context of this latter inquiry, the Supreme Court “ha[s] long recognized that considerable weight should be accorded to an executive department’s construction of a statutory scheme it is entrusted to administer.” *Chevron*,

467 U.S. at 844; *United States v. Rutherford*, 442 U.S. 544, 554 (1979) (“As this Court has often recognized, the construction of a statute by those charged with its administration is entitled to substantial deference.”) (involving FDA).

Similarly, where an agency’s interpretation of its own regulations is under review, the reviewing court must yield an even greater degree of deference. *Thomas Jefferson Univ. v. Shalala*, 623 U.S. 504, 512 (1994) (“We must give substantial deference to an agency’s interpretation of its own regulations.”); *Wyoming Outdoor Council v. United States Forest Serv.*, 165 F.3d 43, 52 (D.C. Cir. 1999) (“Our review in such cases is “more deferential . . . than that afforded under [*Chevron*].”) (quoting *National Med. Ctr. v. Shalala*, 43 F.3d 691, 697 (D.C. Cir.1995)). In the words of the Supreme Court:

Our task is not to decide which among several competing interpretations best serves the regulatory purpose. Rather, the agency’s interpretation must be given “controlling weight unless it is plainly erroneous or inconsistent with the regulation.” . . . In other words, we must defer to the Secretary’s interpretation unless an “alternative reading is compelled by the regulation’s plain language or by other indications of the Secretary’s intent at the time of the regulation’s promulgation.”

Thomas Jefferson, 623 U.S. at 512 (citations omitted); *Wyoming Outdoor Council*, 165 F.3d at 52 (“A court need not find that the agency’s construction is the only possible one, or even the one that the court would have adopted in the first instance. . . . So long as an agency’s interpretation of ambiguous regulatory language is reasonable, it should be given effect.”).

“This broad deference is all the more warranted when . . . the regulation concerns ‘a complex and highly technical regulatory program,’” *Thomas Jefferson*, 512 U.S. at 512 (citation omitted), such as the Hatch-Waxman Amendments. As the Federal Circuit stated last month in affirming a decision of this Court:

Deference is due to an administrative agency's regulations particularly when the subject matter of the regulatory authority is a "highly detailed" regulatory program to which the agency has brought its "specialized expertise," . . . a characterization that aptly describes the FDA's role in the context of the regulatory scheme created pursuant to the Hatch-Waxman Act.

Apotex, Inc. v. Thompson, ___ F.3d ___, 2003 WL 22427772, at *14 (Fed. Cir. Oct. 27, 2003).^{6/}

2. An ANDA Submission Containing A Paragraph IV Certification Must Be "Complete" Before It Is Assigned A Priority Date For Purposes Of Entitlement To Exclusivity

Purepac cites the exclusivity statute, 21 U.S.C. § 355(j)(5)(B)(iv), as if it exists in a vacuum, and ignores the long-established requirement that an ANDA submission containing a Paragraph IV certification must be "complete" before it can qualify for an award of exclusivity. For example, in the preamble to its 1989 proposed rule, FDA stated:

Although the [180-day exclusivity] provisions could be read to permit the mere submission of the first certification of invalidity or non-infringement to delay the effective date of subsequent ANDA's, regardless of the completeness of the application, the legislative history of the 1984 Amendments makes clear that such an interpretation would be inconsistent with the purposes of the patent certification and notification scheme.

54 Fed. Reg. 28,872, 28,895 (July 10, 1989). FDA's implementing regulation relating to exclusivity codifies this "completeness" requirement:

^{6/} In light of Purepac's recent argument to the D.C. Circuit in the *TorPharm* litigation that the FDA's letter decision with respect to gabapentin was "entitled to *Chevron* deference," Proof Brief of Purepac Pharmaceutical Co., filed in *TorPharm, Inc. v. Thompson*, Appeal Nos. 01-5410 & 03-5121 (Aug. 18, 2003), p. 21 (*See Decl. of M. Browder, Ex. 3*) its suggestion that FDA's letter decision in this case does "not warrant *Chevron*-style deference" because it is a mere "letter ruling" (Purepac Br. at 10) is disingenuous at best. Indeed, as the Federal Circuit recently recognized, *Chevron* deference is particularly appropriate in evaluating agency action pursuant to the Hatch-Waxman Amendments in light of the complexity and highly technical nature of the statutory and regulatory scheme, and the FDA's "specialized experience" in administering it. *Apotex*, 2003 WL 22427772, at *14.

If an abbreviated new drug application contains a [Paragraph IV certification] and the application is for a generic copy of the same listed drug for which one or more *substantially complete* abbreviated new drug applications were previously submitted containing a [Paragraph IV certification with respect to] the same patent..., approval of the subsequent abbreviated new drug application will be made effective no sooner than 180 days from whichever of the following dates is earlier: (i) The date the applicant submitting the first application first commences commercial marketing of its drug product; or (ii) The date of a decision of the court holding the relevant patent invalid, unenforceable, or not infringed.

