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Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

**Comment of Apotex Corp. In Response To
Docket No. 2004N-0087: Request For Public Comment On
Additional Regulatory Action Concerning The Approval Of ANDAs**

Apotex Corp. ("Apotex") develops and manufactures generic prescription drugs for sale in the United States, subject to the requirements of the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §§ 301 *et seq.*, as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended at 21 U.S.C. § 355 and 35 U.S.C. § 271) (more commonly known as "the Hatch-Waxman Amendments" or "Hatch-Waxman"). Apotex respectfully submits this comment in response to the Food and Drug Administration's ("FDA") March 3, 2004, request for public comment (Docket No. 2004N-0087) on whether additional regulatory actions should be taken concerning the approval of abbreviated new drug applications ("ANDAs") in view of recent amendments to Hatch-Waxman.

Introduction

On December 8, 2003, President Bush signed into law the Medicare Prescription Drug Improvement and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2016, Sec. 1102(b)(2) (2003) (amending 21 U.S.C. § 355 and 35 U.S.C. § 271) ("the Medicare Act"), in which Congress revisited Hatch-Waxman for the first time since 1984. Title XI of the Medicare Act, entitled "Access to Affordable Pharmaceuticals," made changes to sections 505(a), (b) and (j) of the FDCA (21 U.S.C. §§ 355(a), (b) and (j)) in order to, among other things: (1) eliminate the multiple and unwarranted automatic 30-month stays that brand-name companies had used to delay generic competition; and, (2) just as importantly, further promote and encourage generic competition by securing and protecting 180-day generic marketing exclusivity.

Congress originally enacted this powerful exclusivity incentive to increase generic competition by "encourage[ing] generic drug makers to incur the potentially substantial litigation costs associated with challenging pioneer drug makers' patents." *Mylan Pharms., Inc. v. Shalala*, 81 F. Supp. 2d 30, 33 (D.D.C. 2000); *see also Purepac*

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Pharm. Co. v. Thompson, 354 F.3d 877, 878 (D.C. Cir. 2004) (“To encourage the marketing of low-cost generic drugs, the 1984 Hatch-Waxman Amendments to the Food, Drug, and Cosmetic Act grant companies that successfully challenge drug patents the right to sell their generic drugs without competition for 180 days.”). In the recent amendments to Hatch-Waxman, Congress reaffirmed that the 180-day exclusivity statutory entitlement is an indispensable part of the carefully crafted Hatch-Waxman balance of protecting legitimate patent rights (thus encouraging innovation) and promoting early generic entry (thus providing lower-priced generic drugs to the consuming public). In its request for public comment, FDA stated that it is considering what additional regulatory steps, if any, are warranted in light of these statutory changes.

Apotex submits this comment to address a clear and present threat to the generic drug industry that has placed the 180-day exclusivity incentive in serious jeopardy: namely, the marketing and distribution of so-called “authorized generic” versions of branded drugs during the first ANDA applicant’s 180-day exclusivity period under 21 U.S.C. § 355(j)(5)(B)(iv). By “authorized generic,” we mean, for example, a licensed, private-label version of the brand-name product that is manufactured by the brand-name company under its NDA, but sold and passed off by the licensee as a “generic”—which is launched and marketed during the first ANDA applicant’s 180-day exclusivity period. The purpose of the “authorized generic” is manifest: to cripple and eliminate any benefit derived from the ANDA applicant’s 180-day exclusivity. The danger to the industry presented by authorized generics has already been recognized by the Generic Pharmaceutical Association, whose Board of Directors voted overwhelmingly at the 2004 annual meeting to oppose the use of authorized generics during the 180-day exclusivity period.

To prevent further erosion of the 180-day exclusivity entitlement and reward that Congress intended and that the Medicare Act was designed, in part, to protect, Apotex proposes that FDA implement a policy prohibiting the marketing and distribution of any “authorized generic” version of a brand-name product until the expiration of any 180-day generic marketing exclusivity to which an ANDA applicant is statutory entitled.

