DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

JUL 2 2004

Stuart A. Williams
Chief Legal Officer
Mylan Pharmaceuticals Inc.
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, W.V. 26505

James N. Czaban
Heller Ehrman
White & McAuliffe LLP
1666 K Street, N.W.
Washington, D.C. 20006

Re: Docket Nos. 2004P-0075/CP1 & 2004P-0261/CP1

Dear Messrs. Williams and Czaban:

This letter responds to the citizen petition submitted by Mylan Pharmaceuticals Inc. (Mylan) dated February 17, 2004 (Mylan Petition), the supplement to the Mylan Petition dated June 28, 2004 (Supplement), and the citizen petition submitted on behalf of Teva Pharmaceuticals USA, Inc. (Teva) dated June 9, 2004 (Teva Petition). The Mylan Petition asks that the Food and Drug Administration (FDA or the Agency) prohibit the marketing and distribution of "'authorized generic' versions of brand name products" until after the expiration of any "180-day exclusivity"[1] applicable to an abbreviated new drug application (ANDA) for the drug product. The Teva Petition asks that the Agency: (1) require Pfizer Inc. (Pfizer) to submit a pre-approval supplemental new drug application (sNDA) before marketing or distributing any version of its Accupril (quinapril) product changed in any way "such that the product purports to be, resembles, or could be

[1] *See* 21 U.S.C. 355(j)(5)(B)(iv); 21 C.F.R. 314.107(c). Amendments made to section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Pub. L. 108-173) (MMA) altered the eligibility requirements and triggering events for 180-day exclusivity and established circumstances under which forfeiture of exclusivity can occur. The MMA did not, however, substantively alter the statutory language upon which the Agency has based its determination that it is permissible to market an authorized generic during a 180-day exclusivity period applicable to that drug product under an ANDA. Also, the relevant Title XI provisions concerning 180-day exclusivity apply only to drug products for which the first ANDA containing a paragraph IV certification to a listed patent was submitted after December 8, 2003. *See* MMA, Pub. L. No. 108-173, section 1102(b)(1), 117 Stat. 2066, 2460 (2003). Accordingly, the non-amended version of section 505(j)(5)(B)(iv) governs 180-day exclusivity for Accupril/quinapril. The Agency requested public comment regarding the need for regulatory action to address these and other amendments made to section 505 by the MMA. *See* 69 FR 9982 (March 3, 2004) (comments were due by May 3, 2004).

confused with, a generic (unbranded) version of Accupril"; and (2) delay approval of such an sNDA until the expiration of Teva's 180-day exclusivity period for its generic quinapril drug products. This letter also considers the comments submitted on behalf of Apotex Corp. (Apotex), by Johnson & Johnson, by the Generic Pharmaceutical Association, and on behalf of Pfizer, dated, respectively, March 24, May 11, May 21, and June 23, 2004.

The Agency understands the marketing of "authorized generics" to refer to the marketing of a product approved under a new drug application (NDA), by that NDA holder, under that NDA, but at a lower price and not under the "brand" name, possibly through a different channel of distribution.[2] Because removing the brand name or changing the channel of distribution is unlikely to pose any threats to the public health, FDA has made clear that applicants generally need not submit any pre-approval notification to the Agency for these changes. FDA does not regulate drug prices and has no legal basis on which to prevent an innovator company from marketing its approved NDA product at a price that is competitive with that charged by a first generic applicant to the market. Nothing in the Federal Food, Drug, and Cosmetic Act (the Act) authorizes FDA to prohibit categorically the marketing of authorized generics during 180-day exclusivity periods. Rather, the Act authorizes the Agency to ensure that any manufacturing changes made to enable the marketing of approved new drugs do not adversely affect the safety or efficacy of the product. FDA does not and cannot use that authority to regulate competition in a manner that has little or no relationship to the public health.

Petitioners argue that specific statutory authorities to approve drug products, to require their listing, and to regulate manufacturing changes, as well as general authorities to enforce the Act, can be used to delay the marketing of authorized generics until after the expiration of 180-day exclusivity periods. Petitioners further contend that existing Agency policy and established principles of statutory construction governing the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman amendments) compel FDA to delay the marketing of authorized generics in this manner. For reasons of both law and policy, we are not persuaded by these arguments. Not only does FDA lack authority to justify delaying the marketing of authorized generics solely to protect 180-day exclusivity, the Agency does not believe their marketing should be delayed in this manner, as this marketing appears to promote competition in the pharmaceutical marketplace, in furtherance of a fundamental objective of the Hatch-Waxman amendments. Accordingly, we deny the petitioners' requests.

