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DOCKET NO. 2004P-0227
COMMENTS OF TEVA PHARMACEUTICAL INDUSTRIES LTD.
AND PUREPAC PHARMACEUTICAL CO.

These comments are respectfully submitted on behalf of Teva Pharmaceutical Industries Ltd. ("Teva") and Purepac Pharmaceutical Co. ("Purepac") in opposition to the May 11, 2004 Citizen Petition filed on behalf of Pfizer Inc. ("Pfizer"), in which Pfizer requests that FDA abandon its long-established and well-founded policy of permitting Abbreviated New Drug Application ("ANDA") sponsors to "selectively waive" or fully relinquish their rights under the statutory 180-day generic exclusivity period. 21 U.S.C. § 355(j)(5)(B)(iv). More specifically, Pfizer asks FDA to refuse to issue final approval of Teva's gabapentin ANDA even if Purepac, which holds the 180-day exclusivity rights for generic gabapentin, waives its exclusivity rights as to Teva. As demonstrated herein FDA's waiver policy:

- Reflects a reasonable interpretation of the statutory exclusivity provision that furthers the purposes and intent of the statutory scheme;
- Has been applied consistently for at least seven years;
- Has been examined and accepted by the courts; and
- Is necessary to avoid absurd results that would be contrary to the statutory purpose.

Moreover, Pfizer's Petition fails to provide any logical or legally persuasive basis to require a change in FDA's waiver policy, and is in fact just the latest in a series of bad-faith tactics to prolong its competitive stranglehold on the gabapentin market. Accordingly, the Petition should be denied expeditiously in order to remove any doubt that FDA's exclusivity waiver policy is, and remains valid, and that there is no barrier to approval of Teva's gabapentin ANDA under any waiver that may be granted by Purepac.[1]

[1] It should be noted that on June 3, 2004, the U.S. District Court for the District of Columbia (Huvelle, J.), in an oral ruling from the bench, granted summary judgment in favor of Purepac and FDA, upholding Purepac's previously established right to the 180-day exclusivity period for generic gabapentin drug products. *Apotex, Inc. v. FDA*, No. 1:04-CV-00605 (D.D.C. filed Apr. 14, 2004) (ESH).

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I. FDA'S LONGSTANDING POLICY ALLOWING WAIVER OR RELINQUISHMENT OF 180-DAY EXCLUSIVITY IS PERMISSIBLE AND MUST BE MAINTAINED

Pfizer argues that the statutory 180-day exclusivity provisions are unambiguous and that they prohibit the waiver or relinquishment of the exclusivity rights by first Paragraph IV ANDA applicants. Pfizer is wrong. As discussed in more detail *infra*, the exclusivity provisions are simply silent on the issue of waivers, *see Boehringer Ingelheim v. Shalala*, 993 F. Supp. 1 (D.D.C. 1997), and in light of this statutory silence, FDA has properly and appropriately developed a policy that effectuates the underlying statutory purpose by filling a "gap" in the exclusivity scheme. FDA's policy is entitled to judicial deference, and indeed must be maintained in order to avoid unintended anticompetitive results.

A. FDA And The Courts Have Long Recognized That The 180-Day Exclusivity Provision Confers Valuable Rights And Benefits Which Can Lawfully Be Waived

The statutory 180-day generic exclusivity period was established under the Hatch-Waxman amendments as a crucial mechanism to encourage generic drug applicants to file Paragraph IV ANDAs challenging the validity or applicability of patents purporting to claim approved brand name drug products. The underlying purpose of the exclusivity incentive is to expedite and maximize the sale of lower priced generic versions of branded drugs. It is clear from the overall structure and purposes of the Hatch-Waxman amendments that the Congressional intent was in fact to create a right and benefit -- specifically a right to market "protection" in the form of exclusivity -- to generic companies who are first to file a Paragraph IV ANDA for a generic version of any particular drug. As one court has noted:

> As an incentive to the first generic maker to expose himself to the risk of costly patent litigation, the Hatch-Waxman regime provides that the first to file a Paragraph IV certified ANDA ("the first filer") is eligible for a 180-day period of marketing <u>protection</u>, commonly known as the 180-day exclusivity period ("the Exclusivity Incentive"). By its terms, the Exclusivity Incentive affords the first filer <u>protection from competition</u> from subsequent generic makers for 180 days beginning from the earlier of a commercial marketing or court decision.

Mylan Pharms., Inc. v. Henney, 94 F. Supp. 2d 36, 40 (D.D.C. 2000) (internal citations omitted) (emphasis added).

The courts and FDA have long recognized the right-conferring intent of the 180-day exclusivity provision. *See Mylan Pharms., Inc. v. Shalala*, 81 F. Supp. 2d 30, 33 (D.D.C. 2000) ("[T]he Hatch-Waxman Amendments provide an added incentive for generic drug producers to file Paragraph IV certifications ... 180-day period of <u>exclusive marketing rights</u> for a generic version of the drug claimed by that patent.") (emphasis added); *see also* 54 Fed. Reg. 28872, 28895 (July 10, 1989) ("The purpose of section 505(j)([5])(B)(iv) of the act is to <u>reward</u> the first

applicant to test the scope or validity of a patent...."). The intended nature of the 180-day exclusivity period as a right to market protection is consistent with the nature of the statutory NDA-based exclusivities as rights to market protection for qualifying NDA sponsors. *Id.* at 28896 ("Sections 505(j)([5])(D) and 505(c)(3)(D) of the act partially protect certain listed drugs, or certain changes in listed drugs, from competition in the marketplace for specified periods by placing a moratorium on the submission of, or by delaying the effective approval of, ANDAs...") (emphasis added).

In recognition that section 505(j)(5)(B)(iv) is a right-conferring provision, both FDA and the courts have consistently permitted the beneficiaries of the 180-day exclusivity right to waive all or part of the protective rights granted by Congress. Since 1997 FDA has applied an exclusivity waiver policy whereby a first applicant may either (1) "selectively waive" its exclusivity with respect to one or more selected subsequent applicants, allowing FDA to approve those applicants' ANDAs during the first applicant's 180-day exclusivity period, or (2) relinquish its exclusivity "as to the world," thereby allowing FDA to grant final approval to any and all subsequent Paragraph IV ANDAs that are otherwise eligible for final approval. 64 Fed. Reg. 151, 42873 (Aug. 6, 1999)[2]. In order to selectively waive exclusivity, FDA requires the exclusivity period to have been triggered (by either the first applicant's commercial marketing of the drug, or by a triggering court decision, 21 U.S.C. § 355(j)(5)(B)(iv))[3]. Relinquishment can be effected regardless of whether the exclusivity period has been triggered. *Id.* In both circumstances, the waiver or relinquishment of exclusivity serves the important statutory purpose of expediting generic competition. In contrast, under the reasoning of Pfizer's Petition, neither waiver nor relinquishment would be available, and the core purposes of Hatch-Waxman would be seriously undermined.

1. FDA Permits The First Exclusivity Waiver For Ranitidine And That Decision Is Upheld By The Courts

The first example of a 180-day exclusivity waiver occurred in 1997 when Beohringer Ingelheim, a non-first Paragraph IV ANDA applicant, obtained a final court decision that its generic ranitidine drug product did not infringe the Orange Book listed patents for the branded drug Zantac® (ranitidine). *See Granutec v. Shalala*, 139 F.3d 889, 1998 U.S. App. LEXIS 6685 (Apr. 3, 1998), *14. That court decision started the running of the 180-day exclusivity period of the first Paragraph IV ranitidine applicant, Genpharm, but Genpharm was unable to utilize its 180-day exclusivity period due to an unexpired 30-month approval stay. Because Genpharm would not be able to enjoy its statutory market protection rights by selling its own product during the 180-day exclusivity period (because it was not yet eligible for approval),

[2] This proposed rule was subsequently withdrawn for reasons unrelated to FDA's exclusivity waiver policy, *see* 67 Fed. Reg. 212, 66593 (Nov. 1, 2002), but as discussed below, this withdrawal has no bearing on the continued validity of FDA's waiver policy.

[3] Under recent amendments enacted as part of the Medicare Prescription Drug Improvement and Modernization Act of 2003, the "court decision trigger" provision of the statute has been revoked.

Genpharm sought to waive its exclusivity rights to Granutec as an alternative means of obtaining at least some of the economic benefit of its exclusivity rights.

FDA agreed that such waiver was permissible and appropriate, and therefore granted final approval of Granutec's ANDA before the end of Genpharm's 180-day exclusivity period. This waiver was challenged in court by another subsequent ANDA applicant, Boehringer Ingelheim, which sought "to undo Genpharm Inc.'s FDA-approved waiver of its statutory [180-day] exclusivity in favor of Granutec, Inc." *Boehringer*, 993 F. Supp. at 1. The court emphatically rejected Boehringer's arguments. As the court framed and answered the issue, "plaintiff argues that there is no waiver provision within the statute and that the FDA's interpretation of the statute as containing such a waiver provision is baseless and contrary to law. **The Court cannot agree**. . . .The statute is simply silent on the point, and certainly does not clearly express a statutory policy precluding waivers." *Id.* at 2 (emphasis added).