21 C.F.R. 314.107(c)(1) (emphasis added).

In the next paragraph, the regulation goes on to amplify the “substantial completeness” requirement as follows:

For purposes of paragraph (c)(1) of this section, the “applicant submitting the first application” is the applicant that submits an application that is both *substantially complete and* contains a certification that the patent was invalid, unenforceable, or not infringed prior to the submission of any other application for the same listed drug that is both substantially complete and contains the same certification. A “substantially complete” application must contain the results of any required bioequivalence studies, or, if applicable, a request for a waiver of such studies.

21 C.F.R. 314.107(c)(2) (emphasis added).

Purepac badly misreads the last sentence of this regulation to mean that “there is *only one* requirement for an application to be ‘substantially complete’ under the regulation, and that is that it ‘contain the results of any required bioequivalent studies or, if applicable, a request for waiver of such studies.’” Purepac Br. at 12 (emphasis added). There is nothing in the language of the regulation that *limits* the requirement of completeness to the inclusion of such studies or a waiver. This conclusion is confirmed by 21 C.F.R. § 314.101(b) and (d), which address when an ANDA is deemed “sufficiently complete” for substantive review. Among other criteria, FDA may conclude an ANDA is “incomplete because it does not on its face contain information required under... [21

U.S.C. § 355(j)].” 21 C.F.R. § 314.101(d)(3). Section 355(j) sets forth *all* the requirements for an ANDA, including substantive content requirements in § 355(j)(2)(A) *and*, in the event of amendment of a pending ANDA to include a new Paragraph IV certification, the requirement for simultaneous notice in § 355(j)(2)(B)(iii).

Similarly, Purepac’s reliance on the last sentence of 21 U.S.C. § 355(j)(2)(A), which provides that “the Secretary may not require that an abbreviated application contain information in addition to that required by [the preceding] clauses (i) through (viii),” could hardly be more misplaced. According to Purepac, that sentence prohibits FDA from requiring compliance with the notice-giving requirements contained in § 355 (j)(2)(B)(i) - (ii) in determining whether an application or amended application is complete when filed, because such requirements are not contained in clauses (i) through (viii) of § 355(j)(2)(A). Purepac Br. at 14. If this were true, however, it would render the notice requirements contained in § 355 (j)(2)(B) – the very next subsection of the statute – absolutely meaningless and unenforceable, notwithstanding Congress’ explicit *command* in that subsection that an original ANDA filer “*shall include in the application* a statement that [it] will give notice” to the patent holder as required by § 355(j)(2)(B)(i). In other words, Purepac would have this Court read the statute to mean that FDA is powerless to require that an application “contain” something that Congress has mandated that the applicant “shall include in the application.”

Such a construction would put these two statutory provisions in direct conflict with each other, and is absurd on its face. *See Louisiana Pub. Serv. Comm’n v. Federal Communications Comm’n*, 476 U.S. 355, 370 (1986) (“In interpreting §§ 151 and 152(b), we are guided by the familiar rule of construction that, where possible, provisions of a statute should be read so as not to create a conflict.”); *Smith v. Babcock*, 19 F.3d 257, 263 (6th Cir. 1994) (“We are mindful of the principle that interpretations which yield internal inconsistencies or render some portion of the text

superfluous are to be avoided.”); *Gager v. Mobil Oil Corp.*, 547 F. Supp. 854, 862 (D. Conn. 1982) (“Separate parts of a statute should be reconciled wherever possible to avoid rendering any portion of the statute meaningless.”); *American Cyanamid Co. v. Ladd*, 225 F. Supp. 709, 711 (D.D.C. 1964) (“[D]ifferent sections of statutes should be read and interpreted to conform one with the other, rather than to make one the alpha and omega.”).

As explained below, FDA correctly concluded that because of the different notice-giving schemes mandated by Congress for original versus amended ANDA filers, IVAX’s original ANDA was complete when filed, and that Purepac’s amended ANDA was not.

(a) The Notice Requirements For Original ANDA Filers.

At the heart of Purepac’s attack on the legality of FDA’s actions is its refusal to acknowledge that *Congress* – not FDA – specifically chose to impose different notice-giving requirements upon original ANDA filers who submit Paragraph IV certifications, and those who amend existing applications to include a Paragraph IV certification.

For ANDA filers (like IVAX) who submit an original ANDA containing a Paragraph IV certification with respect to a listed patent, Congress made clear that such filers are *not* required to give notice to the patent holder at the time of filing, but only need include a “statement that [it] will give the notice” at some later date:

An applicant who makes a [paragraph IV certification] shall include in the application *a statement that the applicant will give the notice required by clause (ii) to - (I) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and (II) the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.*

21 U.S.C. § 355(j)(2)(B)(i)(emphasis added); *see also* 21 C.F.R. § 314.94 (“The [paragraph IV] certification shall be accompanied by a statement that the applicant *will comply* with the [notice] requirements”) (emphasis added).

FDA’s implementing regulation addressed to original filers like IVAX makes it clear that notice is not only *not* required at the time of the original filing in order for such filing to be deemed “complete,” but indeed that notice is not even *permitted* at the time of such filing:

The applicant *shall* send the notice required by paragraph (a) of this section *when it receives from FDA an acknowledgment letter* stating that its abbreviated new drug application is *sufficiently complete* to permit a substantive review.