---

[2] For convenience, the term "authorized generic" is used throughout this response. Solely for purposes of this response, the Agency defines the term (consistent with the scope of activities it understands the petitioners challenge) as any marketing by an NDA holder or authorized by an NDA holder, including through a third-party distributor, of the drug product approved under the NDA in a manner equivalent to the marketing practices of holders of an approved ANDA for that drug. For example, an NDA holder might change the product's label or imprint (*e.g.*, to reference a distributor) or market the product through commercial channels routinely used by generics. We understand the essential distinction that is of concern to petitioners in the marketing of an authorized generic is the lowering of the price for this version of the drug product relative to the price of the brand version sold by the NDA holder under the same NDA.

I. An Overview of Regulatory Controls on Marketing of Approved New Drugs During 180-Day Exclusivity Periods

Pharmaceutical companies make a variety of competitive arrangements to market their approved products, without interference from FDA. For example, holders of approved ANDAs routinely arrange with other parties, such as other drug manufacturers, to distribute the ANDA holder's approved product, including under the distributing entity's label or trade name. The parties might enter into such arrangements for numerous reasons, such as to expand the ANDA holder's marketing capacity or ability to service a geographic market, or to fill a gap in the distributor's product line.

The Agency is aware that NDA holders also make various arrangements to market and distribute their products. These include selling authorized generic versions of their products at a reduced price, as patent and other marketing exclusivities expire and ANDA applicants begin to be able to market their own, lower-priced versions of the drug. In particular, NDA holders sometimes market authorized generic versions of their products during 180-day exclusivity periods in which eligible ANDA applicants can market their versions of the drug without competition from certain other applicants.

FDA ordinarily does not regulate or restrict these business arrangements. As a general matter, the Act does not authorize the Agency to regulate directly the timing for marketing of previously approved drug products, including whether such NDA products may be marketed during 180-day exclusivity periods applicable to an ANDA for the drug.

Specifically, section 505(j)(5)(B)(iv) of the Act provides only that a first ANDA applicant to include with its application a certification of its belief that a patent is invalid or not infringed by its product (a "paragraph IV" certification)[3] becomes eligible to market its product for 180 days before subsequent ANDA applicants that have made paragraph IV certifications may obtain marketing approval. 21 U.S.C. 355(j)(5)(B)(iv). Like other provisions of the Act establishing forms of marketing exclusivity,[4] section 505(j)(5)(B)(iv) provides for the delaying of product approval only for specific categories of applicants—in this case subsequent ANDA applicants that make paragraph IV certifications. The provision does not contemplate or countenance delaying the marketing of authorized generics. Nor does it delay the marketing of products approved

---

[3] More precisely, an ANDA applicant submitting a "paragraph IV" certification (named for the statutory paragraph establishing the certification requirement) asserts that the listed patent (i.e., the patent listed in *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book) as claiming the approved drug (listed drug) on which the ANDA relies) is invalid and/or that the ANDA applicant's product does not infringe it. *See* section 505(j)(2)(A)(viii) of the Act; 54 FR 28,872, 28,885-88 (July 10, 1989).

[4] *See* 21 U.S.C. 355(c)(3)(D), (j)(5)(D) (establishing exclusivity periods to benefit the first applicants to market new chemical entities and to market products supported by new clinical investigations); *see also* 21 U.S.C. 355a(a), (c) (extending exclusivity periods to benefit applicants who have submitted pediatric studies). These exclusivity provisions delay the marketing of products approved under ANDAs or pursuant to section 505(b)(2) of the Act.

pursuant to section 505(b)(2) of the Act (21 U.S.C. 355(b)(2), under which an applicant may rely, in part, upon data or information that the applicant does not own and/or to which it does not have a right of reference), or even of all later ANDAs under some circumstances.[5] As discussed more fully below, we see no statutory basis for broadening the reach of this exclusivity beyond that which Congress expressly established.[6]

FDA has authority to regulate changes made to an approved product, but this authority does not permit the Agency categorically to prohibit or delay the marketing of the product with those changes, except as appropriate to ensure the safety and effectiveness of the product. Section 506A of the Act establishes requirements for notice, approval, and validation of "manufacturing"[7] changes, as appropriate to address the potential "effects of the change on the identity, strength, quality, purity or potency of the drug as [these characteristics] may relate to the safety or effectiveness of the drug." *See* 21 U.S.C. 356a(c)(2). The Act specifically authorizes the Agency to permit applicants to notify in their annual reports non-"major" changes.[8] In its regulations, the Agency has identified categories of manufacturing changes to be described in annual reports. 21 C.F.R. 314.70(d), (g)(3). Examples include editorial and other minor labeling changes, the addition of code imprints on a solid dosage form, or minor changes to imprints. *Id.* In guidance, the agency has identified examples of such minor changes, including labeling changes to add a distributor's name. *See* FDA guidance for industry on *Changes to an Approved NDA or ANDA* at 26 (April 2004) (FDA's guidances are available on the Internet at http://www.fda.gov/cder/guidance/index.htm).