The validity of Genpharm's selective exclusivity waiver to Granutec was also subsequently recognized by the Fourth Circuit in *Granutec v. Shalala*, 1998 U.S. App. LEXIS 6685 (4th Cir. Apr. 3, 1998), which also involved generic ranitidine products. In that case, the primary issue was the validity of FDA's "successful defense" rule, which granted 180-day exclusivity only to first ANDA applicants who had also successfully defended a patent infringement action, but the court took notice of the fact that "Genpharm [had] waived any entitlement to exclusivity in favor of Granutec." *Id.* at *16. Importantly, the court's decision relied, in part, upon its acceptance of the lawful availability of such exclusivity waivers. Specifically, the court noted that even though in some circumstances a first-filer might be blocked from actually marketing its drug during its exclusivity period, this "does not strip exclusivity of all value. "As Genpharm and Granutec have demonstrated, the ability to waive exclusivity in favor of another generic manufacturer can be quite lucrative." *Id.* at *26 (emphasis added). As the court concluded, "we hold that... Genpharm was entitled to a period of exclusivity that ran from March 3, 1997, until August 29, 1997. Because Genpharm waived its exclusivity with regard to Granutec, and FDA approved Geneva's ANDA as of August 29, 1997, no party has violated Genpharm's period of exclusivity." *Id.* at *30 (emphasis added).

2. *FDA Explains The Purposes And Operation Of Its Exclusivity Waiver Policy And Proposes Formal Regulatory Codification Of That Policy*

Shortly after the decisions in *Boehringer* and *Granutec*, FDA published a comprehensive set of regulatory proposals designed to address various court decisions, particularly *Mova v. Shalala*, 140 F.3d 1060 (D.C. Cir. 1998), that had invalidated certain elements of FDA's original Hatch-Waxman regulations, and created new gaps and ambiguities in the regulatory scheme. *See* 64 Fed. Reg. 42873. In that proposed rulemaking, FDA discussed and explained various existing policies and statutory interpretations, and also proposed several entirely new procedural and interpretive regulations governing the 180-day exclusivity period system. *See id.* at 42875 ("This proposed rule would revise § 314.107 to clarify and modify eligibility requirements for ANDA applicants seeking 180-day marketing exclusivity.") (emphasis added). The proposal specifically discussed FDA's existing policy to allow selective waivers of 180-day exclusivity, and proposed a formal regulatory codification of that policy. As FDA explained the origins of its waiver policy,

> Since publication of the 1994 regulations addressing 180-day exclusivity, FDA has been asked to determine whether an applicant who has obtained 180 days of exclusivity can waive such exclusivity to permit approval during the exclusivity period of a subsequent ANDA, or ANDAs, containing a paragraph IV certification. The agency has determined that waiver of 180-day exclusivity, like waiver of new drug exclusivity, is permitted under the act and at least one ANDA applicant has successfully effected a waiver. That waiver was challenged unsuccessfully in *Boehringer Ingelheim Corp. v. Shalala.*

Id. at 42881 (emphasis added).

In the preamble to the 1999 proposals, FDA also explained why continuation of its exclusivity waiver policy is necessary to effectuate the underlying benefit-conferring purposes of the 180-day exclusivity period provisions and to avoid unintended, anticompetitive results:

> Waiver of exclusivity permits ANDA applicants that have been awarded exclusivity, but are either unwilling or unable to market their products, to nonetheless obtain a benefit from that exclusivity. A waiver may be particularly appropriate, for instance, when the first ANDA applicant is sued and, while its litigation is ongoing, a favorable court decision is rendered in a case involving a subsequent applicant. Exclusivity would be awarded to the first applicant, with the 180-day period starting on the date of a final court decision in the subsequent applicant's litigation. The first applicant's ANDA may not be finally approved, however, and the applicant could not market its product. Under these circumstances, the first applicant may obtain a benefit by waiving its exclusivity period in favor of a subsequent applicant.

Id. (emphasis added).

3. FDA And The Courts Properly Continue To Adhere To FDA's Waiver Policy Even After FDA's Far-Ranging Proposed Rulemaking Was Withdrawn

Pfizer attacks the validity of FDA's waiver policy because the FDA ultimately withdrew the 1999 proposed rule in which FDA explained this policy. Petition at 3, 7. Pfizer's thinly veiled suggestion that the withdrawal of the proposed rule rescinded FDA's exclusivity waiver policy is without merit.

Because the exclusivity waiver policy discussed in the 1999 proposed rule was a pre-existing FDA policy, FDA's explanation of the necessity of that policy as set forth in the proposal, and as previously upheld by the courts in *Boehringer* and *Granutec*, maintains its full force and effect notwithstanding the fact that the overall proposal was later withdrawn for

reasons unrelated to the validity of the exclusivity waiver policy. *See* 67 Fed. Reg. at 66593 ("Since the proposed rule was published, there have been additional court decisions that address FDA's interpretation of the Act, including the interpretation described in portions of the proposed rule. In light of these decisions, FDA is withdrawing the August 1999 proposed rule..."). Importantly, none of the decisions that led FDA to withdraw the proposed rule addressed (much less questioned) the exclusivity waiver policy. Thus, the withdrawal had no effect on the pre-existing waiver policy. Indeed, FDA has consistently granted exclusivity waiver and relinquishment requests both before publication the 1999 proposed rule, and in the years since the proposal was withdrawn.

As noted above, the 1999 proposals included both explanations of existing policies, and completely new proposals. With respect to pre-existing policies for which FDA proposed to issue formal implementing regulations the effect of the withdrawal of the rulemaking *writ large* is simply that FDA may continue to apply its pre-existing policies, including its pre-existing exclusivity waiver policy. Indeed, this is exactly what FDA announced in its notice of withdrawal of the 1999 proposal. *See* 67 Fed. Reg. at 66593 ("FDA will continue to regulate directly from the statute and applicable FDA regulations and make regulatory decisions on an issue-by-issue basis."). Under Pfizer's logic however, numerous other pre-existing FDA policies would no longer be applicable (because, like the waiver policy, FDA had proposed to codify those other policies in the now-withdrawn 1999 proposal). For example, FDA proposed to codify its policies that:

- The first Paragraph IV applicant is eligible for exclusivity even if it is not sued by the patent holder for infringement, 64 Fed. Reg. at 42876;
- The first applicant loses exclusivity if it loses its patent infringement lawsuit, *id.*;
- The 180-day exclusivity period ends on the date the relevant patent expires, *id.* at 42877; and
- FDA may award separate exclusivity periods for separate strengths of the brand name drug, *id.* at 42881.

FDA continues to apply each of these policies, notwithstanding that the 1999 proposal to codify them was withdrawn. If, as Pfizer implies, the withdrawal of the 1999 proposal negated all pre-existing policies discussed or proposed to be codified in the 1999 proposal, FDA has been acting unlawfully in virtually every area of its exclusivity policy. Such a conclusion is of course absurd. Thus, Pfizer's attempt to attribute a negative inference to the FDA's pre-existing waiver policy based on its withdrawal of the 1999 proposed rule is nonsensical and ignores the FDA's current practices.

More specifically, FDA has in fact properly continued to apply its waiver policy and the courts have continued to recognize the validity of such exclusivity waivers. *See, e.g., Dr. Reddy's Labs., Inc. v. Thompson*, 302 F. Supp. 2d 340 (D.N.J. 2003). In that case, Dr. Reddy's Laboratories ("Dr. Reddy") challenged FDA's decision that Dr. Reddy was no longer entitled to 180-day exclusivity rights for its 40 mg omeprazole drug product because Dr. Reddy had been

adjudicated to have infringed the relevant patents and was therefore enjoined from actually selling its generic product. As a threshold jurisdictional question, the court had to determine whether Dr. Reddy's exclusivity claim was moot due to Dr. Reddy's inability to sell its own generic product. Dr. Reddy argued that review was still necessary and permissible because Dr. Reddy "would be able to sell the rights to that exclusivity to another generic drug maker who does not infringe [the patent]." *Id.* at 349. The court agreed that Dr. Reddy would be entitled to waive or relinquish any exclusivity rights to which it was entitled, and that the court therefore had jurisdiction to decide whether Dr. Reddy's retained any exclusivity rights at all. As the court stated:

> [I]t appears that Reddy could sell to another generic maker who could use any exclusivity period to which Reddy is entitled under the law, just as Andrx and Genpharm have done with respect to their exclusivity rights for the 10 and 20 mg [omeprazole] products.

Id. at 350. Although the court ultimately decided that Dr. Reddy had lost its exclusivity rights, the court's finding that any such rights could have been waived or relinquished for consideration was a crucial legal finding, as it formed the basis for the court's determination that it had jurisdiction to decide the underlying dispute.

Other recent examples of FDA-approved exclusivity waivers and relinquishments include:

- FDA permitted Copley Pharmaceuticals to selectively waive its exclusivity rights to Teva for generic nabumetone 750 mg tablets. *See* Exhibit A, Letter to Teva Pharmaceuticals USA from FDA (Sept. 24, 2001) at 2.