21 C.F.R. § 314.95(b)(emphasis added).

This approach is consistent with the intent of Congress. As FDA explained in the preamble to its 1989 proposed rule to implement these provisions:

The statute and legislative history of Title I demonstrate that Congress did not intend incomplete application submissions to trigger legal action by a patent owner or approved application holder.

The agency therefore proposes that the notice be sent only upon submission of a “complete” application. An applicant must first submit an ANDA and certify in the application that it will provide the required notice to the patent owner or its representative and the pioneer application holder. After receipt of the application, the agency will determine if the application is acceptable for review.

54 Fed. Reg. at 28, 887.

(b) IVAX's ANDA Was “Complete” The Day It Was Filed

Because an original ANDA filer like IVAX is not required (nor even permitted) to give notice of its Paragraph IV certification at the time of filing under the statutory and regulatory scheme, but instead is only required to submit “a statement that [it] *will* give the notice” to the patent holder at a later date, 21 U.S.C. § 355(j)(2)(B)(i); 21 C.F.R. § 314.95(d), FDA logically and appropriately did

not look to the actual date that IVAX gave notice in determining whether its ANDA was “complete” as of the date it was received by FDA – November 26, 2002. As FDA explained in its 1989 rulemaking preamble:

FDA believes that to fulfill the purposes of the patent provisions of the statute, the *date of submission* of a previous application under [21 U.S.C. § 355(j)(5)(B)(iv)] must therefore be the date on which the previous applicant submitted a substantially complete ANDA, and thus *was in a position to notify* the patent owner.

54 Fed. Reg. at 28,895 (emphasis added).

It is undisputed on this record that when IVAX filed its original ANDA, the submission complied with all of the statutory and regulatory requirements imposed by § 355(j)(2)(A) and (B) and 21 C.F.R. § 314.94 (entitled “Content and Format of Abbreviated Applications”), including the requisite “statement that [it would give] notice” to the patent holder (BMS) at a later date. As a result, its application was complete for all relevant purposes on November 26, 2002 – the day it was received by FDA. Indeed, the “completeness” of its application as of that date was confirmed when it received from FDA the January 14, 2003 acknowledgment of completeness letter described in 21 C.F.R. § 314.95(b). As detailed below, in accordance with the different statutory provisions applicable to original ANDA filers, the actual giving of notice by IVAX was a *subsequent* requirement that needed to be undertaken only *after* the completeness of its application had *already* been established.

FDA’s implementing regulations make clear that the ultimate giving of notice for an original ANDA filer is irrelevant for purposes of whether the original ANDA was complete when filed. To reiterate, 21 C.F.R. § 314.94, entitled “Content and Format of an Abbreviated Application,” provides in relevant part that an original ANDA containing a Paragraph IV certification:

. . . shall be accompanied by a statement that the applicant will comply with the requirements under § 314.95(a) with respect to providing a notice to each owner of the patent or their representatives and to the holder of the approved application for the listed drug, and with the requirements under § 314.95(c) with respect to the content of the notice.

21 C.F.R. § 314.94(a)(12)(i)(A)(4).

Significantly, while the regulation requires that such “statement” promise compliance with the notice requirements contained in § 314.95(a) and (c), it conspicuously *omits* any reference to compliance with § 314.95(b). Subparagraph (b), of course, is the notice-related provision that governs the *timing* of when an original ANDA applicant, like IVAX, is required to give notice of its Paragraph IV certification to the patent holder, and upon which Purepac premises its “IVAX didn't comply either so why are we the only ones being punished?” argument. In making this argument, Purepac simply ignores that FDA, consistent with the timing of notice distinctions drawn by Congress for original versus amended ANDA filers, specifically chose *not* to include the timing requirement in § 314.95(b) as one of the conditions for which original ANDA filers had to provide assurances of compliance *at the time of the filing* of an original ANDA. As such, there is direct textual support in both the statute *and* the regulations that the timing of when an original ANDA holder actually gives notice to the patent holder is *irrelevant* to whether the original application was complete when it was filed. As a result, under any level of *Chevron* analysis, the FDA's decision to treat IVAX's ANDA as complete when filed cannot be considered arbitrary, capricious, an abuse of discretion or contrary to law.

(c) **The Notice Requirements For Amended ANDA Filers**

By contrast, Congress clearly imposed a different notice-giving requirement upon an amended ANDA filer (like Purepac) who amends a pending application to include a Paragraph IV certification:

If an application is amended to include a [paragraph IV certification], the notice required by clause (ii) *shall be given when the amended application is submitted.*

21 U.S.C. § 355(j)(2)(B)(iii) (emphasis added). FDA's implementing regulations track this simultaneous notice requirement for amended ANDA filers:

If an abbreviated application is amended to include [a paragraph IV certification], the applicant *shall* send the notice required by paragraph (a) of this section *at the same time that the amendment to the abbreviated application is submitted to FDA.*