In addition, section 510 of the Act requires manufacturers and distributors to update their drug listings with the Agency if any changes are made to product characteristics that

---

[5] If the patent claims a use of the product, as opposed to the product itself, an ANDA applicant may be able to "carve out" from its own labeling the portion of the labeling for the listed drug relating to the use. As a result, an ANDA applicant may be able to avoid having to make a paragraph IV certification, but still potentially be able to market the product (without the labeling relating to the patented use) during the patent term (and, thereby, during the 180-day exclusivity period). *See* 21 U.S.C. 355(j)(2)(A)(v); 21 C.F.R. 314.94(a)(8)(iv), 314.127(a)(7).

[6] We note as well that petitioners' request for the Agency to prevent marketing of authorized generics until after applicable 180-day exclusivity periods, in fact, requests a ban on marketing of authorized generics for substantially more than a 180-day period. The 180-day exclusivity period does not begin until patent protection and other marketing exclusivities no longer apply to the reference listed drug. Accordingly, although we are not aware of any instances in which NDA holders have attempted to market authorized generic versions of their product substantially earlier, preventing the marketing of an authorized generic until after the applicable 180-day exclusivity period expires could require prohibiting the marketing of such alternate versions of the NDA holder's product for several years before the 180-day exclusivity period would begin.

[7] Agency regulations refer to these changes as "supplements and other changes to an approved product." 21 C.F.R. 314.70.

[8] *See* 21 U.S.C. 356a(d)(2)(B). Major changes are those the agency has determined have a "substantial potential to adversely affect the identity, strength, quality, purity, or potency of the drug as [these characteristics] may relate to the safety or effectiveness of a drug." 21 U.S.C. 356a(c)(2).

clearly distinguish one version of the product from another. 21 U.S.C. 360(j)(2)(D). Agency regulations further clarify that registrants must update their drug listings "[i]f any change occurs in those product characteristics that clearly distinguish one product version from another" and, therefore, requires a new NDC (new drug code) number. 21 C.F.R. 207.35(b)(4). An NDC number is composed of three segments, identifying the manufacturer or distributor, the drug formulation, and the trade package size and type.

Accordingly, as appropriate to ensure the safety and efficacy of marketed drug products, FDA oversees the changes that holders of approved ANDAs and NDAs make to their products to enable the marketing arrangements they wish to pursue. *See* 21 U.S.C. 356a; 21 C.F.R. 314.70. Typically, such changes may include adjustments to the label (for example, to indicate a distributor) and alteration of the imprint on the dosage form (for example, to that of a distributor). Ordinarily, these changes do not raise significant safety or efficacy concerns; they do not substantively alter the content of the label or make the dosage form any less safe or effective. Consequently, consistent with section 506A (and section 505) of the Act and with the Agency's regulations, FDA generally permits the ANDA or NDA holder to notify the Agency of such changes in that registrant's annual report. *See* 21 U.S.C. 356a; 21 C.F.R. 314.70; *Changes to an Approved NDA or ANDA* at 15, 26. However, changes to the product label or imprint to indicate the distributor, for example, "clearly distinguish" the version of the product and, therefore, the distributor or manufacturer, as appropriate, must update its drug listing with the Agency in accordance with section 510 of the Act. 21 U.S.C. 360; 21 C.F.R. 207.

FDA does not consider the underlying marketing objectives or the competitive implications of the changes being made, only their implications for the public health. ANDA applicants routinely and frequently make such minor manufacturing changes to facilitate distribution arrangements with third parties. Accordingly, the great majority of notifications reflect changes made by these applicants. However, NDA holders have long made such manufacturing changes as well. Although the Agency does not track what marketing considerations might have prompted the changes made, we are aware of numerous instances over many years in which NDA holders have made such changes to enable marketing of authorized generics.[9]

Significant changes to Agency policies on manufacturing changes might require a notice and comment rulemaking. *See, e.g., Alaska Professional Hunters Ass'n v. FAA*, 177 F.3d

[9] Examples include: in 1992-93, Stewart Pharmaceuticals Division of ICI Americas (now AstraZeneca LP) arranging for marketing of an authorized version of Nolvadex (tamoxifen) by Barr Laboratories Inc. (Barr); in 1994, Smith Kline Beecham Pharmaceuticals (now GlaxoSmithKline (GSK)) arranging for marketing of an authorized generic version of Dyazide (triamterene/hydrochlorothiazide); in 1995, marketing by Dey LP of an authorized generic version of GSK's Ventolin (albuterol) inhaler, and by Warrick Pharmaceuticals (a subsidiary of Schering Corp.) of an authorized generic of Schering's Proventil (albuterol) inhaler; Barr's marketing of an authorized generic of Bayer Pharmaceuticals Corp.'s Cipro (ciprofloxacin) in 1997; Mylan Laboratories Inc.'s marketing of an authorized generic of Pfizer Inc.'s Procardia XL (nifedipine) in 1999; Par Pharmaceuticals Inc.'s marketing of an authorized generic of GSK's Paxil (paroxetine hydrochloride) and Glucophage (metformin hydrochloride) in 2003; and in 2004, Watson Pharmaceuticals Inc.'s marketing of an authorized generic of Proctor and Gamble Pharmaceuticals Inc.'s Macrobid (nitrofurantion) and Teva's marketing of an authorized generic of Bristol-Myers Squibb Co.'s Paraplatin (carboplatin).

