HellerEhrman
ATTORNEYS

James N. Czaban
jczaban@hewm.com
Direct (202) 912-2720
Main (202) 912-2000
Fax (202) 912-2020

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March 13, 2003

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

Re: Docket No. 03P-0089

Dear Sir or Madam:

Wyeth respectfully submits these comments to the above-referenced Citizen Petition filed February 27, 2003 by Andrx Pharmaceutical, Inc. ("Andrx"). Wyeth is the sponsor of ANDA No. 75-822 for loratadine orally disintegrating tablets, 10 mg., which received final effective approval on February 10, 2003. This ANDA was the first ANDA to be submitted with a Paragraph IV Certification to all relevant Orange Book-listed patents for this drug product. Accordingly, as FDA has already determined, and as Andrx admits, Wyeth is entitled to the 180-day exclusivity period under 21 U.S.C. § 355(j)(5)(B)(iv).

In its Petition, however, Andrx notes that Wyeth has been marketing a loratadine orally disintegrating tablet, Alavert™, under the authority of a separate and unrelated New Drug Application under 21 U.S.C. § 355(b)(2) (a "505(b)(2) NDA"), which received final approval on December 19, 2002. Based on this, Andrx requests FDA "to declare that Wyeth has been commercially marketing generic loratadine under the name Alavert since December 19, 2002, and to declare further that 180 days after that date, [Andrx's] ANDA [for loratadine orally disintegrating tablets] will be eligible for full approval." As demonstrated herein, Andrx's request is wholly unsupportable as a matter of fact and as a matter of law, and its Petition should therefore be denied. However, as further discussed below, Wyeth will not claim any exclusivity with respect to its loratadine orally disintegrating tablets ANDA beyond August 9, 2003, the date that is 180 days after Wyeth's ANDA received final approval.

Marketing of a Drug Under a New Drug Application (NDA) Cannot Trigger The 180-Day *Generic* Drug Exclusivity Period

The statutory provisions governing the 180-day exclusivity period have been the subject of many legal challenges. In most cases the courts have hewed closely to the literal

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statutory language, notwithstanding more expansive interpretations that have been advanced by FDA or individual applicants. *See, e.g., Mova Pharmaceuticals v. Shalala*, 140 F.3d 1060 (D.C. Cir. 1998), *Mylan Pharmaceuticals v. Henney*, 94 F. Supp. 2d 36 (D.D.C. 2000). Of particular importance here, the statute specifically and unequivocally ties the start of the 180-day exclusivity period to commercial marketing under the authority of an *ANDA*. The governing exclusivity provision, section 505(j)(5)(B)(iv), applies by its terms only to "application[s]" that "contain[] a certification described in subclause (IV) of paragraph (2)(A)(vii)," – i.e., 21 U.S.C. § 355(j)(2)(A)(vii), the statutory provision setting forth the required contents of an "abbreviated application for a new drug." The parallel, but legally distinct, certification that applies to a 505(b)(2) NDA under 21 U.S.C. § 355(b)(2)(A) does not give rise to any counterpart exclusivity period. Thus, when Congress created the commercial marketing trigger for the 180-day exclusivity period in section 505(j)(5)(B)(iv)(I), its reference to the "first commercial marketing of the drug under the previous application" can only have been intended to mean commercial marketing conducted under the authority of an approved ANDA, and not, as Andrx would have it, marketing of another drug product under another type of application such as a 505(b)(2) NDA.

As FDA and Andrx are aware, FDA's December 19, 2002 approval of Wyeth's Alavert product was granted pursuant to Wyeth's 505(b)(2) New Drug Application, and not pursuant to Wyeth's ANDA. Because 505(b)(2) NDAs are distinct and independent types of applications that bear no legal connection to ANDAs, it is factually and legally impossible for Wyeth to have marketed Alavert "under" its ANDA – and thereby have triggered the start of its exclusivity period – before that ANDA was approved.[1]

FDA's Prior Decision Regarding Nifedipine Exclusivity
Is Irrelevant To The Timing Of Wyeth's Loratadine Exclusivity

Recognizing that the plain language of the statute is contrary to its requested agency action, Andrx seeks instead to rely upon FDA's response to a previous Citizen Petition involving wholly different factual circumstances, and a preliminary district court decision denying a motion to enjoin the agency's Petition response (*Mylan v. Thompson*, 207 F. Supp. 2d 476 (N.D. W.Va. 2001)). As shown below, those proceedings do not support Andrx's contention that Wyeth's marketing of a branded OTC loratadine product under the wholly separate 505(b)(2) NDA scheme constitutes "commercial marketing" of a "generic" product under Wyeth's ANDA.