21 C.F.R. § 314.95(d) (emphasis added).

Obviously, Congress's statutory command that an amended ANDA filer give simultaneous notice to the patent holder at the time of filing is mandatory and unambiguous. The non-discretionary nature of this obligation is equally clear from the face of the regulation, and is supported by sound policy considerations. One purpose of the Hatch-Waxman Amendments to the FDCA was "to get generic drugs into the hands of patients at reasonable prices – fast." *In re: Barr Laboratories, Inc.*, 930 F.2d 72, 76 (D.C. Cir. 1991). In the case of a pending ANDA, a newly issued patent can be listed in the Orange Book very close to the time that the ANDA would otherwise be eligible for final approval and the start of commercial marketing. If the ANDA sponsor concludes that it is entitled to begin marketing before expiration of the newly issued patent because the patent is invalid or will not be infringed, it must amend its ANDA with a Paragraph IV certification to the newly issued patent and give notice to the NDA sponsor and patent holder. The patent holder has a 45-day window to file a patent infringement action; the 45-day window begins

on the day notice of the Paragraph IV certification is received. 21 U.S.C. § 355(j)(5)(B)(iii). If no suit is brought, the ANDA may be eligible for final approval after expiration of the 45-day period.
Id.

Thus, in the interest of speeding the availability of generic drugs to the public, there are sound public policy and public health reasons to *require* sponsors of pending ANDAs to give notice at the same time the ANDA is amended to include the Paragraph IV certification. This approach helps ensure that generic drugs will be approved and marketed as quickly as possible. In comparison, a newly submitted original ANDA must first be acknowledged as sufficiently complete by the FDA so as to not trigger unnecessary legal action by the patent holder. There is no such intervening event applicable or necessary for an amended ANDA filer.

In any event, because the statutory command to an amended ANDA filer is clear and unambiguous, it obviously must be enforced by the courts and the agency as written. *See, e.g., Kokechick Fisherman's Ass'n v. Secretary of Commerce*, 839 F.2d 795, 802 (D.C. Cir. 1988) (recognizing that an agency may not adopt an interpretation that "clearly has the effect of avoiding the stricture of the [applicable statute] and congressional intent").

(d) Purepac's Amended Filing Was Incomplete And Ineffective Until The Day Purepac Complied With Its Statutory Notice Obligation

In this case, on this record, Purepac does not and cannot dispute that it did not comply with the statutory requirement that mandated, *at the time of filing of its amendment*, that notice had to be given to the patent holder simultaneously. As a result of that failure, as explained below, it was entirely appropriate for FDA to treat Purepac's ANDA as incomplete at the time of filing for purposes of any entitlement to exclusivity, and to conclude that its effective date of filing did not occur until it complied with its concomitant statutory obligation to send notice.

Although Purepac is understandably reluctant to acknowledge it, this was precisely Judge Huvelle's conclusion in *TorPharm, Inc. v. Thompson*, 260 F. Supp. 2d 69, 78-81 (D.D.C. 2003). In that case, on indistinguishable facts, Judge Huvelle found that it was well within the Agency's lawful authority to conclude, for purposes of determining "first filer" entitlement to exclusivity in the context of an amended ANDA filing, that it was the date that the amended filer complied with its statutory notice obligations, *not* the date of the amended filing itself, that controlled for purposes of determining entitlement to exclusivity:

Here, the FDA has exercised that discretion reasonably. In its Decision Letter, the agency determined that where a certification is submitted without simultaneous notice, *that certification does not become effective for exclusivity purposes until the notice is actually sent*. In other words, where notice is provided after the certification is received, the agency's policy constructively moves the certification's "submission" date to the day on which the applicant mailed the notice.

Id. at 80 (emphasis added). As Judge Huvelle further explained, in those circumstances where an amended ANDA filer like Purepac fails to give simultaneous notice, it was entirely appropriate for the FDA to respond to "an applicant's failure to furnish simultaneous notice by refusing to make its solitary certification effective upon receipt by the Agency. *Those who heed the notice provision reap the benefit of instant acceptance; those who do not, do not.*" *Id.* (emphasis added).^{2/}

Ironically, the amended filer who failed to timely comply with its simultaneous notice obligations in *TorPharm* was none other than Purepac. However, because of the factual circumstances of that case, FDA's conclusion to toll the effective date of Purepac's amended

^{2/}In reaching this conclusion, Judge Huvelle clearly recognized the different notice-giving requirements applicable to original versus amended ANDA filers at the time of filing. *See TorPharm*, 260 F. Supp. 2d at 69 (comparing different notice-giving requirements applicable to original and amended ANDA filers created pursuant to clauses (i) and (iii) of 21 U.S.C. § 355(j)(2)(B)).