- FDA permitted Andrx to relinquish its exclusivity for a generic version of Wellbutrin SR 150 mg tablets (bupropion hydrochloride) allowing the FDA "to approve any [bupropion hydrochloride extended release 150 mg tablet] without regard to the 180-day exclusivity period specified in Section 505(j)(5)(B)(iv)." Exhibit B, Letter to Eon Labs, Inc. from FDA (March 22, 2004) at 4.

- Andrx and Genpharm were granted "shared exclusivity" for generic omeprazole delayed-release capsules, but were unable to immediately market due to a district court finding of infringement. FDA permitted Andrx and Genpharm to relinquish their shared exclusivity to allow FDA to approve the subsequent ANDA of Kremers Urban Development Co ("KUDCo"), whose ANDA was held to not infringe. *See* Exhibit C, Letter to Kremers Urban Development Co. from FDA, (November 1, 2002) at 3.

Thus, the fact that FDA has withdrawn the 1999 proposed rule, in which it explained the exclusivity waiver policy, has no effect on the continued validity of the exclusivity waiver policy, and FDA should continue to apply that policy and deny Pfizer's petition.

B. Maintenance of The 180-Day Exclusivity Waiver Policy, Both Generally, And With Respect to Purepac's Gabapentin Exclusivity, is Required to Effectuate The Purposes of Hatch-Waxman

FDA must continue to apply its longstanding exclusivity waiver policy, both generally, and with respect to Purepac's gabapentin exclusivity, in order to assure that the purposes of the exclusivity period provisions are fulfilled. Purepac is a relatively small generic drug company which made a substantial investment to be the first ANDA applicant to challenge Pfizer's listed patents for its Neurontin® (gabapentin) drug product. Pfizer has used every tactic available to prolong the inevitable day when Purepac and other generic companies would begin providing American consumers with more affordable generic versions of Neurontin®. Pfizer began its assault in June of 1998 when it sued Purepac for infringement of two patents, U.S. Patent Nos. 4,894,476 (the "'476 patent") and 5,084,479 (the "'479 patent). Pfizer had listed both patents in the Orange Book, despite the fact that the '479 patent claimed an unapproved method for treating neurodegenerative diseases. In 2003 FDA determined that the '479 patent was improperly listed in the Orange Book and this determination was affirmed on appeal. *See Torpharm, Inc. v. Thompson*, 260 F. Supp. 2d 69, 76-77 (D.D.C. 2003), *aff'd by sub nom. Purepac Pharm. Co. v. Torpharm, Inc.*, 354 F.3d 877 (D.C. Cir. 2004).

Pursuant to 21 U.S.C. 355(j)(5)(B)(iv), Purepac submitted a Paragraph IV certification to the '476 patent, triggering a thirty-month stay of approval. The '476 litigation continued for almost two years when in April of 2000, the Patent and Trademark Office issued to Pfizer another gabapentin patent, U.S. Patent No. 6,054,482 (the "'482 patent"). The '482 patent was a "submarine" patent that had been pending in the PTO, unbeknownst to the generic companies, since 1990. Pfizer listed the '482 patent in the Orange Book and Purepac was again required to submit a Paragraph IV certification to its ANDA. Pfizer thus received an additional thirty-month extension for its gabapentin monopoly. The '482 patent litigation is still pending in the United States District Court for the District of New Jersey. The thirty month stay of approval expired in December 2002 for Purepac and in February 2003 for Teva. Purepac received final approval for its gabapentin capsule product in September 2003.

Although Purepac and Teva believe strongly in the ultimate validity of their challenges to the '482 patent, litigation always involves risk and uncertainty. In order to reduce its potential liability if and when it decides to begin commercially marketing its product, Purepac has entered an agreement with Teva whereby Purepac can selectively waive its exclusivity, under FDA's established policy, to allow Teva's ANDA to be approved during Purepac's exclusivity period, so that both companies could begin marketing at the same time, and thereby share the risk of a potential future finding of infringement.

Anticompetitive delay tactics of the sort practiced by Pfizer with gabapentin only increase the necessity of FDA maintaining its exclusivity waiver policy generally, and with respect to gabapentin. Generic companies who are first to file Paragraph IV Certifications may nevertheless face any number of last-minute obstacles to launching their product, including operational difficulties (raw material supply or plant capacity limitations, conflicting production priorities, etc.), unresolved patent issues, or minor product-specific technical issues that will eventually be overcome (e.g., stability or bioequivalence problems). Where such obstacles arise

and delay the ability of the first-filer to launch its product, it makes no sense from a public policy perspective to prevent the company from waiving its exclusivity rights in order to allow a subsequent applicant to begin supplying its generic product to American consumers at lower cost. Indeed, that is the very purpose of the 180-day exclusivity period -- to expedite the availability of generic drugs. *See Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 676, 110 S. Ct. 2683, 2691 (1990) (Waxman-Hatch was designed "to enable new drugs to be marketed more cheaply and quickly."); *Glaxo*, 110 F.3d at 1568 (Congress enacted the Hatch-Waxman Act in 1984 "to benefit makers of generic drugs, research-based pharmaceutical companies, and not incidentally, the public.") (citing H.R. Rep. No. 98-857, pt. I, at 14-15 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2647-48); *Teva v. FDA*, 182 F.3d 1003, 1004 (D.C.Cir. 1999), *remand* 1999 U.S. Dist. LEXIS 14575 (D.D.C. Aug. 18, 1999), *aff'd by* 254 F.3d 316 (D.C. Cir. 2000) ("Under the so-called Hatch-Waxman amendments, an abbreviated new drug application process allows applicants, upon meeting certain requirements, to proceed more quickly to the marketplace.") (emphasis added). Thus, FDA's exclusivity waiver policy must be maintained, and the Teva/Purepac agreement must be allowed to be implemented, because it will serve the purposes of the 180-day exclusivity period by: (1) facilitating earlier and greater availability of lower cost generic gabapentin products than would otherwise be the case if Purepac were not permitted to waive its exclusivity as to Teva, *see Teva, supra*, 182 F.3d at 1004; (2) preserving the incentive/reward purposes of the 180-day exclusivity period, *see Mylan, supra,* 81 F. Supp. 2d at 33; and (3) assuring that Purepac receives appropriate value from its exclusivity through the waiver mechanism, *see* 64 Fed. Reg. at 42881, *Granutec, supra,* at *26.

II. PFIZER'S PETITION IS WITHOUT MERIT

Pfizer's Petition seeks a radical departure from FDA's longstanding and reasonable policy of permitting 180-day exclusivity waivers and relinquishment, and the courts' uniform acceptance of that policy. Specifically Pfizer argues (1) that the statutory exclusivity provision is unambiguous and that its "plain language" precludes the possibility of a waiver that would allow FDA approval of a subsequent applicant; (2) that FDA's established policy allowing waivers of 180-day exclusivity is based on a flawed analogy to the agency's policy allowing waiver of 5-year and 3-year NDA exclusivities; and (3) that allowing waiver of 180-day exclusivity would create unintended and inappropriate consequences by encouraging the filing of unapprovable ANDAs. Pfizer's position is incorrect as a matter of law, internally inconsistent and self-defeating, and relies upon a surprisingly uninformed view of how generic companies do business under the Hatch-Waxman scheme.

A. The Statute Does Not Prohibit Waiver Of 180-Day Exclusivity

Pfizer's first line of attack is to point out that the statutory provision that established the 180-day exclusivity period operates by imposing a statutory "waiting period" on FDA approval of Paragraph IV ANDAs other than the ANDA of the applicant which filed the first Paragraph IV Certification for the drug at issue. Thus, Pfizer argues that the 180-day exclusivity period is not a "property right" subject to waiver or relinquishment, and that the "plain language must govern and defeat Purepac's effort to turn the benefit it derives from the statutory bar against final approval of Teva's application into a marketable asset comparable to a *bona fide* property right." Petition at 4-5. Under Pfizer's theory, no exclusivity-eligible ANDA applicant could ever

consent to FDA approval of another ANDA (whether by selective waiver or complete relinquishment of exclusivity) until a full 180 days after its exclusivity had been "triggered" because, as Pfizer argues, "nothing in Section 505(j)(5)(B)(iv) admits of any exception to this waiting period." Petition at 4. Pfizer's statutory "plain language" argument is unfounded.