I. Authorized Generics Violate The Letter And Spirit Of Hatch-Waxman.

The practice of marketing authorized generics during the 180-day exclusivity period violates the letter and intent of Hatch-Waxman. Under any reasonable interpretation of the statute, approving an authorized generic for marketing during a first applicant’s exclusivity period denies that applicant the marketing exclusivity to which it is statutorily entitled.

The statute, as amended, now explicitly acknowledges and defines the term “180-day exclusivity period” as follows:

- (II) DEFINITIONS— In this paragraph
- (aa) 180-DAY EXCLUSIVITY PERIOD— The term ‘180-day exclusivity period’ means the 180-day

period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.

21 U.S.C. § 355(j)(5)(B)(iv)(II), as amended. In turn, this language refers to the immediately-preceding clause:

(iv) 180-DAY EXCLUSIVITY PERIOD—

(I) EFFECTIVENESS OF APPLICATION— Subject to subparagraph (D) [relating to forfeiture], 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.

21 U.S.C. § 355(j)(5)(B)(iv)(I), as amended. In sum, the 180-day exclusivity period is defined clearly as the period of time during which FDA is prohibited from finally approving ANDAs other than the first applicant's. Notably, however, the 180-day exclusivity period is not defined as necessarily arising from the prohibition on FDA's approval of later-filed ANDAs under section 355(j)(5)(B)(iv)(I). Stated otherwise, the 180-day exclusivity period is defined only by its duration and the fact that it is an "exclusivity" period.

Any reasonable interpretation of the term "exclusivity" means an exclusivity against all generics, including "authorized generics." By definition, a shared exclusivity with an authorized generic is not an "exclusivity" at all. But FDA's current interpretation of section 355(j)(5)(B)(iv) allows brand-name companies to render any exclusivity utterly meaningless, because FDA would allow them to license not only one authorized generic licensee, but any number of third-parties to share the first ANDA applicant's valuable exclusivity. This simply cannot be correct. The Medicare Act was enacted, in part, to prevent further erosion of this important statutory entitlement of exclusivity. The marketing of any authorized generic during the 180-day exclusivity period is inconsistent with the concept of "exclusivity," and threatens to obliterate this entitlement altogether.

That such arrangements are inconsistent with the plain meaning of section 355(j)(5)(B)(iv) is most evident where an authorized generic licensee previously filed its own ANDA containing a paragraph IV certification for the drug that it proposes to sell under license from the brand-name company. In such a case, this late-filing generic applicant purports to end-run the 180-day exclusivity period by abandoning its ANDA for a license under the brand-name company's NDA and selling an "authorized generic," thus nullifying the statutory benefit of the true first applicant that undertook the

substantial risks and costs of designing around or invalidating blocking patents. Congress clearly did not intend for such gaming of the system.

In addition, the statutory language creating the first generic applicant's 180-day exclusivity period is similar to the language creating Hatch-Waxman's new chemical entity exclusivity under section 355(c)(3)(E) and the pediatric exclusivity under section 355a. The 180-day exclusivity is no less an exclusivity than those other exclusivities created by Congress to offer incentives to brand-name companies. FDA should not countenance brand-name companies' efforts to devalue and erode that exclusivity through the use of authorized generics.

II. FDA Already Treats "Authorized Generics" As True Generics Under The Statute And Regulations, And So Should Compel "Authorized Generics" To Respect 180-Day Exclusivity Rights.

On August 9, 2000, Teva Pharmaceuticals USA, Inc. submitted a Citizen Petition arguing that Mylan Pharmaceuticals, Inc.'s ("Mylan") 180-day exclusivity period was triggered by Mylan's marketing of Pfizer's extended-release nifedipine tablets under Pfizer's NDA—in other words, an "authorized generic" version of Pfizer's NDA product. *See* Teva's 8/9/2000 Citizen Petition (Docket No. 00P-1446, entered on August 11, 2000). FDA agreed with Teva that Mylan's marketing of a "generic," whether under its own ANDA or Pfizer's NDA, triggered the exclusivity. *See* FDA 2/6/2001 Resp. to Teva Citizen Petition (Docket No. 00P-1446, entered on March 5, 2001). FDA explained:

Whether Mylan markets the product approved in its ANDA or the product approved in Pfizer's NDA is of little import to the statutory scheme; Mylan has begun commercial marketing of generic nifedipine. Permitting Mylan to market nifedipine without triggering the beginning of exclusivity would be inconsistent with the intent of the statutory scheme.