Paragraph IV certification nevertheless resulted in FDA awarding exclusivity to Purepac.^{8/} It is not surprising, therefore, that Purepac's briefing to Judge Huvelle in that case contains arguments such as:

- “Under a second-step *Chevron* analysis, FDA's January 28 Decision must be upheld, because its determination was based on a reasonable interpretation of the statute.”
- “FDA's decision was a permissible construction of the Exclusivity Statute and the Notice Statute.”
- “[U]nder its ‘*completeness*’ approach, FDA correctly determined that Purepac was the ANDA applicant eligible for exclusivity.” (emphasis added)
- “FDA's interpretation of its own regulation, 21 C.F.R. section 314.95(d), is entitled to ‘substantial deference.’”
- “It was proper for FDA to determine that Purepac had complied with both the certification and notice requirements *as of the date that it sent notice* to Warner-Lambert” (emphasis added)

See Purepac's Memorandum in Opposition to TorPharm's Motion for Preliminary Injunction in *TorPharm, Inc. v. Tommy G. Thompson*, Civil Action No. 03-254 (ESH) (D.D.C.) (Mar. 5, 2003), at pp. 17-18, 21-22 (*see* Decl. of M. Browder, Ex. 2).

It is also not surprising that, in the appellate brief it filed with the D.C. Circuit urging *affirmance* of Judge Huvelle's decision, Purepac has advanced the following arguments:

- “Exercising its discretion, FDA refused to recognize Purepac's certification *until it sent notice*.” (emphasis added).
- “In *TorPharm*, the district court correctly ruled that Purepac is eligible for 180-day exclusivity on the ‘482 patent because Purepac both certified against it and sent

^{8/}In disobedience of the statutory requirement for sending notice at the time the Paragraph IV ANDA amendment is sent to FDA, Purepac (like in this case) waited over two weeks before sending notice to the patent holder in that case. Nevertheless, the *TorPharm* court found that Purepac's priority date (the date on which it belatedly sent notice and *not* the date of its amendment) was still earlier than the date on which the other ANDA sponsor had amended its ANDA and gave notice, as required by § 355(j)(2)(B)(iii). On this basis, the *Torpharm* court upheld FDA's decision to award Purepac 180-day exclusivity.

notice before anyone else. The court rightly recognized that Hatch-Waxman specifies no penalty for delayed notice and *gave suitable deference to FDA's delayed recognition* of Purepac's certification." (emphasis added)

- "Accurately observing that Hatch-Waxman does not address the precise question at issue – *an appropriate penalty for delayed notice* – the district court correctly concluded that 'the agency had considerable flexibility' in deciding an appropriate consequence." (emphasis added)
- "The district court soundly determined that FDA reasonably exercised its discretion in *delaying the effective date* of Purepac's paragraph IV certification." (emphasis added)
- "In light of statutory silence, FDA's decision to credit Purepac's paragraph IV certification as complete for exclusivity purposes upon satisfaction of *both* conditions was a reasonable interpretation of the statute entitled to *Chevron* deference." (emphasis added)

See Purepac's Brief, Appeal Nos. 02-5410, 03-0254 (D.C. Cir.) (Aug. 18, 2003), at pp. 1-2, 20-21 (*see* Decl. of M. Browder, Ex. 3).

What *is* surprising is that Purepac is simultaneously advancing to *this* Court precisely the opposite argument, namely that FDA's determination of the effective date of Purepac's non-complying ANDA amendment in the exact same way it did in the *TorPharm* action is arbitrary, capricious and unlawful. While "[c]ourts do not relish the prospect that an adept litigant may succeed in proving a proposition in one action, and then succeed in proving the opposite in a second," 18B C. Wright & A. Miller, *Federal Practice & Procedure* § 4477 (2003), what is truly remarkable is that Purepac takes these irreconcilably inconsistent positions in the context of a case where it is complaining of supposedly inconsistent treatment by FDA. Apparently, Purepac believes that the determinative factor in deciding the legality of FDA's actions is whether the Agency's decision is helpful or harmful to Purepac in any particular situation. We submit that the Court should apply a less arbitrary and capricious standard – one that is not only consistent with Judge Huvelle's decision, but is more faithful to the unambiguous commands of the statute and regulations.

It is also ironic that Purepac complains that FDA supposedly imposed an additional requirement upon Purepac to obtain exclusivity that, it says, is not contemplated by statute (in fact, it is not just contemplated, but *mandated* by statute) when it is *Purepac* that attempts in its brief to impose upon *IVAX* an additional condition of “completeness” that is contrary to the notice-giving scheme created by Congress and FDA for original ANDA filers. In that regard, Purepac’s reliance on *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060 (D.C. Cir 1998) is, if nothing else, puzzling. If *Mova* stands for anything, it is that it would be improper to impose the additional “completeness” requirement that Purepac wishes to impose upon an original filer like *IVAX* when Congress specifically chose to *exempt* such a filer from that requirement at the time of filing.

Similarly, while Purepac urges this Court to treat this as an equal protection case by arguing, in essence, that “*IVAX*’s notice was given later than ours” and “if we are to be punished for late notice, so should they,” this tit-for-tat argument can only be advanced by ignoring *Congress*’ decision to require Purepac to give notice immediately, and to not require *IVAX* to give notice until *after* its application was *already* complete. Because it was *Congress* who chose to impose different requirements upon amended ANDA filers, Purepac’s exhortations that “FDA appears to have created two separate exclusivity tracks, one for new ANDAs and a second, more arduous track for amended ANDA filers,” Purepac Br. at 19, simply miss the mark. Indeed, given that Purepac was so focused on trying to be the first in line that it filed amendments to its ANDA *every day* over a 20-day period, it is difficult to understand why it would have been so “arduous” for Purepac to simply send the notice that Congress commanded it to simultaneously send – *just once* – during that 20-day span.