1030 (D.C. Cir. 1999). In any event, we believe our policy is consistent with the scope and nature of FDA's statutory authority and the Agency's public health mission. Moreover, this approach enables the Agency to avoid becoming unnecessarily and inappropriately involved with private business arrangements or their marketplace effects.

II. Petitioners Offer No Persuasive Arguments in Support of Agency Authority to Prohibit the Marketing of Authorized Generics During 180-Day Exclusivity Periods

The Mylan and Teva Petitions offer various proposals to establish approval requirements and other measures to delay the marketing of authorized generics until after the expiration of any 180-day exclusivity period applicable to an ANDA for the drug product. As explained below, existing statutory and regulatory authority would not permit FDA to institute any of these proposed measures. Further, the petitioners are incorrect that marketing of authorized generics during a 180-day exclusivity period contravenes existing Agency policy or established principles of statutory construction.

A. Approval Requirements

Mylan proposes that the Agency establish an approval process for authorized generic products under which the sponsors would be required to submit pre-approval supplements for certain changes. Certain products would receive only tentative approval if there were an ANDA applicant eligible for 180-day exclusivity for the same drug product. The Agency would grant final approval for the change only when any 180-day exclusivity period had expired. Mylan asserts that this process is necessary to protect the statutory 180-day exclusivity incentive, that authorized generics are marketed like products approved under ANDAs, and, therefore, authorized generics should also be approved and subject to 180-day exclusivity.

Section 505 of the Act forbids the marketing of a new drug that has not been approved under either an NDA in accordance with subsection 505(b), or an ANDA in accordance with subsection 505(j). 21 U.S.C. 505(a). Nowhere does the Act, however, prohibit an ANDA or NDA holder's use of alternative marketing practices for its own approved new drug (so long as any related manufacturing changes do not pose safety or effectiveness concerns as discussed above).

Further, it is well-settled law that a separate approval is not required as a general matter for third-party distribution of an approved drug. In *United States v. Kaybel*, 430 F.2d 1346 (3d. Cir. 1970), the Third Circuit Court of Appeals found that the repackaging of an approved solid oral dosage form drug did not require a separate drug approval, stating that "it would require an unwarranted distortion of the normally understood meaning of this rather simple language [of section 505(a) of the Act] . . . to characterize the product marketed by the [repackagers] . . . as a drug different from the 'new drug' for which approval already had been obtained . . . ." *Kaybel*, 430 F.2d at 1347. The court's reasoning clearly extends to the authorized distribution by a third party of an NDA holder's product (let alone to alternate marketing practices adopted by the NDA holder

itself) where the drug is packaged and labeled before it leaves the NDA holder's facility and is distributed exactly as received. Accordingly, public health considerations would provide even less justification for Agency efforts to impose approval requirements for the marketing of authorized generics.

Section 505(d) establishes numerous, express grounds for refusal to approve applications, and section 505(e) establishes numerous grounds for compelling the withdrawal of previously approved products. However, neither provision addresses marketing arrangements in any manner. *See* 21 U.S.C. 355(d), (e). Further, a third party need not have its own FDA-approved drug application to ship or sell an FDA-approved drug product in domestic commerce. Indeed, Congress has enacted several provisions in the Act that specifically address wholesale distribution of drug products by such parties. *See, e.g.*, 21 U.S.C. 353(e)(1)(A), (2)(A).

The Agency has authority to alter its product review and approval procedures to ensure the safety and effectiveness of drug products. If such a change to Agency procedures were warranted, the Agency could undertake the appropriate administrative and regulatory process to address particular safety or efficacy concerns raised by authorized, third-party marketing of approved new drugs, or other practices associated with the marketing of authorized generics (as well as with distribution of products under ANDAs). However, the Agency has no existing statutory authority to establish approval requirements for authorized generics solely to prevent their marketing in anticipation of—and during—a 180-day exclusivity period.[10]

In short, there is no statutory basis for imposing categorical approval requirements for the marketing of authorized generics, as a means to prevent their marketing during a 180-day exclusivity period applicable to the drug under an ANDA.[11]