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[1] Andrx specifically declines to argue in its Petition that there has been a "triggering" court decision that would start the running of Wyeth's ANDA exclusivity period under the "court decision" exclusivity trigger of 21 U.S.C. § 355(j)(5)(B)(iv)(II).

In *Mylan*, the exclusivity holder (Mylan) had received final effective approval of its ANDA for nifedipine prior to settling its Paragraph IV ANDA patent litigation with the patentee. Pursuant to that settlement, Mylan abandoned its patent challenge in exchange for the right to market an AB-rated "generic" nifedipine product under a license and supply agreement with the innovator company, which it proceeded to do in lieu of marketing a generic product under its own approved ANDA. In contrast, here Wyeth has concluded no agreement with the patent holder, Schering, to terminate the loratadine patent infringement litigation; indeed, that litigation is still ongoing in the Court of Appeals for the Federal Circuit. Thus, Wyeth's marketing of its OTC loratadine product to date has occurred not as the result of any settlement of Paragraph IV ANDA litigation with the patent holder, but as the result of a separate approved application under an entirely distinct statutory provision, namely section 505(b)(2) of the Act.

The nifedipine situation is also irrelevant here because prior to its settlement and distribution agreement with the patent holder, Mylan had received final effective approval of its nifedipine ANDA that would have allowed it to begin commercial marketing "under" its ANDA. Thus, its "marketing" of the innovator's nifedipine product could be tied to its legal authority to market a generic product under its ANDA. In stark contrast, here it was factually and legally impossible for Wyeth to have begun marketing loratadine under its ANDA prior to the effective approval date of February 10, 2003. The fact that Wyeth was able to market a similar product under a wholly separate 505(b)(2) application cannot, therefore, have triggered Wyeth's 180-day exclusivity period, even under an expansive interpretation of *Mylan*.

* * *

Thus, neither the plain language of the statute, nor a fair reading of the *Mylan* case, supports the position that Wyeth's 180-day exclusivity period under section 505(j)(5)(B)(iv) was somehow triggered by Wyeth's marketing of its 505(b)(2)-approved loratadine product beginning last December. Wyeth's ANDA for loratadine orally disintegrating tablets only received final effective approval on February 10, 2003. Because the commercial marketing trigger requires marketing of the drug product approved "under the" relevant ANDA, it is impossible for Wyeth's 180-day exclusivity period to have started by virtue of "commercial marketing" prior to that date. To hold otherwise would be, in effect, to penalize Wyeth for having taken the initiative to submit a 505(b)(2) application for an OTC loratadine product in an effort to expedite the availability of such a product to consumers at a time when there was no OTC reference listed drug against which to submit an ANDA. Indeed, any other applicant, including Andrx, could have filed a similar 505(b)(2) NDA for a loratadine reditab product and received final approval without being subject to a 180-day exclusivity period. The fact that Andrx chose not to do so should not entitle it to the unjustified windfall of a market entry prior to the expiration of Wyeth's lawfully obtained 180-day exclusivity period.

Wyeth Will Not Claim Exclusivity Beyond August 9, 2003

Although Wyeth has not yet begun marketing a product under the authority of its ANDA, Wyeth does plan to do so in the near future, at which time its 180-day exclusivity period will officially begin. In the interest of fairness, however, after that exclusivity period has begun, Wyeth will waive or relinquish any remaining portion of its 180-day exclusivity period after August 9, 2003, the date that is 180 days after the date of final approval of the ANDA. In this way, subsequent ANDA applicants for loratadine orally disintegrating tablet products will be eligible for final effective approval on that date, i.e., as if Wyeth's exclusivity period under that ANDA had been triggered immediately upon the date of final approval. Wyeth will notify FDA separately both at the time the 180-day exclusivity is triggered, pursuant to 21 C.F.R. § 314.107(c)(4), and at the time the company actually waives or relinquishes the remaining exclusivity period, i.e., immediately prior to August 9, 2003.

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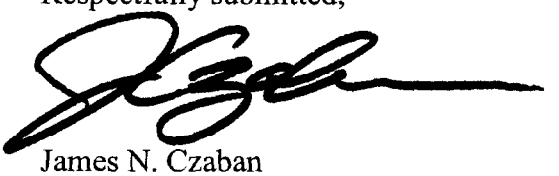
For the foregoing reasons, Andrx's Petition should be denied.

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