At best, therefore, Purepac’s wounds are self-inflicted, and it should not be heard to complain that FDA’s actions were unlawful because of its own inexplicable failure to comply with the statute.

Again, as Judge Huvelle aptly put it, “[t]hose who heed the notice provision reap the benefit of instant acceptance, those who do not, do not.” *TorPharm*, 260 F. Supp. 2d at 80.

B. Purepac Has Failed to Establish Immediate Or Non-Speculative Harm

In this Circuit, “[i]rreparability of injury is,” without question, “a very high standard.” *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212, 220 (D.D.C. 1996) (quoting *American Coastal Line Joint Venture, Inc. v. United States Lines, Inc.*, 580 F. Supp. 932, 936 (D.D.C. 1983)).

First, the alleged injury “must be both certain and great; it must be actual and not theoretical.” *Wisconsin Gas Co. v. Federal Energy Regulatory Comm’n*, 758 F.2d 669, 674 (D.C. Cir. 1985); *Leboeuf, Lamb, Greene & Macrae, LLP v. Abraham*, 180 F. Supp. 2d 65, 72 (D.D.C. 2001). Of equal importance, the alleged injury must be either ongoing or imminent. In the words of the D.C. Circuit:

Injunctive relief “will not be granted against something merely *feared* as liable to occur at some indefinite time,” . . . the party seeking injunctive relief must show that “[t]he injury complained of [is] of *such imminence* that there is a ‘clear and present’ need for equitable relief to prevent irreparable harm.”

Wisconsin Gas, 758 F.2d at 674 (citations omitted) (both alterations in original) (emphasis added); *Mead Johnson Pharm. Group v. Bowen*, 655 F. Supp. 53, 56 (D.D.C. 1986) (“Plaintiff has not demonstrated the existence of *imminent* irreparable injury.”), *aff’d*, 838 F.2d 1332 (D.C. Cir. 1988).

Moreover, “[i]mplicit in each of these principles is the further requirement that the movant substantiate the claim that irreparable injury is ‘likely’ to occur.” *Wisconsin Gas*, 758 F.2d at 674.

Bare allegations of what is likely to occur are of no value since the court must decide whether the harm *will in fact occur*. The movant must provide *proof* that the harm has occurred in the past and is likely to occur again, or proof indicating that harm is *certain* to occur in the *near future*.

Id. (emphasis added).

Applying these principles, Purepac's claim of irreparable harm cannot withstand scrutiny. Indeed, it fails in its premise. Although Purepac's filed its ANDA before IVAX (a fact it is fond of trumpeting), for reasons Purepac has not chosen to share with the Court it has yet to receive even *tentative* approval (a crucial fact nowhere even *mentioned* in its brief). In other words, it has yet to persuade FDA that its metformin ER product is safe, effective, and otherwise suitable to be released for human consumption.^{2/} Thus, even if this Court were to grant the requested injunctive relief, Purepac would still be unable to sell the drug to the public.

Because there is no guarantee Purepac's ANDA will *ever* receive such approval from FDA, Purepac's claimed irreparable injury – the “loss” of exclusivity – is far from certain or imminent. To the contrary, as it is unclear whether Purepac will ever be in a position to experience the effects of an alleged loss of exclusivity, its claim of injury is based entirely upon speculation.

C. The Balance Of Hardships Tips Strongly In IVAX's Direction

In stark contrast to the foregoing, it needs hardly be said that extending the TRO-imposed suspension of IVAX's metformin ER final approval for an additional undefined period of time would have serious adverse effects on IVAX in a number of different ways.

First of all, IVAX would lose much if not all of the huge investment it made in the preparation for the October 2003 launch of its metformin ER product. As indicated above, that cost was in excess of \$20 million. Decl. of C. Hogan, ¶¶ 14, 18.

In addition, IVAX would likely be forced to recall all IVAX metformin ER product in the possession of its customers. Decl. of C. Hogan, ¶ 19. The financial cost alone of the recall would likely be in excess of \$200,000. *Id.*

^{2/} Meanwhile, according to FDA's website, in addition to IVAX's final ANDA approval, Andrx Corporation, Barr Laboratories, Geneva Pharmaceuticals, Ranbaxy Pharmaceuticals, and Teva Pharmaceuticals Industries have all received tentative ANDA approval for metformin ER.