1. The Statute Is Silent With Respect To Exclusivity Waivers. Because FDA's Waiver Policy Furthers The Congressional Intent, It Is Permissible and Entitled to Deference

Pfizer confuses the concept of a statutory provision that has an affirmative "plain meaning" with one which is silent with respect to a particular question or issue. Here, the statute is *silent* with respect to whether a first Paragraph IV applicant may selectively waive the rights Congress granted by way of the 180-day exclusivity period provision. But, that is very different from saying that the statute unambiguously prohibits FDA's policy of allowing such waivers. Where, as here, the statute is silent on the specific issue, the agency's policy implementing the statute must be upheld so long as it is reasonable. As the court in *Boehringer, supra,* has previously noted with respect to the precise exclusivity waiver issue raised by Pfizer,

> The statutory provision in question does contain mandatory language. <u>However</u>, that language does not speak to the precise issue at hand. <u>Section 355 says nothing about waivers of exclusivity</u>. There is nothing to indicate that Congress even thought about waivers in drafting the section. <u>The statute is simply silent on the point, and certainly does not clearly express a statutory policy precluding waivers</u>. In cases such as this, the Court is guided by *Chevron v. NRDC*, 467 U.S. 837 (1984), where the Supreme Court explained:
>
>> ...if the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on a permissible construction of the statute.

Boehringer, 993 F. Supp. at 3-4 (emphasis added). Thus, the statute does not ("plainly" or otherwise) prohibit FDA's longstanding policy of allowing selective waiver of 180-day exclusivity. Rather, that policy is sound, reasonable, and should be adhered to.

FDA cannot adopt Pfizer's "plain language" argument because it is based on reading the exclusivity provisions in isolation from the overall context of the statutory scheme. Contrary to Pfizer's approach, when interpreting a provision of a complex regulatory statute such as Hatch-Waxman, it is not sufficient to look merely to whether Congress specifically considered and addressed a particular factual scenario (such as wavier of 180-day exclusivity), and declare that the failure to provide detailed rules to address such a scenario means that the statute forbids all but a literal interpretation of the statutory provision. In fact, to do so would negate Congress' express mandate to the Secretary of Health and Human Services to "promulgate ... such regulations as may be necessary for the administration of section 505 of the Food, Drug and Cosmetic Act... ." 21 U.S.C. § 355 note, Pub.L. No. 98-417, § 105, 98 Stat. 1585 (1984); *see also United States v. Mead Corp.*, 533 U.S. 218, 229, 121 S.Ct. 2164, 2172 (2001) ("Yet it can

still be apparent from the agency's generally conferred authority and other statutory circumstances that Congress would expect the agency to be able to speak with the force of law when it addresses ambiguity in the statute *or fills a space in the enacted law,* even one about which 'Congress did not actually have an intent' as to a particular result.")(quoting *Chevron*, 467 U.S. at 845)) (emphasis added). Moreover, as the Supreme Court has recently explained,

> In determining whether Congress has specifically addressed the question at issue, a reviewing court should not confine itself to examining a particular statutory provision in isolation. The meaning -- or ambiguity -- of certain words or phrases may only become evident when placed in context. *See Brown v. Gardner*, 513 U.S. 115, 118, 115 S. Ct. 552 (1994) ("Ambiguity is a creature not of definitional possibilities but of statutory context."). It is a "fundamental canon of statutory construction that the words of a statute must be read in their context and with a view to their place in the overall statutory scheme." *Davis v. Michigan Dept. of Treasury*, 489 U.S. 803, 809, 109 S. Ct. 1500 (1989). A court must therefore interpret the statute "as a symmetrical and coherent regulatory scheme," *Gustafson v. Alloyd Co.*, 513 U.S. 561, 569, 115 S. Ct. 1061 (1995), and "fit, if possible, all parts into an harmonious whole." *FTC v. Mandel Brothers, Inc.*, 359 U.S. 385, 389, 79 S. Ct. 818 (1959).

FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 132-33, 120 S. Ct. 1291, 1300-01 (2000).

Contrary to Pfizer's assertions, because the exclusivity provisions are silent with respect to waivers, FDA is authorized to adopt a policy with respect to the waiver issue. FDA's waiver policy should be maintained, and would be upheld in any new judicial challenge, because it is based on a permissible construction of the 180-day exclusivity period provisions, and is appropriately grounded in the context of, and with the necessary view to the place of the exclusivity within, the overall Hatch-Waxman scheme.

2. *Pfizer's Plain Language Argument Fails Because FDA's 180-Day Exclusivity Waiver Policy Is Consistent With Its Policy To Allow Waivers Of Similar NDA-Based Exclusivities*

Pfizer attempts to bolster its "plain language" argument against 180-day exclusivity waivers by pointing out that the 180-day exclusivity operates by means of a statutorily-imposed "waiting period" imposed upon FDA's ability to approve subsequent Paragraph IV ANDAs. Petition at 4-5. Pfizer's argument glosses over a key point, specifically, that the statutory provisions granting the NDA and ANDA exclusivities are structurally similar -- in that they impose "waiting periods" on the FDA approval of certain ANDAs for specified periods of time -- yet FDA has consistently permitted waivers of new drug exclusivities. The following table illustrates the common structural elements of the various exclusivity "waiting periods":

NCE Exclusivity § 505(j)(5)(D)(ii)	**3-Year Exclusivities** § 505(j)(5)(D)(iii), (iv)	**180-day exclusivity** § 505(j)(5)(B)(iv)
"If an [NDA] for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other [NDA], is approved..., no [ANDA] may be submitted...which refers to the drug for which the [NDA] was submitted before the expiration of five years from the date of the approval of the [NDA] ...."	"If an [NDA] submitted for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another [NDA], is approved... and if such [NDA] contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an [ANDA] effective before the expiration of three years from the date of the approval of the [NDA] for such drug." * * * "If a supplement to an [NDA] is approved...and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an [ANDA] for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement."	[As codified prior to December 8, 2003]: "If the [ANDA] contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous [ANDA] has been submitted under this subsection [containing] such a certification, the [subsequent ANDA] shall be made effective not earlier than one hundred eighty days after – (I) the date the Secretary receives notice from the applicant under the previous [ANDA]of the first commercial marketing of the drug under the previous [ANDA], or (II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier." [As codified as of December 8, 2003]: (I) Effectiveness of application. — Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

Because all three exclusivity types operate in functionally symmetrical ways, to the extent Pfizer argues that the "plain language" of the 180-day exclusivity period provision does not "admit[] of any exception to" the procedural waiting period, the same argument would have to apply to, and preclude waiver of, new drug exclusivities. However, as Pfizer is forced to concede, FDA does allow waivers of new drug exclusivities and has relied upon that policy in justification of its policy to also allow waivers of 180-day exclusivity. *See* Petition at 6-7; 64 Fed. Reg. at 42881 ("The agency has determined that waiver of 180-day exclusivity, like waiver of new drug exclusivity, is permitted under the act."). Because FDA has determined that the statute permits waivers of the NCE and 3-year exclusivity "waiting periods," it must reject Pfizer's argument and continue to allow waivers of the 180-day exclusivity period "waiting period." *See Brown & Williamson, supra* ("A court must therefore interpret the statute 'as a symmetrical and coherent regulatory scheme.'") (citing *Gustafson v. Alloyd Co.*, 513 U.S. 561, 569 (1995)).

3. Pfizer's Reliance on Mova, Teva, TorPharm, and Granutec Is Misplaced

Pfizer cites to various cases in support of its proposition that FDA must apply the allegedly "plain language" of the statute to preclude waiver of 180-day exclusivity. *See* Petition at 4-5, citing *Mova v. Shalala*, 140 F.3d 1060 (D.C. Cir. 1998), *Teva v. FDA*, 182 F.3d 1003 (D.C. Cir. 1999), *TorPharm v. Shalala*, 1997 WL 33472411 (D.D.C. Sept. 15, 1997), and *Granutec v. Shalala*, 1998 U.S. App. LEXIS 6685 (4th Cir. Apr. 3, 1998). None of those cases even remotely questioned the validity of FDA's 180-day exclusivity waiver policy, and indeed as discussed above, *Granutec* actually endorsed the policy. Rather, the cases dealt primarily with disputes over the baseline eligibility for, and the events that would trigger the start of, the exclusivity period.[4] Pfizer's reliance on these cases is unavailing.

In *Mova* and *Granutec* the courts rejected an FDA regulation that had the effect of *eliminating* the 180-day exclusivity period altogether by allowing FDA approval of subsequent Paragraph IV ANDAs without the first applicant's consent before one of the statutory exclusivity triggering events had occurred. *See Mova*, 140 F.3d at 1070 ("The FDA thus construes the commercial marketing trigger to potentially hurt, but never benefit, the first ANDA applicant. There is no indication in the text or history of section 355(j)(5)(B)(iv) that the commercial marketing trigger is supposed to function in that one-sided manner."); *accord Granutec*, 1998 U.S. App. LEXIS 6685 at *21-22 ("[T]he idea that any 180-day exclusivity period must be premised on the successful defense of an infringement suit results in the evisceration of 21 U.S.C. § 355(j)(4)(B)(iv)(I), which clearly contemplates an exclusivity period beginning -- whether or not an infringement suit has come to resolution -- on the date of the first commercial marketing by the first ANDA filer."). FDA's exclusivity waiver policy is fully consistent with the *Mova* and *Granutec* courts' interpretation of the 180-day exclusivity period provisions, because FDA's waiver policy protects and promotes the value of exclusivity to deserving first

[4] As noted below, *TorPharm* did not even interpret the operative statutory exclusivity provision at issue in this Petition proceeding.

applicants. And, because FDA's waiver policy requires that there have been a triggering event before a selective waiver may be effectuated, this policy avoids the "plain language" violation that led to the invalidation of FDA's successful defense regulation in *Mova*. Thus, FDA's waiver policy protects the same interest that the *Mova* court sought to protect, and *Mova* in no way precludes continued operation of FDA's waiver policy.