B. Statutory Listing Requirements

The Mylan Petition asserts that existing authority allows the Agency to require listing of authorized generics and to forbid their marketing until the expiration of any 180-day

---

[10] Mylan argues that 21 CFR 314.101 provides FDA with discretion to accept applications for authorized generic products. Section 314.101 expressly states that, as a general matter, the Agency will not accept an ANDA for a drug product that "is already covered by an approved application" held by the ANDA applicant or if the ANDA applicant is "merely a distributor and/or repackager of the already approved drug." § 314.101(d)(8). FDA has in the past permitted holders of approved drug applications to obtain ANDAs for their already approved drug products. However, the Agency retains the regulatory authority to refuse to file such applications and does not believe that it has the legal authority to compel NDA holders to submit such applications to market or arrange for distribution of an authorized generic. Further, the Agency continues to consider it unnecessary and inappropriate for third parties to obtain a separate drug approval merely to market an already approved product as authorized by the holder of the existing drug approval.

[11] Where a statutory provision is silent or ambiguous, the Agency may apply a permissible interpretation. *See Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060, 1068 (D.C. Cir. 1998) (citing *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 843 (1984)).

exclusivity period for the drug based on this listing requirement. As noted above, listing of authorized generics is required if the labeling, imprint, or other changes produce a "clearly distinguishable" version of the product. *See* 21 U.S.C. 360(j)(2)(D); 21 C.F.R. 207.35(b)(4). These are ministerial, record-keeping requirements, however, that enable the Agency to monitor the marketing of products and take action as needed to address public health concerns.[12] The Agency does not approve drug listings or updates to them. These drug listing requirements do not allow the Agency to delay the marketing of authorized generics to protect 180-day exclusivity.

C. Requiring and Delaying Approval of sNDAs

The Teva Petition argues that the Agency can and should exercise its authority under section 506A of the Act to (1) require NDA holders to submit sNDAs if they wish to market or distribute a version of their product that "purports to be, resembles, or could be confused with, a generic (unbranded) version" during a 180-day exclusivity period, and (2) delay approving these sNDAs until the exclusivity period expires. Teva Petition at 1.

Section 506A does not allow the Agency to require pre-approval of the kinds of manufacturing changes typically associated with the marketing of an authorized generic. As noted above, such changes might include changing the imprint or the labeling of the product. Agency regulations generally characterize such changes as "minor" and permit applicants to notify FDA of these changes in their annual reports. *See* 21 C.F.R. 314.70(d), (g)(3); *see also Changes to an Approved NDA or ANDA* at 16, 25. Teva argues that such changes should not be considered "minor" when made to enable an NDA holder to market a "generic" version of its product because that marketing "significantly harms" ANDA applicants eligible for 180-day exclusivity. Teva Petition at 12.

As explained above, section 506A establishes requirements to address the potential of a manufacturing change to affect "the identity, strength, quality, purity, and potency of the drug as [these characteristics] may relate to the safety or effectiveness of the drug." 21 U.S.C. 356a(c)(2). Accordingly, FDA sees no basis for inferring any statutory authorization for the Agency to delay implementation of a manufacturing change except as appropriate to address any potential the change may have to affect the safety or effectiveness of the product. *See* 21 U.S.C. 356a(c)(2); 69 FR 18,728 (April 8, 2004). As noted above, significant revision of this Agency policy could require notice and comment rulemaking. In any event, the Agency does not agree that this statutory authority can be relied upon to delay categorically the marketing of authorized generics until after the expiration of 180-day exclusivity periods.[13]

---

[12] *See* 66 FR 59,138-39 (November 27, 2001) (explaining the rationale for expanding registration requirements to foreign establishments to ensure consistent compliance with drug listing requirements and the Agency's ability to track the source of specific products as needed to address safety and effectiveness considerations).

[13] Teva argues in the alternative that FDA could impose sNDA requirements for such manufacturing changes under section 506A(d) even if the changes are deemed "minor." This argument fails, however, for the same reason, that section 506A authorizes the Agency only to address the potential that a change will adversely affect "the identity, strength, quality, purity, or potency of the drug as [these characteristics] may

D. General Enforcement Authority

Teva argues that the Agency could rely upon its general "effective enforcement" authority under section 701(a) of the Act (21 U.S.C. 371(a)) to delay marketing of authorized generics until after the expiration of 180-day exclusivity periods. This is unpersuasive. Such an action would not further effective enforcement of the Act, particularly as the statute does not impose any duty to prohibit such marketing or any right to such protection.