IVAX would also likely lose the ability to sell the approximately 130 million metformin ER tablets it has manufactured to date, which have a sales value of approximately \$52 million. Decl. of C. Hogan, ¶ 20. Although the shelf life of metformin ER is twenty-four (24) months, most of IVAX's customers typically expect product with greater than twelve (12) months of shelf life remaining, leaving less than twelve (12) months to get the product to the customer. In this instance, however, commercial production having commenced in July of 2003, much of IVAX's metformin ER product is already several months old; and, if the requested injunction is entered, there is no telling when IVAX would again be able to offer the product for sale. Thus, if the requested injunction is entered, it is unlikely that IVAX would ever be able to sell any recalled or current metformin ER inventory, in which case it would be required to destroy it at significant expense. *Id.*

IVAX would also lose the ability to make what is expected to be an enormous amount of metformin ER sales during the 180-day market exclusivity period. Decl. of C. Hogan, ¶ 21. The principal value of the exclusivity period is the ability to sell a generic product either without any generic competition, or with only minimal generic competition in the event that the NDA holder decides to license its branded product for "generic" distribution. Based on IVAX's substantial experience in the introduction and marketing of brand-equivalent drugs, and its projections regarding estimated sales and profits on metformin ER during the 180-day exclusivity period, IVAX estimates that its metformin ER sales during the exclusivity period would likely be: (i) in the range of \$100 million, with a profit of \$80 million, assuming no entry of a licensed branded "generic" product; and (ii) in the range of \$70 million, with a profit of \$50 million, if a licensed branded "generic" product was launched early on during the exclusivity period. If the requested injunction is entered, IVAX will at the very least lose the time value of these expected profits, and could lose the profits

themselves if during the suspension of its final approval a licensed branded "generic" product were launched. *Id.*

IVAX would relatedly lose the benefit of an even larger metformin ER market share beyond the 180-day market exclusivity period. Decl. of C. Hogan, ¶ 22. Because the manufacturer of an exclusive generic drug has the opportunity to establish valuable and lasting customer relationships and product placements, often manifesting in long-term contracts, it generally establishes a market dominance that is difficult for subsequent entrants to overcome. In other words, the manufacturer of an exclusive generic drug typically maintains a significantly larger market share than other generic competitors after the conclusion of the exclusivity period. Thus, if IVAX was deprived of its approval and exclusivity period, it would not only lose metformin ER sales during that period, but beyond that period as well. *Id.*

IVAX would also lose incremental sales of other non-metformin ER products which would likely be facilitated by the 180-day market exclusivity period. Decl. of C. Hogan, ¶ 23. As a general matter, it is a common practice in the industry for generic drug manufacturers to offer "bundled" product offerings, in which the manufacturer and purchasers negotiate purchasing terms for multiple products in the same offering. The "bundled" products are then sold to the purchaser at the agreed-upon price for the term of the agreement, often a period of multiple years. A manufacturer with an exclusive product, therefore, has the unique ability to offer a "bundle" featuring a generic product which no other company can sell, and to obtain a commitment by the customer to purchase not only the exclusive product but others as well, for a term extending well beyond the exclusivity period. In fact, prior to the October 29, 2003 TRO, IVAX had already offered such a program to customers. *Id.*

Finally, IVAX's reputation and goodwill among customers would also be injured. For not only would IVAX be deprived of the prestige of the 180-day market exclusivity period and suffer the stigma of having a suspended final approval, customers will undoubtedly react with additional – and likely enhanced – anger and frustration at the prospect of having to continue enduring BMS's monopoly pricing, when a lower-cost generic metformin ER product was so recently within their grasp. Decl. of C. Hogan, ¶ 24.

D. An Injunction Would Be Inimical To The Public Interest

Similarly, it cannot seriously be disputed that the public interest will be served by denying the preliminary injunction Purepac seeks, and harmed if an injunction is entered. “The purpose of the Hatch-Waxman Amendments was, after all, ‘to increase competition in the drug industry by facilitating the approval of generic copies of drugs.’” *Serono Labs.*, 158 F.3d at 1326 (quoting *Mead Johnson Pharm. Group v. Bowen*, 838 F.2d 1332, 1333 (D.C. Cir. 1988)); *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212 (D.D.C. 1996) (“The Hatch-Waxman Amendments . . . aimed to increase competition in the drug industry by creating an administrative regime pursuant to which the approval of generic drugs would be facilitated.”); *In Re Barr Labs.*, 930 F.2d 72, 76 (D.C.Cir. 1991) (“Congress sought to get generic drugs into the hands of patients at reasonable prices – fast.”). And “the public interest [favors] receiving generic competition to brand-name drugs as soon as is possible.” *Boehringer Ingelheim Corporation v. Shalala*, 993 F.Supp. 1, 2-3 (D.D.C. 1997).

Here, the *only* obstacle keeping IVAX from marketing its generic metformin ER tablets is this Court's October 29, 2003 TRO. If this Court denies Purepac's motion for a preliminary injunction and the TRO is dissolved, IVAX is poised to make its product available to retail pharmacies, and ultimately diabetes patents, immediately.

Indeed, as indicated above, substantial quantities of IVAX's metformin ER product were transported to commercial distributors and pharmacy chains upon IVAX's receipt of final ANDA approval, but (as a result of this Court's TRO) were quarantined before the product was dispensed to patients. Decl. of C. Hogan, ¶¶ 13, 15. This product could be released within hours of a decision by this Court denying Purepac's motion for a preliminary injunction.