In *TorPharm v. Shalala*, the court addressed the question of whether the 30-month stay of ANDA approval is terminated only by a "final" unappealable court decision holding that the patent challenged by the first Paragraph IV filer was invalid or not infringed (as FDA's regulations then required), or whether a district court decision of invalidity or non-infringement terminates the stay and allows final approval of the ANDA. There was no question of whether the first applicant could waive its exclusivity; in fact, the court interpreted a completely different provision of the Act – section 505(j)(5)(B)(iii) rather than the 180-day exclusivity period provision of section 505(j)(5)(B)(iv). As the court noted, "the dispositive question in this case is whether plaintiff is entitled to invoke one of the[] statutory exceptions [to the 30-month approval stay]." *TorPharm*, 1997 WL 33472411, at *1. The court further stated that "the dispute...turns on the meaning of the phrase "the court" in 21 U.S.C. § 355(j)([5])(B)(iii)." *Id.* at *3. Thus, *TorPharm* is irrelevant to, and does not support, the interpretation proposed in Pfizer's Petition.

Pfizer is particularly off base in its reliance on *Teva v. FDA*. In that case, FDA in fact adopted what it thought was a literal "plain language" interpretation of the 180-day exclusivity period triggering provisions by refusing to treat a jurisdictional dismissal of a declaratory judgment action as a court decision "holding" that the relevant patent was invalid or not infringed. The court rejected FDA's narrow interpretation because it was inconsistent with the purposes of the Hatch-Waxman amendments and would create unintended, competition-delaying consequences. Particularly apropos to Pfizer's Petition, the D.C. Circuit noted that "a narrow interpretation cannot be reasonable simply because it is narrower than it *could* be; to the contrary that interpretation may in fact be narrower than it *should* be given the purposes of the statutory scheme and congressional intent." *Teva*, 182 F.3d at 1011 (italics in original, underscores added). Thus, not only does *Teva* not stand for the proposition that the 180-day exclusivity period must be read literally, it is a strong example of why FDA and the courts must look to the underlying Congressional intent even when faced with "plain language" arguments under Hatch-Waxman.

B. FDA's Justification For 180-Day Exclusivity Waiver Is Sound

Pfizer seeks to discredit FDA's decision to treat new drug exclusivities and 180-day exclusivity similarly for purposes of waivers by arguing that "unlike the NDA holder who owns the proprietary data on which all ANDA filers rely, and who can transfer or assign rights in those data at its discretion, the first-filed ANDA applicant holds no transferable asset, and 'no property right to exclusivity itself.'" Petition at 7. Pfizer's argument is flawed in two respects.

First, Pfizer's argument ignores the fact that 180-day exclusivity period is unquestionably intended as a benefit for ANDA applicants who have engaged in the statutorily rewarded activity of being the first to challenge a branded company's patent. *See, supra*, § I.A. Similarly, the corresponding new drug exclusivities are intended as a benefit to NDA sponsors who engage in

the statutorily rewarded activities of bringing new drug products (and significant improvements to approved products) to the market. In both circumstances, Congress set up a task/reward system whereby a company is given exclusivity rights when it undertakes statutorily mandated steps. It is irrelevant to the waiver question that Congress required NDA sponsors to do one thing (develop new products) to earn their reward, and required ANDA holders to do another thing (develop generic drugs and challenge listed patents) to earn their reward. Each respective activity was intended to be rewarded, and they were in fact rewarded by functionally and procedurally similar mechanisms. There is no basis whatsoever to conclude that Congress intended to restrict the rights of *either* NDA or ANDA sponsors to waive their respective exclusivities, much less that Congress meant to restrict waivability of 180-day exclusivity but not similarly restrict new drug exclusivities.

Second, Pfizer's argument that 180-day exclusivity is not waivable because it is not tied to any "transferable asset" is simply incorrect. A generic applicant does hold transferable assets which underlie its exclusivity – specifically, its particular product formulation (which is often proprietary or even patented), as well as the proprietary data generated in order to develop, test, and obtain FDA approval of the generic product. All of those assets are readily transferable, so even if Pfizer's "transferable asset" test for exclusivity waivability was valid (which it is not) generic applicants could readily meet that test. Under either FDA's current waiver policy, or under Pfizer's erroneous interpretation, waivability of 180-day exclusivity period rights would not require any actual transfer of such assets.

C. No Court Has Ever Ruled That The Statutory Exclusivity Language Precludes Exclusivity Waivers and *Mova* Did Not Overrule *Boehringer*

Pfizer attempts to escape the compelling decision in *Boehringer, supra,* in which the court upheld FDA's 180-day exclusivity waiver policy, by suggesting that *Mova* overturned *Boehringer.* Petition at 8-9. Pfizer's argument is desperate, distorted, and dead wrong. In arguing that the court in *Mova* "considered and rejected the rationale of *Boehringer*" Pfizer confuses the *mode of statutory construction* used in the two cases, with the *substantive bases* for the courts' decisions. While it is true that the *Mova* court based its decision on a "literal reading" of the statute, whereas the *Boehringer* court found the statute to be "silent," it is crucial to note that the courts were considering very different specific issues. *Boehringer* directly addressed whether waiver of 180-day exclusivity is precluded by section 505(j)(5)(B)(iv) (and correctly found that such waiver is not precluded), whereas *Mova* addressed whether a first Paragraph IV filer could be deprived of exclusivity if it failed to win its patent infringement case before a subsequent applicant's ANDA was otherwise ready for FDA approval. The fact that the *Mova* court found that the plain statutory language precluded FDA from involuntarily depriving an applicant of its exclusivity rights in no way precludes the possibility that the same statutory provision does not plainly answer the very different question of whether a first filer can voluntarily waive its exclusivity rights. Thus, Pfizer's argument that *Mova* requires that in all

cases "the plain words of the statute govern the approval of ANDAs under section 505(j)(5)(B)(iv)" is simply incorrect.[5]

D. FDA's 180-Day Exclusivity Waiver Policy Does Not Abrogate Pfizer's Protectable Interests, Nor Will It Create Perverse Consequences

In a final last ditch effort to cast doubt on the propriety of FDA's 180-day exclusivity waiver policy, Pfizer argues that this policy does not support the overall objectives of the Hatch-Waxman amendments. Petition at 9-10. Here too, Pfizer's arguments are without merit.

First, Pfizer argues that FDA's waiver policy is unlawful because it violates the "statute's intent of 'protecting both the interests of drug manufacturers who produce new drugs and the interests of generic drug manufacturers and their consumers,'" and "does not acknowledge the statutory protection accorded NDA holders' proprietary data." Petition at 3, 9. This argument is a complete distortion. Just because the Hatch-Waxman Amendments *as a whole* were intended to benefit both branded and generic companies, in no way means that each discrete provision of Hatch-Waxman has such a dual purpose. Indeed, the various exclusivity provisions of Hatch-Waxman are all clearly directed toward benefiting one or the other segment of the industry, but not both at the same time.[6] More specifically, the 180-day exclusivity period is universally understood by FDA, industry, and the courts, as being a benefit specifically directed to *generic* drug companies, and is intended to increase the speed and degree of generic competition – i.e., to more quickly and completely reduce the branded company's stranglehold on the market for the drug at issue. *See, supra,* § I.A.

Although Pfizer appears to argue that the exclusivity period might, in some cases, provide a *de facto* benefit to branded companies by limiting the number of competitors for the first six months of generic competition, any such windfall to branded companies -- to the extent that it exists at all -- is not an *intended* or required effect of the statute. *See Mova*, 140 F.3d at 1075 (the 180-day exclusivity period provision "is not intended to benefit pioneer drug companies directly. Indeed, quite the opposite is true: the provision is intended to reward generic drug manufacturers who challenge pioneer drug companies' patents. Thus, ...[a pioneer drug company] cannot show that it is an 'intended beneficiary' of section 355(j)(5)(B)(iv).") (emphasis added) (citations omitted). Pfizer's Petition is an ill-founded attempt to usurp undeserved value -- in the form of lessened or delayed initial generic competition -- from a

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[5] Indeed, as noted above, subsequent to *Mova* the D.C. Circuit rejected an FDA interpretation that was based on the allegedly "plain words" of the same statutory provision. *Teva v. FDA*, 182 F.3d 1003 (D.C. Cir. 1999).