E. Agency Precedent

Both the Mylan and Teva Petitions argue that Agency precedent compels FDA to prohibit marketing of an authorized generic during a 180-day exclusivity period for the drug product. Specifically, they point to the Agency's response to a citizen petition submitted by Teva in August 2000.[14]

The situation addressed in the citizen petition involved Mylan's 180-day exclusivity for a nifedipine product. In that case, Mylan had begun marketing a version of Pfizer's Procardia (nifedipine) product pursuant to an agreement with Pfizer to settle patent infringement litigation for the drug. At that time, under section 505(j)(5)(B)(iv) of the Act, the 180-day exclusivity period was triggered by the earlier of a court decision finding the patent at issue not infringed or invalid, or the commercial marketing of the drug product under an eligible ANDA. *See* 21 U.S.C. 355(j)(5)(B)(iv) (2003); *see also* note 1 *supra*. Mylan argued that the 180-day period had not yet been triggered because no such court ruling had issued and Mylan was marketing a version of Pfizer's product, rather than Mylan's own nifedipine product for which it had sought approval in the ANDA. Teva filed a citizen petition requesting that the Agency determine either that the 180-day exclusivity period had expired or that Mylan had lost its eligibility for the exclusivity. *See Mylan v. Thompson*, 207 F. Supp. 2d 476, 481-83 (N.D. W. Va. 2001).

---

relate to the safety and effectiveness of the drug." *See* 21 U.S.C. 356a(c)(2); 21 C.F.R. 314.70; 69 FR 18,728.

[14] Citizen Petition submitted by Teva Pharmaceuticals USA, Inc., Docket No. 00P-1446/CP1 (Aug. 9, 2000) (Nifedipine Petition). Teva also attempts to rely on (1) a proposed regulation addressing patent licensing by ANDA applicants, included with the 1989 Hatch-Waxman proposed rulemaking, and (2) the Agency's discussion, in the preamble to the 1994 Hatch-Waxman final rule, of the applicability of the 180-day exclusivity period to ANDA applicants having such patent licenses. The proposed regulation and discussion, however, concerned when an ANDA applicant that made a paragraph IV certification and had a licensing agreement with the patent holder could market its product. *See* 54 FR at 28,923-24 (proposed 21 C.F.R. 314.94(a)(12)(v)); 59 FR 50,338, 50,346-47, 50,353 (October 3, 1994). It has no bearing on the ability of NDA holders to market their own products during 180-day exclusivity periods. As the Agency stated in the preamble to the 1994 final rule, "FDA believes that the negotiations surrounding licensing agreements and the parties entering into such agreements are outside the scope of this rule." 59 FR at 50,351.

FDA determined that the exclusivity period no longer blocked other ANDAs, relying on two alternative rationales: either (1) Mylan had effectively abandoned its challenge to the patent by entering into the agreement with Pfizer and, therefore, had lost its eligibility for the exclusivity period, or (2) Mylan had triggered the exclusivity period by marketing Pfizer's product.[15] In subsequent litigation, a court upheld the Agency's determination, rejecting the first rationale but accepting the second. *Mylan*, 207 F. Supp. 2d at 487-88. In short, this case established that the marketing of an NDA holder's product by the holder of an approved ANDA that is eligible for 180-day exclusivity for that same drug product constitutes marketing under the ANDA for purposes of beginning the exclusivity period under section 505(j)(5)(B)(iv)(I) of the Act. 21 U.S.C. 355(j)(5)(B)(iv)(I) (2003).

Mylan and Teva both argue that the Agency's response to that petition establishes a broader policy of treating "brand generics as the legal and functional equivalents of ANDA generics for purposes of applying and enforcing the 180-day exclusivity period . . . ." Teva Petition at 3; *see* Mylan Petition at 3. This conclusion is incorrect, as is apparent from the statutory interpretation upon which the Agency relied for its decision. The Agency relied upon an interpretation of section 505(j)(5)(B)(iv)(I), which provided that the 180-day exclusivity period could be triggered by the "first commercial marketing" of "the drug" "under" an ANDA eligible for 180-day exclusivity. The Agency concluded that the provision could permissibly be construed to treat "first commercial marketing of the drug under the previous application [the ANDA eligible for 180-day exclusivity]" to include the marketing of the NDA holder's drug product (which is the same drug product as that for which the ANDA applicant seeks approval) by that ANDA holder. The Agency found this interpretation to be consistent with the two-fold legislative intent of the provision, to (1) benefit the consuming public "through the prompt availability of lower cost generic drugs" and (2) allow the eligible ANDA applicant to reap the benefits of 180 days of marketing exclusivity (as Mylan had by marketing Pfizer's product for 180 days without competition from other ANDA applicants). *Nifedipine Petition Response* at 7-8.

Despite petitioners' assertions to the contrary, the Agency position described in the Teva Nifedipine Petition Response and affirmed in *Mylan* provides no basis for concluding that an NDA holder cannot itself market or otherwise arrange for the distribution of authorized generic versions of its own product during a 180-day exclusivity period.[16]

---

[15] *See* Letter from Janet Woodcock, Director, Center for Drug Evaluation and Research, to Deborah A. Jaskot, Senior Director, Regulatory Affairs, Teva Pharmaceuticals USA, Inc. 5-8 (Feb. 6, 2001) (responding to Nifedipine Petition) (Nifedipine Petition Response).