Id. at 7-8; *see also Mylan Pharms., Inc. v. Thompson*, 207 F. Supp. 2d 476, 488 (N.D. W. Va. 2001) (quoting FDA's response to Teva's Citizen Petition). Thus, FDA treated the "authorized generic" as a true generic for exclusivity purposes, and refused to permit an end-run around the strictures of section 355(j)(5)(B)(iv) through such an arrangement.

The same reasoning applies with equal force here. If an "authorized generic" is treated as a true generic under the statute for exclusivity purposes and is not permitted to avoid the triggering mechanism for 180-day exclusivity, then it should not be permitted to avoid another 180-day applicant's exclusivity either. There is no basis in the statute or FDA's regulations to distinguish the two situations. FDA should continue to apply the line of reasoning from *Mylan* by prohibiting the marketing of an authorized generic during the 180-day exclusivity period.

III. Authorized Generics Undermine The Incentives Congress Created For True Generics Under Hatch-Waxman.

By enacting section 355(j)(5)(B)(iv), Congress created an incentive for generic firms to challenge and invent around drug patents, in the form of a 6-month opportunity to be the sole supplier of a generic version of the innovator's drug. Authorized generics, however, rob true generics of this incentive to fulfill the goals of Hatch-Waxman and are designed to cripple the first ANDA applicant's exclusivity.

Indeed, Apotex has already been the target of an authorized generic license agreement for Paxil[®] (paroxetine hydrochloride) that was clearly designed to destroy Apotex's exclusivity. Apotex was the first generic company to file an ANDA for paroxetine containing a paragraph IV certification challenging a listed patent, in this case GlaxoSmithKline's ("GSK") primary blocking patent for paroxetine hydrochloride hemihydrate. As a reward and incentive for undertaking the substantial risk and expense of challenging GSK's patent, Apotex was statutorily entitled to the 180-day exclusivity period for that drug. And in fact, Apotex was sued four different times and subjected to successive 30-month stays arising out of improperly listed GSK patents. Apotex spent years and many millions of dollars defending and prevailing in resource-draining patent litigation against GSK, ultimately invalidating GSK's main blocking patent, as well as several others, for the benefit of entire generic industry. As a result, Apotex reasonably expected to enjoy a true 180-day exclusivity period as Congress intended.

But on the same day Apotex launched its AB-rated generic paroxetine, Par Pharmaceutical, under license from GSK, launched an "authorized generic" version of Paxil[®] under GSK's NDA, though packaged with a "generic" label and sold at a generic price—all calculated to compete with Apotex and destroy its exclusivity. Apotex expected sales for its paroxetine product to be in the range of \$600 million during the 180-day exclusivity period. Given competition from Par's authorized generic product, however, Apotex only generated about \$265 million in total sales. There is no question that Par's "authorized generic," manufactured and supplied by GSK under its NDA, crippled Apotex's 180-day exclusivity, reducing Apotex's entitlement by over half. Par, on the other hand—which had undertaken no risk whatsoever and done nothing to clear the way for generic competition—enjoyed a windfall to the tune of hundreds of millions of dollars for its end-run around Apotex's exclusivity.