[6] *See e.g.*, 21 U.S.C. §§ 355(j)(2)(A)(vii) and 355(j)(5)(B)(iii) (benefiting branded companies by requiring generic applicants to certify to brand company patents and imposing a 30-month stay of generic approval if the brand company files a patent infringement lawsuit within 45 days of a Paragraph IV Notification); 21 U.S.C. § 355(j)(5)(D) (benefiting branded companies by imposing a 5-year "NCE exclusivity and 3-year new product or supplemental approval exclusivities to block submission and approval of competing generic products). Pfizer agrees that the NDA exclusivity provisions do not serve a dual purpose, but are "intended to protect the interests of pioneer companies holding NDAs...." Petition at 6. In contrast, the 180-day exclusivity period is intended as a benefit to generic drug companies, not to branded companies. *See Mova*, 140 F.3d at 1075.

statutory provision whose fundamental purpose is to shift market value away from branded companies and to generic companies.

Moreover, Pfizer's data protection concerns are unfounded because "the statutory protection[s] accorded NDA holders' proprietary data" is fully operable even under an exclusivity-waiver system. This is because brand company data are protected by (1) the Paragraph IV patent certification/notification requirements, and the 30-month ANDA approval stay available when the brand company asserts its patent rights against a Paragraph IV ANDA applicant. 21 U.S.C. § 355(j)(5)(B)(iii). A first-filer generic cannot selectively waive its exclusivity to another applicant whose ANDA is still subject to a 30-month stay, or against whom the branded company has obtained a preliminary injunction, because final approval and marketing of such an ANDA continues to be blocked for the benefit of the branded company. And, although ANDAs can be approved after expiration of the 30-month stay even if litigation is ongoing (absent an injunction), in such circumstances branded companies have already enjoyed the full measure of their regulatory protection since the statute clearly provides for final approval when the stay expires. 21 U.S.C. § 355(j)(5)(B)(iii). Branded companies' data interests are also protected under FDA's waiver policy because FDA approval of a subsequent ANDA filer under a waiver does not preclude the branded company from asserting its patents and recovering damages if a marketed generic product is found to infringe the brand company's patents.

Finally, Pfizer propounds two hypothetical "serious policy concerns" that it believes would arise from FDA's exclusivity waiver policy. Petition at 9-10. Specifically, Pfizer argues that exclusivity waivers would encourage ANDA applicants to either file ANDAs that are "not ultimately approvable," or to file unmeritorious patent challenges, in both cases "encourag[ing] speculation in 'exclusivities,' not investment in development of ANDA products that don't infringe...valid patents." Petition at 10. Pfizer speculation is wrong, and its expressed policy concerns exist only in Pfizer's imagination. Since FDA has applied its 180-day exclusivity waiver policy for nearly seven years, Pfizer's failure to point to any specific examples of the types of "speculation in exclusivities" is compelling proof that its concern is unfounded. Second, Pfizer fails to appreciate that under the recent amendments to the Hatch-Waxman exclusivity provisions, ANDAs that are "not ultimately approvable" will result in a forfeiture of exclusivity because the applicant will fail to obtain tentative approval within 30 months of submitting the ANDA. 21 U.S.C. § 355(j)(5)(D)(IV). Third, a Paragraph IV ANDA applicant with a "weak patent position" will, upon losing its patent infringement case, be forced to amend its ANDA to include a Paragraph III certification, thereby forfeiting exclusivity. 21 U.S.C. § 355(j)(5)(D)(III). Thus, Pfizer's uninformed speculation about adverse effects of FDA's exclusivity waiver policy does nothing to support its requested change in policy.

III. CONCLUSION

Pfizer's petition is a meritless attempt to thwart the pro-competitive intent of the Hatch-Waxman amendments by restricting the amount of generic competition Pfizer will initially face for its Neurontin brand gabapentin products. The statutory exclusivity provisions have been properly interpreted by FDA and the courts for the last seven years to permit generic exclusivity waivers, and no court decision or policy "concern" changes that fact. If Pfizer's Petition were granted, the adverse consequences to Purepac's and Teva's interests, and to the American public,

would be severe and irreparable. Those consequences are even more significant here than in other situations involving anti-generic citizen petitions, because Pfizer has made clear that it will imminently begin a "switch" campaign to convince doctors and patients to stop using Neurontin® and instead use Pfizer's follow-on product, pregabelin. When such switch tactics are initiated in advance of vigorous generic competition, the result is often to greatly diminish the total volume of sales of generic versions of the original product.[7]

Although FDA is not obligated to answer the petition before approving Teva's ANDA, for the reasons set forth herein, Pfizer's Petition should be denied promptly to remove any possibility of inappropriate delay to Purepac's and Teva's ability to exercise their rights to jointly market generic gabapentin during the term of Purepac's exclusivity period.

Respectfully submitted,

James N. Czaban
Shannon M. Bloodworth
HELLER EHRMAN
WHITE & MCAULIFFE LLP
1666 K Street N.W.
Washington, D.C. 20006

[7] *See* Exhibit D, *Anticonvulsants: Pfizer's Pregabalin to Top Success*, http://www.avytal.com ("the imminent loss of patent protection [for Neurontin] means that this cash cow will soon be subject to imminent challenges from cheap copycat versions from generic manufacturers. In order to stave off this threat and so maintain and grow its share of the anticonvulsant market, Pfizer must ensure that a follow-on pregabalin compound is launched before Neurontin loses its patent. Such a strategy would be typical of Pfizer, which has maintained leadership in other CNS markets, such as depression and pain, through the successful launch of follow-on products.").

EXHIBIT A

ANDA 75-189/S-001, S-002 September 24, 2001

TEVA Pharmaceuticals USA
Attention: Deborah A. Jaskot
1090 Horsham Road
PO Box 1090
North Wales, PA 19454

Dear Madam:

This is in reference to your supplemental new drug applications dated August 28, 2001, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act for Nabumetone Tablets, 500 mg and 750 mg.

Reference is also made to the Tentative Approval letter for Nabumetone Tablets 500 mg and 750 mg issued by this office on December 24, 1998, and to the approval letter for Nabumetone Tablets 500 mg dated May 26, 2000.

These supplemental applications, submitted as "Prior Approval Supplements-Expedited Review Requested," provide for the final approval of Nabumetone Tablets 750 mg:

S-001 An additional strength - Nabumetone Tablets 750 mg; and

S-002 Revised labeling to incorporate the 750 mg tablet strength.

We have completed the review of these supplemental abbreviated applications and have concluded that the 750 mg strength of the drug product is safe and effective for use as recommended in the submitted labeling. Accordingly, the supplemental applications are approved. The Division of Bioequivalence has determined your Nabumetone Tablets, 750 mg, to be bioequivalent and therefore therapeutically equivalent to the listed drug (Relafen Tablets, 750 mg, of SmithKline Beecham Pharmaceuticals). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

The listed drug product (RLD) noted above and referenced in your application, Relafen Tablets of SmithKline Beecham Pharmaceuticals, is subject to a period of patent protection which expires on December 13, 2002, (U.S. Patent No. 4,420,639 [the '639 patent]). Your application contains a patent certification under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of this drug product will not infringe on the '639 patent or that the patent is

otherwise invalid. You further informed the agency that litigation is currently underway in the United States District Court for the District of Massachusetts involving a challenge to the '639 patent (SmithKline Beecham Corporation, and Beecham Group, p.l.c. v. Teva Pharmaceuticals USA, Civil Action No. 97 CV12541 RCL). Thus, this approval is partially based upon the Agency's recognition that the 30-month period identified in Section 505(j)(5)(B)(iii) of the Act, during which time FDA was precluded from approving your application, has expired.

As noted in the Agency's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book"), an abbreviated new drug application for Nabumetone Tablets, 750 mg strength, was approved for Copley Pharmaceuticals Inc. (Copley) on June 6, 2000. This application also contained a Paragraph IV Certification and was the first application received by the Agency for the 750 mg strength. Upon approval, Copley became eligible for 180 days of market exclusivity for the 750 mg strength which would be triggered by the occurrence of one of the two events stated below. The Act provides that approval of a subsequent abbreviated new drug application such as yours that also contains a Paragraph IV Certification under Section 505(j)(2(A)(vii)(IV) and that provides for approval of the same drug product as that for which another abbreviated application containing a Paragraph IV Certification was previously received, shall be made effective not earlier than:

1. One hundred and eighty (180) days after the date the Secretary receives notice from the applicant of the previous application that commercial marketing of the drug product approved in that application has commenced, or

2. the date of a decision of a court holding the patent which is the subject of the certification to be invalid or not infringed; whichever option occurs first [Section 505(j)(5)(B)(iv)].

Based upon the regulations cited above, this supplemental application for Nabumetone Tablets 750 mg would not be eligible for final approval until one of the precipitating events has occurred. However, you have notified the Agency that the 180-day exclusivity for this drug product commenced on August 27, 2001, upon the first comemrcial marketing of the product under Copley's application. Furthermore, you have also notified the agency that as the owner of both the Copley and the Teva ANDAs, you are selectively transferring the remainder of Copley's 180-day generic drug exclusivity awarded under Copley's ANDA 75-179 to Teva under this application.

We remind you that you must comply with the requirements for an approved abbreviated application described in 21 CFR 314.80-81

and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

The material submitted is being retained in our files.