[16] For similar reasons, Mylan's argument, that FDA could preclude the marketing of authorized generics through a rulemaking process similar to that pursued by the Agency to eliminate multiple "30-month stays" on approval of ANDA applications, fails. *See* 68 FR 36,676 (June 18, 2003). Section 505(j)(5)(B) provides for the Agency to stay final approval of an ANDA containing a paragraph IV certification, generally for 30 months, if the NDA or patent holder sues the ANDA applicant within 45 days of receiving notice of the certification. The Agency relied upon interpretation of specific statutory language regarding amendments to NDAs (*see* 21 U.S.C. 355(j)(2)(B)(iii) (2003) as authority for this rulemaking. *See* 67 FR 65,448, 65,454-456 (October 24, 2002); 68 FR at 36,688-694. In contrast, Mylan requests that the Agency prohibit marketing of authorized generics solely on the basis of "the spirit and intent of the Hatch-Waxman Amendments." Supplement at 2. The Agency does not consider the requested marketing prohibition

Even if prohibiting the marketing of authorized generics were desirable, FDA lacks the statutory authority to establish such a policy. In any event, the Agency's actions in the nifedipine matter did not establish such a broad policy precedent.[17] That FDA did not establish such a policy is further demonstrated by the Agency's having continued its prior practice, as noted above, of allowing NDA holders to make manufacturing changes, including labeling and imprint changes, that permit the marketing of authorized generic versions of their products during 180-day exclusivity periods. *See* note 9 *supra* and accompanying text.

F. Established Principles of Statutory Construction

Teva argues that FDA must interpret the Act to prohibit marketing of authorized generics during 180-day exclusivity periods to satisfy core interpretive principles regarding the Hatch-Waxman amendments, first articulated by a district court and then referenced in the Agency's response to Teva's nifedipine petition. Specifically, these principles provide that the statute should be interpreted to (1) maintain Hatch-Waxman incentives, (2) avoid interpretations that excessively favor either first ANDA applicants or innovators, and (3) avoid an interpretation that enables the patent holder to determine whether an ANDA applicant is entitled to exclusivity. *See* Nifedipine Petition Response at 5 (citing *Mylan Pharms., Inc. v. Henney*, 94 F. Supp. 2d 36, 53-54 (D.D.C. 2000)).

Fundamentally, as explained above, the Agency does not believe the statute can permissibly be interpreted as the petitioners request. Further, the Agency believes that its own interpretation is consistent with all of these principles. As explained below, the Agency sees no evidence that the interpretation undermines Hatch-Waxman incentives. The interpretation does not unduly favor either first ANDA applicants or NDA holders; it merely permits NDA holders to pursue competitive marketing strategies, consistent with the objectives of the Hatch-Waxman amendments. In fact, a contrary interpretation arguably would unduly favor first ANDA applicants, to the detriment of the public interest that is promoted through encouragement of competition and, thereby, of lower prices in the pharmaceutical market. Finally, the interpretation does not enable the patent holder to determine whether an ANDA applicant is entitled to exclusivity. ANDA applicants remain able to obtain and benefit from 180-day exclusivity.

---

consistent with the spirit of the amendments, however (*see* section III *infra*), and petitioners offer no equivalent statutory authority upon which to base it.

[17] The Teva Petition goes on to argue that if FDA were to fail to prohibit authorized generics in light of this precedent it would be an unexplained departure from existing policy and, therefore, arbitrary and capricious in violation of the Administrative Procedure Act. Teva Petition at 15-16. This argument fails as well because the precedent does not support the interpretation that both Mylan and Teva attempt to apply. Rather, the Agency is maintaining its consistent, long-standing policy by permitting NDA holders to market authorized generic versions of their products.

III. Marketing of Lower-Priced Versions of Brand Products During 180-Day Exclusivity Promotes Competition in Furtherance of a Fundamental Objective of the Hatch-Waxman Amendments

Although FDA does not regulate competition as a general matter, a fundamental objective of the Hatch-Waxman amendments is promotion of competition in the pharmaceutical marketplace. Consistent with this objective, as discussed above, the Act offers ANDA applicants the opportunity to challenge the applicability or validity of patents that an NDA holder has identified as claiming the drug product. *See* 21 U.S.C. 355(j)(2)(A)(vii); § 314.94(a)(12). Such challenges can promote competition because they enable ANDA applicants to market their products earlier than they could otherwise (before the expiration of the patent term) if such challenges are successful. However, in making such challenges, ANDA applicants expose themselves to the risk of patent infringement litigation. In light of this risk, Congress established 180-day exclusivity as an incentive for ANDA applicants to make patent challenges. *Mova*, 140 F.3d at 1074-75. If more than one ANDA applicant qualifies, the exclusivity can be shared.[18]

If an NDA holder arranges for distribution of an authorized generic version of its product at a reduced price during the 180-day exclusivity period, this might reasonably be expected to diminish the economic benefit to an ANDA holder who has qualified for the exclusivity. This negative economic impact could result from competition between the NDA holder's and ANDA holder's versions of the drug.