IV. Authorized Generics Are Not Pro-Consumer Over The Long Run.

Contrary to claims made by some brand-name companies that authorized generics are pro-consumer, authorized generics are actually anticompetitive in the end because such arrangements significantly devalue 180-day exclusivity and, in turn, eliminate the incentive for true generics to design around and challenge brand patents. In its response to the earlier-mentioned Citizen Petition from Teva, FDA explained that the commercial marketing trigger of the 180-day exclusivity period "is intended to give the first ANDA applicant with a paragraph IV certification the opportunity to market a generic version of the innovator's drug with no competition for 180 days." FDA 2/6/2001 Resp. to Teva

Citizen Petition at 7 (emphasis added). The purpose of section 355(j)(5)(B)(iv), therefore, is to confer an economic benefit on the first generic applicant that has filed a paragraph IV certification, in the form of marketing exclusivity. By granting first applicants this exclusivity period, Congress intended to stimulate the development and marketing of new generic products and, for this reason, the 180-day exclusivity period is best seen as a pro-competitive legislative measure, as its original name clearly indicates: the Drug Price *Competition* and Patent Term Restoration Act. But promoters of authorized generics are attempting to deprive first applicants—and, in turn, the public—of this pro-competitive benefit.

Nor do authorized generics result in the marketing of new and innovative drug products. Rather, all that is accomplished by such arrangement in the long term is a strong disincentive for innovation and challenging invalid patents—the antithesis of the Hatch-Waxman compromise.

V. Authorized Generics Give Brand-Name Companies The Unilateral Right To Do Away With The 180-Day Exclusivity Period.

In its response to Teva's Citizen Petition, FDA also explained that the statute should not be interpreted or applied in a manner that puts the first applicant's entitlement exclusivity in the hands of the patent-holder. *See* FDA 2/6/2001 Resp. to Teva Citizen Petition at 5. But that is precisely what FDA has done by rubberstamping authorized generic arrangements. The brand-name company now has the unilateral power to render meaningless and eviscerate the 180-day exclusivity through the licensing of the listed drug to *one or more* generic competitors.

As Judge Richard W. Roberts of the United States District Court for the District of Columbia recently observed in *TorPharm, Inc. v. FDA*, Civil Action No. 03-2401 (RWR), 2004 U.S. Dist. LEXIS 524 (D.D.C. Jan. 8, 2004) with respect to so-called "shared exclusivity," it would be ironic if Congress meant to give brand-name companies the power to create a shared exclusivity between generic companies by filing additional patents for a drug product when its aim was to get more and cheaper generics on the market faster. Unfortunately, however, that is how FDA is currently regulating with respect to authorized generics.

Consider the case of a brand-name company that has fought generic competition for years, as GSK did in connection with Paxil[®]—in that case, through the relentless listing of questionable patents in the Orange Book. Through such unrelenting anticompetitive efforts, brand-name companies can force generics to incur enormous litigation costs, as GSK did to Apotex. It is patently unreasonable for FDA to then authorize these brand-name companies to frustrate Hatch-Waxman's mechanism for compensating generics for these delays and expenses. If a brand-name company exercises its right under section 355(j)(5)(B)(iii) to stay a generic's ANDA approval by filing an action against that company, it should be precluded from licensing an authorized generic for sale before or during that generic company's 180-day exclusivity period.

Conclusion

For all these reasons, Apotex respectfully suggests that FDA immediately consider changing its approach towards authorized generics. There are various avenues FDA could take, as demonstrated by *Mylan*, that would not require new legislative or rulemaking action to delay the marketing of authorized generics until expiration of the 180-day exclusivity period. Apotex would be delighted to work with FDA and other companies in the generic industry to develop a workable solution.

The Hatch-Waxman Amendments were an "attempt to balance two competing interests: Promoting competition between 'brand name' and 'generic' drugs and encouraging research and innovation." 67 Fed. Reg. 65,447, 65,448 (Oct. 24, 2002). FDA should interpret the statute in a manner that respects the Hatch-Waxman compromise. Apotex submits that FDA's approval of an "authorized generic" drug for marketing during a 180-day exclusivity period obliterates the incentives that Congress chose to give to generic companies to challenge and invent around drug patents. FDA should accordingly implement a policy prohibiting the marketing and distribution of any "authorized generic" version of a brand-name product until the expiration of any 180-day generic marketing exclusivity to which the first ANDA applicant is statutorily entitled.

Respectfully submitted,



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