By contrast, Purepac has not received even tentative approval, which means that it has yet to satisfy all substantive requirements for ANDA approval. If this Court were to conclude that Purepac is entitled to the relief it seeks – an injunction to prevent FDA from issuing final approval to IVAX or any other ANDA sponsor – it is unknown when, *or even if*, American consumers would ever have access to generic metformin ER. Simply stated, Purepac might never receive final ANDA approval, thereby blocking the entire generic market until the '521 patent expires in March 2018.

The economic effect of an injunction on diabetes patients would be – putting it, charitably – very substantial. During the first six months of 2003, BMS's sales of Glucophage[®] XR were approximately \$237 million. Decl. of C. Hogan, ¶ 7. Without generic competition, BMS will be able to continue charging monopoly prices, much to the detriment of American consumers, third party payors, and government insurance programs like Medicaid.

If IVAX's marketing approval and exclusivity are restored, however, IVAX expects that, during the 180-day exclusivity period, it will be able to capture 80% of the total market for the drug, selling at an average price of 60% to 75% of the brand price, assuming no entry of a licensed branded "generic" product. Decl. of C. Hogan, ¶ 26. The resultant savings to purchasers during the 180-day exclusivity period in that scenario would be \$47 to \$75 million. *Id.*^{10/}

^{10/} If a licensed branded "generic" product was launched during the exclusivity period, the savings to purchasers would be even greater. *Id.*

Likewise, assuming the entry of additional generic competitors after the expiration of the 180-day exclusivity period, it can be expected that generic penetration of the market would reach 90%, with an average selling price of approximately 10% to 15% of the brand price, resulting in enormous savings to consumers in the magnitude of approximately \$180-\$190 million. Decl. of C. Hogan, ¶ 27.

Finally, Purepac's contention that “[a]bsent a preliminary injunction, patients and pharmacies would be forced to bear the brunt of FDA's improper award to IVAX if Purepac ultimately prevails . . . because pharmaceutical products are required to have unique physical appearances . . . and retailers would be forced to expend resources educating patients about the new pill,” Purepac Br. at 32-33, rings hollow. Suffice it to say, theoretical, speculative concerns about the possibility of consumer confusion in the event of a switch are no reasons to delay the entry of generic competition, particularly in light of Congress' expressed intent otherwise. Indeed, even if Purepac's contention about a “requirement” for unique physical appearances were correct (which it is not), the “burden” would be no greater than in switching from Glucophage® XR to a generic product.

In sum, if Purepac prevails, BMS's monopoly will continue and generic competition may be delayed indefinitely, as the 180-day exclusivity period does not begin to run until the first filer commercially launches its product. At a minimum, BMS's monopoly will continue until Purepac meets FDA approval requirements. Viewed against the prospect of IVAX commencing commercial marketing immediately, followed by at least several other generic firms 180 days later, it needs hardly be said that the requested injunction would be contrary to the public interest.

V. PUREPAC IS NOT ENTITLED TO ANY EQUITABLE RELIEF BECAUSE IT COMES BEFORE THIS COURT WITH UNCLEAN HANDS

Apart from the foregoing, Purepac's motion should also be denied because it has unclean hands. Courts have long held that a party seeking relief in equity must come to court with clean

hands. See, e.g., *Clarke v. White*, 37 U.S. 178, 193 (1838); *Keystone Driller Co. v. General Excavator Co.*, 290 U.S. 240, 244 (1933). The doctrine of unclean hands “closes the door of a court of equity to one tainted with inequitableness or bad faith relative to the matter in which he seeks relief. . . .” *Precision Instrument Mfg. Co. v. Auto. Maintenance Mach. Co.*, 324 U. S. 806, 814 (1945) (denying company’s relief due to perjury). The fundamental principle is that “one seeking equity must do equity and must show ‘clean hands’ at the threshold.” *Udall v. Littell*, 366 F.2d 668, 675 (D.C. Cir. 1966).

In order to apply the doctrine of unclean hands, the act of bad faith in question must have an “immediate and necessary relation to the equity that he seeks in respect of the matter in litigation.” *Keystone Driller Co.*, 290 U.S. at 245. In this case, Purepac’s unconscionable conduct is directly related to the matter at issue here. Specifically, as set out more fully in the attached Declaration of Monte Browder, Purepac gained knowledge of the facts it has used to support the filing of this lawsuit only as a result of confidential business discussions with IVAX, and is using this information in breach of its confidentiality agreement with IVAX. Declaration of M. Browder, ¶¶ 15-19 ^{11/}

Granting Purepac’s request for a preliminary injunction would be tantamount to sanctioning its unconscionable breach of confidentiality, which has an immediate and necessary relation to the equitable relief requested by Purepac. Thus, the doctrine of unclean hands should keep Purepac from obtaining the equitable relief it seeks.

^{11/}Although one of the documents disclosed by IVAX to Purepac under the confidentiality agreement now appears in FDA’s administrative record in this case, under ordinary circumstances the document would not have been publicly available so quickly, and certainly not just one day after ANDA approval See Decl. of M. Browder, ¶ 18.

VI. CONCLUSION

For the foregoing reasons, Purepac's motion for preliminary injunction should be denied in its entirety.

November 8, 2003.

Respectfully submitted,

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