Sincerely yours,

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

EXHIBIT B

DEPARTMENT OF HEALTH & HUMAN SERVICES

ANDA 75-932/S-001; S-002

Food and Drug Administration
Rockville MD 20857

MAR 22 2004

Eon Labs, Inc.
Attention: Enna Krivitsky
227-15 North Conduit Avenue
Laurelton, NY 11413

Dear Madam:

This is in reference to your supplemental abbreviated new drug applications dated December 18, 2003, submitted under Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), regarding your abbreviated new drug application (ANDA) for Bupropion Hydrochloride Extended-release Tablets USP, 100 mg and 150 mg (Twice-A-Day Dosing).

Reference is made to your correspondence dated March 22, 2004. Reference is also made to our letter dated November 25, 2003, granting final approval to your Bupropion Hydrochloride Extended-release Tablets USP, 100 mg, and designating your Bupropion Hydrochloride Extended-release Tablets USP, 150 mg, as tentatively approved.

The supplemental applications provide for:

S-001: Final approval of your Bupropion Hydrochloride Extended-release Tablets USP, 150 mg; and

S-002: Updated final-printed labeling to include the 150 mg strength.

We have completed the review of these supplemental abbreviated applications and they are approved. Based upon the information you have presented to date, we have concluded that your Bupropion Hydrochloride Extended-release Tablets USP, 150 mg, are safe and effective for use as recommended in the submitted labeling.

The Division of Bioequivalence has determined your Bupropion Hydrochloride Extended-release Tablets USP, 150 mg, (twice-a-day dosing) to be bioequivalent and therapeutically equivalent to the listed drug (Wellbutrin SR® Sustained-Release Tablets, 150 mg, of GlaxoSmithKline). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application. The "interim" dissolution specifications are as follows:

> Dissolution testing should be conducted in 900 mL of [redacted], at 37°C, using USP 26 Apparatus [redacted] (basket) at 50 rpm. The test product should meet the following "interim" specifications:

Time (Hours)	% Dissolved
1	(b)(4)
2	
4	
6	

> The "interim" dissolution tests and tolerances should be finalized by submitting dissolution data for the first three production size batches. Data should be submitted as a "Special Supplement - Changes Being Effected" when there are no revisions to the "interim" specifications or when the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

The listed drug product referenced in your supplemental application, Wellbutrin SR® Tablets, 150 mg, of GlaxoSmithKline, is subject to multiple periods of patent protection. The following United States patents and their expiration dates currently appear in the Agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations, the "Orange Book":

Patent Number	Expiration Date
5,358,970 (the '970 patent)	August 12, 2013
5,427,798 (the '798 patent)	August 12, 2013
5,731,000 (the '000 patent)	August 12, 2013
5,763,493 (the '493 patent)	August 12, 2013

Your application contains paragraph IV certifications to each of these patents under Section 505(j)(2)(A)(vii)(IV) of the Act stating that none of these patents will be infringed by your manufacture, use, offer for sale, or sale of Bupropion Hydrochloride Extended-release Tablets USP, 150 mg. Section 505(j)(5)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately, unless an action is brought against Eon Labs, Inc. (Eon) for infringement of one or more of the patents which were the subjects of the paragraph IV certifications. This action must be brought against Eon prior to the expiration of forty-five (45) days from the date the notice you provided under paragraph (2)(B)(i) was received by the patent and NDA holder(s). You have informed the Agency that Eon complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for infringement of the '970, '000, or '493 patents was brought against Eon within the statutory forty-five day period. You have also informed the agency that with regard to the '798 patent, Glaxo Wellcome, Inc. initiated a patent infringement action against Eon in the United States District Court for the Southern District of New York (Glaxo Wellcome, Inc. v. Eon Labs Manufacturing, Inc.), Civil Action No. 00-CIV-9089. With regard to this litigation, the Agency recognizes that the 30-month period identified in Section 505(j)(5)(B)(iii) of the Act, during which time the FDA was precluded from approving your application, has expired.

Please note that approval is being granted for your Bupropion Hydrochloride Extended-release Tablets USP, 150 mg, even though the Office of Generic Drugs received and filed an ANDA containing paragraph IV certifications to the listed patents for this drug product prior to the receipt of your application. Accordingly, your supplemental application would not be eligible for full approval until 180-days following the earlier of one of the following triggering events:

1. the date the Secretary receives notice from the applicant of the previous ANDA that commercial marketing of the 150 mg strength of the drug product approved in that application was initiated, or

2. the date of a decision of a court holding the patents that were the subjects of the paragraph IV certifications to be invalid or not infringed [Section 505(j)(5)(B)(iv)].

We refer you to the Agency's guidance document entitled "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments" (June 1998). However, in a communication dated March 19, 2004, the holder of the ANDA referred to above as being received and filed prior to your application informed the Agency that it has relinquished its eligibility for 180-day exclusivity with respect to the patents listed above for Bupropion Hydrochloride Extended-release Tablets USP, 150 mg. Thus, by relinquishing its eligibility for 180-day generic drug exclusivity, the prior applicant recognizes that the relinquishment will apply to all ANDAs for Bupropion Hydrochloride Extended-release Tablets USP, 150 mg, and that the Office of Generic Drugs may approve any such application without regard to the 180-day exclusivity period specified in Section 505(j)(5)(B)(iv).

Under Section 506(A) of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change can be made.

Post-marketing requirements for this ANDA for Bupropion Hydrochloride Extended-release Tablets USP, 150 mg are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of your Bupropion Hydrochloride Extended-release Tablets USP, 150 mg.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns for the 150 mg strength. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

(b)(6)

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

EXHIBIT C

ANDA 75-410 NOV 1 2002

Kremers Urban Development Company
Attention: Steven R. Pollock
6140 W. Executive Drive
Mequon, WI 53092

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated July 2, 1998, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Omeprazole Delayed-release Capsules, 10 mg and 20 mg.

Reference is also made to our Tentative Approval letters dated May 3, 2001, and October 4, 2002, and to your amendment dated October 31, 2002, requesting that the agency grant final approval to the application.

The listed drug (RLD) referenced in your application, Prilosec Delayed-release Capsules (Prilosec) of AstraZeneca LP (AstraZeneca), is subject to periods of patent protection and exclusivity. As noted in the agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), AstraZeneca's three-year exclusivity with respect to labeling for the use of Prilosec in pediatric patients two years of age and older, (M-19), is due to expire on January 12, 2006. Section 11 of the Best Pharmaceuticals for Children Act (BCPA), signed into law in January 2002, allows certain portions of AstraZeneca's labeling which is subject to pediatric exclusivity protection to be omitted from the labeling of products approved under Section 505(j). The BCPA also permits the incorporation of language in the labeling of products approved under Section 505 (j) that informs health care practitioners that AstraZeneca's drug product has been approved for pediatric use. The agency has determined that the final printed labeling you have submitted with respect to the pediatric use protected by exclusivity (M-19) is in compliance with the BCPA.

In addition, the following patents are scheduled to expire on November 30, 2005, (U.S. Patent No. 4,636,499); October 20, 2007, (U.S Patent Nos. 4,786,505 and 4,853,230); August 2, 2010, (U.S.

Patent No. 5,093,342); August 4, 2014,(U.S. Patent Nos. 5,599,794 and 5,629,305); April 9, 2019, (U.S. Patent Nos. 6,147,103, and 6,191,148); April 9, 2019, (U.S. Patent No. 6,166,213); and May 10, 2019, (U.S. Patent No. 6,150,380). Please note that the expiration dates of the patents listed above have been adjusted to reflect a 6-month extension as provided for under Section 505A of the Act (pediatric exclusivity extension). Throughout this letter, references to individual patents will be made by use of only the last three digits of the patent.

With regard to these patents, your application contains a patent certification under Section 505(j)(2)(A)(viii) of the Act indicating that the '342, '794, and '305 patents are for method of use patents, and that these patents do not claim any of the proposed indications for which you are seeking approval. In addition, your application contains paragraph IV certifications under Section 505(j)(2)(A)(vii)(IV) of the Act to the '499, '505, '230, '103, '380, '213, and '148 patents stating that your manufacture, use or sale of either strength of this drug product will not infringe on these patents, or that these patents are invalid or unenforceable.

Section 505(j)(5)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately unless an action is brought against Kremers Urban Development Company (KUDCO) for infringement of one or more of these patents which are the subject of the certifications. This action must be brought against KUDCO before the expiration of forty-five days from the date the notice you provided to the NDA/patent holder(s) under paragraph(2)(B)(i) was received. You have notified the agency that KUDCO complied with the requirements of Section 505(j)(2)(B) of the Act, and as a result litigation was initiated in the United States District Court for the Eastern District of Wisconsin involving challenges to the '499, '505, '230, '794, '305, and '342 patents (Astra Aktiebolag, Aktiebolaget Hassle, KBI-I Inc., KBI Inc. and AstraZeneca, L.P. v. Kremers Urban Development Co., and Schwarz Pharma Inc.(Civil Action No. 99-C-0131. This litigation was subsequently consolidated with similar litigation pending in various United States District Courts into the United States District Court for the Southern District of New York (Civil Action No. 99-C-0131), Civil Action No.99 Civ. 8928(BSJ) and No. 99 Civ. 9888(BSJ)), In re Omeprazole M-21-81, MDL Docket No. 1291(BSJ).