Any such adverse economic effect is insufficient to justify the action requested here, even if FDA had the authority to grant the request. In fact, such competition during the 180-day period furthers the Hatch-Waxman objective of enhancing competition overall among drug products. For example, it can be anticipated to encourage ANDA applicants to offer their products at lower prices during the exclusivity period, thereby reducing the substantial "mark-up" ANDA applicants can often apply during the period, before approval of subsequent ANDA applicants increases competition.[19]

---

[18] *See* FDA's guidance for industry on *180-Day Exclusivity When Multiple ANDAs Are Submitted on the Same Day* (July 2003) (regarding sharing of exclusivity where multiple ANDA applicants submit paragraph IV certifications to the same patent on the first day any such certifications are submitted for that patent); letter from Gary Buehler, Director, Office of Generic Drugs, to Diane Servello, Andrx Pharmaceuticals, Inc. (Nov. 16, 2002) (regarding sharing of exclusivity where different ANDA applicants are first to submit paragraph IV certifications to different patents for the same drug) (available on the FDA website at http://www.fda.gov/cder/ogd/shared_exclusivity.htm); *Apotex Inc. v. FDA*, No. 04-0605 (D.D.C. June 3, 2004), *appeal pending* No. 04-5211 (D.C. Cir.). The MMA amends the Act expressly to permit shared exclusivity for applicants that submit paragraph IV certifications on the first day that any paragraph IV certifications are made by any ANDA applicants for that drug. *See* MMA, section 1102(a)(1); 21 U.S.C. 355(j)(B)(iv) (2004).

[19] Mylan argues that the marketing of authorized generics does not benefit consumers as "[n]o pricing data currently supports the bald assertion that authorized generics lower prices at a consumer level." Supplement at 5. Section 505(j)(5)(B)(iv) of the Act and the Hatch-Waxman amendments overall, however, were intended to promote competition, as a means to reduce the costs of drugs to consumers. Failure of competition to achieve this result may warrant Congressional attention, but does not support prohibiting the marketing of authorized generics, any more than it supports prohibiting the sale of generic products under ANDAs.

Moreover, petitioners offer no evidence that generic companies would stop submitting ANDAs just because they faced the prospect of making less money during the 180-day exclusivity period. If 180-day exclusivity were the sole incentive for ANDA submission, FDA would presumably not see, as we do, second, third, and fourth ANDAs filed by generic companies that are aware that they are not first to file an ANDA application including a paragraph IV certification and, therefore, cannot gain 180-day exclusivity. Also, although multiple applicants often submit ANDAs for the same drug, some applicants may not qualify to share 180-day exclusivity, even though they too have challenged patents potentially claiming their products. In fact, it is the existence (and delayed approval) of these ineligible ANDA applicants that also have challenged listed patents that makes 180-day exclusivity valuable. In the absence of evidence to the contrary, the continuing willingness of ANDA applicants to submit subsequent ANDAs and expose themselves to risk of patent infringement litigation—without any prospect of sharing in 180-day exclusivity—also supports the conclusion that the incentives created by 180-day exclusivity remain adequate.

Neither petitioner nor any of the comments offers any evidence that competition from authorized generics has the effect of destroying the intended benefit of the 180-day exclusivity and, thereby, the incentive to challenge patents. Rather, the competitive effect of introducing a lower-priced authorized generic version of an NDA holder's product appears akin to that which one ANDA applicant's product might have relative to that of another ANDA applicant when exclusivity is shared.[20]

IV. Conclusion

The marketing of authorized generics during the 180-day exclusivity period is a long-standing, pro-competitive practice, permissible under the Act. We are not persuaded by petitioners' arguments that the Agency can, must, or should prohibit such marketing. Therefore, we decline to interfere with these business arrangements and practices.

Accordingly, both petitions are denied.

Sincerely yours,

William K. Hubbard
Associate Commissioner
for Policy and Planning

---

[20] For example, Apotex's comments associate competition from an "authorized generic" with a drop in sales during the exclusivity period for its paroxetine product from a projected $530-575 million to $150-200 million. March 24, 2004, comments at 4.

The Agency notes that, as a general matter, the Federal Trade Commission, rather than FDA, has regulatory authority to address anti-competitive marketing practices, including impermissible practices in which entities might engage with respect to marketing of authorized generics.