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April 25, 2003

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: Docket No. 03P-0089 – Wyeth's Supplemental Comments

Dear Sir or Madam:

Wyeth respectfully submits these additional comments to the above-referenced Citizen Petition, in response to Andrx's March 21, 2003 response to Wyeth's initial comments to the Petition

In its Petition, Andrx requested that FDA administratively deem Wyeth to have begun marketing loratadine orally disintegrating tablets under its Abbreviated New Drug Application (ANDA) on December 19, 2002, a date that is nearly two months prior to FDA's approval of that ANDA. As Wyeth pointed out in its original comments, it is legally and factually impossible for FDA to make such a determination. In addition, Wyeth notified FDA and Andrx that Wyeth would not assert exclusivity under the ANDA beyond August 9, 2003, the date that is 180 days after the approval date of the ANDA, even though Wyeth would be fully justified in asserting exclusivity for a longer period, beginning on the date it actually begins marketing loratadine under the authority of the ANDA.

Andrx, in its most recent filing has said it "accepts Wyeth's offer to forsake generic exclusivity after August 9, 2003," but nevertheless requests that FDA "adjudicate the Andrx petition by: (1) deeming Wyeth's commercial marketing of generic loratadine to have begun on February 10, 2003…; (2) declaring the [sic] Wyeth's exclusivity for loratadine will expire on August 9, 2003; and (3) adopting appropriate measures to implement Wyeth's offer." However, as shown herein, there is nothing left for FDA to "adjudicate," and Andrx's further arguments, apparently aimed at eliciting a broad policy announcement from the Agency, are incorrect and should be disregarded.

Andrx's "Bioequivalence Marketing" Argument Is Wrong

Not content to simply accept Wyeth's voluntary good faith commitment, Andrx's supplement requests that FDA rule that "the marketing of a product under section 505(b)(2) satisfies the 'commercial marketing' prong of section 505(j)(5)(B)(iv) if the 505(b)(2) product is *bioequivalent* to the product that is the subject of the 505(j) ANDA."

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Andrx Supp. at 2 (emphasis added). Andrx's position is overly broad, and is based on a fundamental misunderstanding of the 505(b)(2) NDA process, the ANDA process, and the 180-day exclusivity period scheme. Moreover, Andrx's interpretation would impose a new and wholly unworkable rule that would allow 180-day exclusivity periods to be triggered by the marketing of drugs that are not even therapeutically equivalent to the generic product to which exclusivity applies. This is because a true generic product must be identical to the Reference Listed Drug in *several* respects including, but not limited to, bioequivalence. 21 U.S.C. § 355(j)(2)(A). In contrast however, a 505(b)(2) NDA must *differ* from the listed drug in a material way that would preclude approval under an ANDA; FDA regulations specifically prohibit the filing of a 505(b)(2) NDA for a product if at the time of submission of the application the proposed product "is a duplicate of a listed drug and is eligible for approval under section 505(j) of the act." 21 C.F.R. § 314.101(d)(9).[1] However, because bioequivalence can exist between products independently of whether all of the ANDA "sameness" criteria exist, *see* 21 C.F.R. § 320.1(e) (recognizing bioequivalence of pharmaceutical alternatives), the marketing of a 505(b)(2) product that happens to be bioequivalent to an ANDA product does not satisfy the letter or intent of the "commercial marketing" trigger under 21 U.S.C. § 355(j)(5)(B)(iv).

Andrx's radical proposed interpretation would have unintended and perverse consequences. For example, if marketing of a 505(b)(2) product would trigger exclusivity for any bioequivalent ANDA product, it would actually create an incentive for generic companies to strategically file 505(b)(2) NDAs for a slight change to an innovator product (for example a different but clinically unimportant new dosing regimen) solely for the purpose of triggering another generic applicant's 180-day exclusivity period on a therapeutically inequivalent product. Moreover, Andrx's approach would not be limited to 505(b)(2) NDA products, but could also apply to generic versions of different innovator products that contain the same active ingredient but which happen to meet the "same rate and extent" criteria of bioequivalence. Such a system would make the Hatch-Waxman scheme even more difficult for FDA to administer, but would not by any stretch of the imagination effectuate the Congressional intent behind the 180-day exclusivity period system. Accordingly, Andrx's interpretation should be rejected.

In addition, despite Andrx's repeated protestations, FDA's decision with respect to Mylan's nifedipine ANDA exclusivity is inapposite here, for the reasons set forth in Wyeth's initial comments. Moreover, that situation is also irrelevant to Andrx's 505(b)(2)/bioequivalence argument because in that case Mylan's product was not approved under a 505(b)(2) NDA, but had final approval as a true "duplicate" generic version of the innovator drug Mylan marketed under its settlement agreement with the innovator. Because 505(b)(2) products are not, by definition, true duplicate generic products, the Mylan scenario does not support Andrx's proposed interpretation.

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[1] In the case of Wyeth's Alavert 505(b)(2) NDA, at the time of filing, the Reference Listed Drug (Claritin) was labeled for prescription sale only, whereas Wyeth sought OTC status for Alavert. The serendipitous fact that Schering chose to convert Claritin to OTC status after learning of Wyeth's Alavert NDA does not justify the radical statutory redrafting espoused by Andrx.

There Is Nothing For FDA To "Adjudicate"

In its original Petition comments Wyeth offered to notify FDA when it actually begins marketing a product under the legal authority of its ANDA, and to subsequently waive or relinquish any portion of its exclusivity beyond August 9, 2003. Although this offer was completely voluntary, and does not constitute a concession of any sort, as alleged by Andrx, Andrx Supp. at 2, Wyeth stands by that commitment, and will follow through accordingly at the appropriate time. It is beyond dispute that an exclusivity holder has the right to choose whether, *and when*, to waive or relinquish its exclusivity, and such a voluntary commitment is not itself commercial marketing. Moreover, nothing in the statute or FDA's regulations gives FDA the authority to preemptively waive or relinquish an exclusivity on behalf of an applicant merely because it has expressed the intent to do so in the future. For FDA to "adjudicate" Andrx's petition as requested in Andrx's supplement would require the Agency to venture into treacherous interpretative waters for no practical or prudential purpose.

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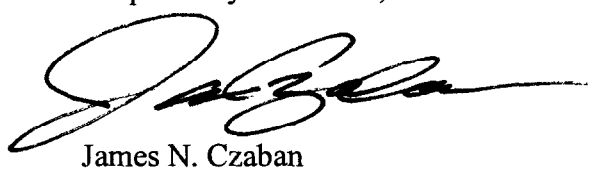
For the foregoing reasons, and the reasons stated in Wyeth's original Petition comments, Andrx's Petition should be denied, both because it is legally insupportable, and because it is effectively moot.

Respectfully submitted,



James N. Czaban
Counsel for Wyeth

cc: Geoffrey M. Levitt, Vice President & Chief Regulatory Counsel, Wyeth Pharmaceuticals
Kathy A. Gleason, Assistant General Counsel, Wyeth; Senior Vice President, Wyeth Consumer Healthcare