The agency recognizes that the 30-month period identified in Section 505(j)(5)(B)(iii) of the Act, during which time FDA was precluded from approving your application with respect to the litigation noted in the preceding paragraph, has expired. We also note that no action for patent infringement was brought

against KUDCo within the statutory forty-five day period with respect to the '103, '380, '213, and '148 patents.

Furthermore, the Act provides that approval of an abbreviated new drug application that contains a certification described in section 505(j)(2)(A)(vii)(IV) (a paragraph IV certification) and that provides for approval of the same drug product as that for which another abbreviated application containing a Paragraph IV Certification was previously received, shall be made effective not earlier than one hundred and eighty (180) days after:

1. the date the Secretary receives notice from the applicant of the previous application that commercial marketing of the drug product approved in that application was initiated, or

2. the date of a decision of a court holding the patent which is the subject of the certification to be invalid or not infringed; whichever option occurs first [Section 505(j)(5)(B)(iv)].

The Office of Generic Drugs received and filed ANDAs containing a paragraph IV certification to the various listed patents for Omeprazole Delayed-release Capsules, 10 mg and 20 mg prior to the filing of your application. Accordingly, your application would not be eligible for full approval until 180-days following the earlier of event 1. or 2. noted above. We refer you to the Agency's guidance document entitled "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments" (June 1998).

In a communication dated October 31, 2002, the holders of the ANDAs referenced above as having been received and filed prior to your application informed the Agency that they have relinquished their eligibility for the 180-day exclusivity with respect to Omeprazole Delayed-release Capsules, 10 mg and 20 mg. Thus, by relinquishing their eligibility for 180-day exclusivity, the Office of Generic Drugs is permitted to approve any ANDA for these drug products that is otherwise ready for approval, without regard to the 180-day exclusivity period specified in Section 505(j)(5)(B)(iv).

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Omeprazole Delayed-release Capsules, 10 mg and 20 mg, to be bioequivalent, and therefore, therapeutically equivalent to the listed drug (Prilosec Delayed-release Capsules, 10 mg and 20 mg, of AstraZeneca LP). The FDA recommended

dissolution and acid-resistance testing should be incorporated into your stability and quality control programs. In "interim" tests and tolerances are:

(i) The dissolution testing should be conducted in 900 mL of 0.1N HCl for 2 hours [Acid stage]; followed by 900 mL of 0.05M phosphate buffer, pH 6.8 [Buffer stage], at 37°C using USP apparatus I (basket) at 100 rpm. The test product should meet the following specification:

> NLT [redacted] (Q) of the drug in the capsule is dissolved in 45 minutes [at the end of the Buffer stage].

(ii) Separate acid resistance testing should be conducted in 900 mL of 0.1N HCl for 2 hours [Acid stage]. The omeprazole content of the granules should be analyzed at the end of the Acid stage, and the test product should meet the following specification:

> NMT [redacted] of the drug in the capsule is dissolved in 120 minutes, as determined by the difference between the average potency assay (without acid exposure) and the potency assay of the remaining granules at the end of the Acid stage.

The "interim" dissolution test and tolerances should be finalized by submitting dissolution data for the first three production size batches in a supplemental application. The supplemental application should be submitted under Section 505(j) of the Act as a Changes Being Effected (CBE-0) supplement when there are no revisions to the interim specifications or when the final specifications are tighter than the interim specifications. In all other instances the supplement should be submitted under 505(j) of the Act as a prior approval supplement.

Under Section 506(A) of the Act, certain changes in the conditions described in this ANDA require approved supplemental application before the change may be made.

Post-marketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that your submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FDA 2253

(Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

/S/

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

11/1/02

EXHIBIT D

04 June 2004

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Summary

Ever since it first came to market in 1993, the anticonvulsant drug Neurontin has consistently been one of Pfizer's top earners, generating considerable sales and driving strong growth for the New Yor

Ever since it first came to market in 1993, the anticonvulsant drug Neurontin has consistently been one of Pfizer's top earners, generating considerable sales and driving strong growth for the New York-based company. With this drug set to lose patent protection Pfizer is gearing up to launch its replacement. Datamonitor investigates whether pregabalin will allow Pfizer to maintain its market share.

In the brief **Pregabalin: Follow-On Strategy a Winner for Pfizer** Datamonitor analyzes why **Pfizer** s developing pregabalin, through analysis of the blockbuster Neurontin. It predicts the outlook of pregabalin in three main markets it is expected to enter; namely epilepsy, anxiety, and neuropathic pain, by analyzing clinical trial data and competitive activity. The pros and cons of off-label prescriptions are discussed, and forecasts are provided for Neurontin and pregabalin to 2010.

Neurontin, whose active ingredient is gabapentin, is approved in more than fifty countries worldwide for a variety of indications, including the adjunctive treatment of epilepsy and a range of neuropathic pain conditions. Since its launch, the treatment has rapidly grown to blockbuster status generating sales of over $2 billion in 2002 alone. But the imminent loss of patent protection means that this cash cow will soon be subject to imminent challenges from cheap copycat versions from generic manufacturers.

Delaying tactics

In order to stave off this threat and so maintain and grow its share of the anticonvulsant market, Pfizer must ensure that a follow-on pregabalin compound is launched before Neurontin loses its patent. Such a strategy would be typical of Pfizer, which has maintained leadership in other CNS markets, such as depression and pain, through the successful launch of follow-on products.

Neurontin's patent originally expired in 2001, although, just prior to this, Pfizer produced a production patent that granted the drug protection until 2014. However, this patent has since been challenged by several generic manufacturers in the courts, with accusations that Pfizer was illegally seeking to perpetuate their monopoly on the drug.

In response, Pfizer has sued the generic manufacturers to prevent them from manufacturing generic versions of Neurontin. Pfizer has therefore secured itself additional time to effectively prepare pregabalin for launch. The company is doubtless aware that as soon as Neurontin finally loses patent protection sales will drop dramatically.

The FDA has already granted **Alpharma** market exclusivity for generic gabapentin. The exclusivity currently applies to 100mg, 300mg and 400mg capsules, but the company anticipates that the FDA will extend it to include 600mg and 800mg gabapentin tablets as well. Alpharma, however, expected to wait for a court ruling on the validity of Pfizer's production patent before entering the market.

Pregabalin groundwork

Like Neurontin, its planned replacement is a 3-substituted analog of gamma-amino butyric acid (GABA). It is thought the two compounds share similar mechanisms of action, binding to the calcium channels, modulating calcium influx, and resulting in analgesic, anxiolytic, and anticonvulsant activity. Studies have shown two key differences between the drugs: Pregabalin provides equivalent efficacy at lower doses, and because of this, pregabalin is unlikely to be associated with dose-related adverse events, such as fatigue.

Pfizer has already begun laying the groundwork for pregabalin's product lifecycle by using Neurontin to establish its position in a number of key markets. Pfizer's strategy is to establish Neurontin in markets that pregabalin will be launched into, so the acceptance by physicians of the new compound is high. This has been approached either through an actual indication (e.g. neuropathic pain) or through the publication of clinical trial data to encourage off-label use.

Datamonitor expects off-label prescriptions of pregabalin to be a profitable source of sales, as has been the case with Neurontin. However, this is a risky strategy and Pfizer must consider several key issues surrounding off-label usage to avoid negative publicity.

Off-label use refers to the use of an approved drug for any purpose other than what is described in the drug's labeling, and over 70% of Neurontin sales come from off-label prescriptions. In essence, the more versatile a drug is, the greater its revenue generating potential, and Pfizer expects pregabalin will be used as a safer alternative to Neurontin.

Another blockbuster?

However, to avoid lawsuits, loss of reputation and bad publicity, Datamonitor recommends that Pfizer drives off-label pregabalin usage through the presentation of clinical information in respected peer-reviewed medical journals and independent clinical studies.

Datamonitor believes pregabalin will provide Pfizer with yet another blockbuster product. Sales are expected to cannibalize Neurontin following launch in 2003, as Pfizer minimizes generic erosion by convincing physicians to switch therapies. Datamonitor forecasts pregabalin to achieve blockbuster sales by 2010.

Due to the fact it offers a superior clinical profile to its predecessor, physicians are expected to switch from full priced Neurontin to pregabalin. While Neurontin is only indicated as an adjunctive therapy in the treatment of partial seizures in epilepsy, wider approved treatment indications will ensure a greater patient potential for pregabalin and allow Pfizer to market the new drug directly to physicians and patients for these indications, rather than depend on off-label use.

If you found this week's Expert View useful, you may be interested in Datamonitor's reports, all available from www.datamonitor.com/healthcare/

- · **Pregabalin:** Follow-On Strategy a Winner for Pfizer priced $1,500
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Michael Randle

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