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November 9, 2007

Division of Dockets Management  
U.S. Food and Drug Administration  
Department of Health and Human Services  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

**EMERGENCY PETITION FOR STAY OF ACTION**

On behalf of Cobalt Laboratories Inc. and Cobalt Pharmaceuticals Inc. (collectively, "Cobalt"), the undersigned respectfully submits this petition requesting that the Agency stay approval of any abbreviated new drug application ("ANDA") for Acarbose Tablets 25 mg, 50 mg, and 100 mg unless and until such ANDA contains sufficient evidence and data from the required *in vivo* testing to establish bioequivalence in accordance with 21 U.S.C. § 355(j), 21 C.F.R. § 320.21, and 21 C.F.R. § 320.23.

The basis for this Petition for Stay of Action is set forth below, and in Cobalt's accompanying Citizen Petition, dated November 9, 2007, which is submitted herewith and incorporated herein by reference, which requests that FDA: (1) require all applicants submitting an ANDA referencing Bayer's NDA No. 20-482 for Precose® (acarbose) to conduct the required *in vivo* bioequivalence tests and studies comparing the proposed generic product to Precose®, the reference listed drug; (2) refrain from granting any *in vivo* bioequivalence waiver for any ANDA referencing Bayer's NDA No. 20-482 for Precose®; and (3) require that the results of such tests and studies establish the *in vivo* bioequivalence of any generic Precose® product sufficient to permit final approval of any such ANDA pursuant to 21 U.S.C. § 355(j)(8)(A)(ii) and 21 C.F.R. § 320.21.

As required by 21 C.F.R. § 10.20, we include an original and 4 copies of this emergency petition for stay of agency action.

2007P-0448

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**A. Decision Involved And Action Required.**

This petition pertains to all ANDAs for acarbose tablets in any strength, all of which are subject to the bioequivalence requirements set forth in 21 U.S.C. § 355(j), 21 C.F.R. § 320.21, and 21 C.F.R. § 320.23. As explained in Cobalt's Citizen Petition, FDA may not waive the requirement for the submission of evidence demonstrating *in vivo* bioequivalence for proposed generic acarbose tablets under either FDA's regulations or guidance documents. FDA must, therefore, delay approval of all acarbose ANDAs unless and until each such ANDA is supported by an adequate *in vivo* bioequivalence study or studies mandated by the aforementioned statutory and regulatory provisions. This stay of approval is necessary to protect the public health and interest, and to prevent irreparable harm to Cobalt. See 35 U.S.C. § 355(q)(1)(A)(ii); 21 C.F.R. § 10.35. The requirements for such a stay are met here.

**B. Statement Of Grounds.**

**1. Cobalt Will Suffer Irreparable Injury.**

Cobalt faces imminent substantial and irreparable injury in the absence of a stay. Cobalt indisputably submitted the first ANDA for acarbose tablets in all strengths referencing Bayer's NDA No. 20-482 for Precose® (acarbose) tablets. In conjunction with the submission of its ANDA, Cobalt conducted the necessary *in vivo* bioequivalence studies as required by FDA and 21 U.S.C. § 355(j) to establish that Cobalt's acarbose product is bioequivalent to the brand product, Precose®. It is Cobalt's understanding, however, that other ANDA applicants may not have conducted the necessary *in vivo* studies to show bioequivalence, and that FDA nevertheless is considering approving such applications.

Any approval of an ANDA that lacks the required *in vivo* studies demonstrating bioequivalence would be arbitrary, capricious, an abuse of discretion, and contrary to law. See *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 28 (D.D.C. 1997) ("The disparate treatment of functionally indistinguishable products is the essence of the meaning of arbitrary and capricious.") As explained in Cobalt's Citizen Petition, FDA cannot lawfully waive *in vivo* bioequivalence requirements for acarbose. The Agency cannot lawfully force Cobalt to compete with applicants that, unlike Cobalt, have not satisfied all necessary requirements for approval, including *in vivo* bioequivalence testing. Such unlawful approvals will cause Cobalt devastating and irreparable harm, for which it has no adequate remedy at law against the Agency.

**2. Cobalt's Case Is Not Frivolous And Is Being Pursued In Good Faith.**

Cobalt's case is not frivolous, and it is being pursued in good faith. Under the controlling statute and regulations, FDA must enforce the requirements for establishing *in vivo* bioequivalence before approving any ANDAs, and a biowaiver is not available here.

**3. Cobalt Has Demonstrated Sound Public Policy Grounds Supporting The Stay.**

Sound public policy grounds support the requested stay. An ANDA applicant must establish, *inter alia*, that its proposed drug product is “bioequivalent” to the reference listed drug (“RLD”). See 21 U.S.C. § 355(j)(2)(A)(iv).<sup>1</sup> Demonstrating bioequivalence to the RLD is, in fact, critical to obtaining FDA approval: “A major premise underlying the [Hatch-Waxman Amendments] is that bioequivalent drug products are therapeutically equivalent, and therefore, interchangeable.” (FDA, *Approved Drug Products with Therapeutic Equivalence Evaluations*, p. vii (27th ed. 2007)). Proof of bioequivalence provides the necessary assurances that an ANDA product will be safe and effective. And, where, as here, a biowaiver may not be granted, bioequivalence must be established through *in vivo* testing.

In addition to the obvious safety concerns, the public also has an interest in requiring FDA to act lawfully, to fulfill its obligations under its governing statutes and implementing regulations, and to fairly and equally treat regulated parties.

**4. The Delay Resulting From The Stay Is Not Outweighed By Public Health Or Other Public Interests.**

“[T]he public’s interest in the ‘faithful application of the laws’ outweigh[s] its interest in immediate access to [a competing] generic product.” *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998). This is particularly true where, as here, health and safety concerns demand that bioequivalence be adequately established through *in vivo* testing. The public interest therefore strongly supports a stay of approval of any ANDAs referencing Bayer’s NDA No. 20-482 for Precose<sup>®</sup> until the necessary *in vivo* studies are conducted, and further demands that FDA refrain from granting any biowaivers for such ANDAs. Moreover, a temporary stay will not harm others. Cobalt is entitled to 180-day generic exclusivity under 21 U.S.C. § 355(j)(5)(B)(iv) and currently there are no approved acarbose ANDAs. Subsequent

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<sup>1</sup> A generic drug product is “bioequivalent” when:

(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

applicants, therefore, cannot claim harm from staying an approval to which they currently are not statutorily entitled in the first place.

**C. Conclusion.**

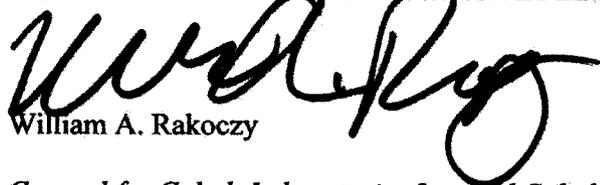
For the reasons set forth above and in the aforementioned Citizen Petition, the undersigned requests that the Commissioner stay approval of any and all ANDAs referencing Bayer's NDA No. 20-482 for Precose® (acarbose) until and unless *in vivo* bioequivalence studies comparing the proposed generic product to Precose® sufficiently establish the bioequivalence of any generic acarbose product to permit final approval of any such ANDA.

**D. Certification.**

Pursuant to 21 U.S.C. § 355(q)(1)(H), I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: October 2007. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: Cobalt. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.

Respectfully submitted,

RAKOCZY MOLINO MAZZOCHI SIWIK LLP



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