APOTEX CORP.

October 19, 2007

Division of Dockets Management
Food and Drug Administration
Room 1061 (HFA-305)
5630 Fishers Lane
Rockville, MD 20852

Re: Docket 2007N-0382 (Generic Ramipril Capsules –180-Day Exclusivity Issues)

Dear Sir or Madam:

This comment is submitted by Apotex, Corp. (Apotex) in response to the agency's notice posted on its website, asking for comments regarding 180-day generic drug exclusivity for ramipril capsules. Apotex is commenting because of the importance of the issues involved and the public interest in preventing a generic sponsor entitled to 180-day exclusivity from settling patent infringement litigation and "parking" its 180-day exclusivity, thereby blocking other generic versions of the innovator product from entering the market. Permitting a generic sponsor to indefinitely block generic competition and lower prices severely injures American consumers and other generic companies. These issues are important both with regard to ramipril capsules and more generally, in light of the Food and Drug Administration's (FDA) practice of proceeding on a case-by-case basis on exclusivity issues, where those case-by-case decisions are often based on prior agency decisions.

As Apotex understands the facts concerning ramipril, Cobalt Pharmaceuticals, Inc. (Cobalt) submitted the first Paragraph IV abbreviated new drug application (ANDA) for ramipril capsules, thereby entitling Cobalt to 180-day exclusivity. Cobalt was sued by the patent owner for patent infringement. Rather than continuing to defend that litigation, Cobalt admitted

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infringement of the patent and subsequently settled the lawsuit, resulting in voluntary dismissal of the case without prejudice. Apparently as part of its settlement of litigation, Cobalt entered into an agreement with King Pharmaceuticals, Inc. (King), the innovator drug sponsor. Under that agreement, Cobalt will distribute an "authorized generic" version of King's Altace, the innovator product, at a time and under conditions which have not been publicly disclosed.

Cobalt received final ANDA approval almost two years ago, in October 2005, and settled its patent litigation in April 2006. However, Cobalt has never marketed its generic product and apparently has no intention of doing so at this time. In fact, Cobalt's ANDA is currently listed in the "discontinued" section of FDA's *Orange Book*. Yet, Cobalt continues to maintain its Paragraph IV certification, even though Cobalt is no longer actively pursuing its patent case. The bottom line is that Cobalt's actions have blocked the entire market for generic ramipril capsules, contrary to the public interest and contrary to the intent of the Hatch-Waxman Amendments.

Consistent with a prior agency decision, FDA should conclude that Cobalt's actions have, as a matter of law, converted Cobalt's Paragraph IV certification to a Paragraph III certification. Without a Paragraph IV certification in its ANDA, it follows that Cobalt is no longer eligible for 180-day exclusivity. Once the 180-day block is removed, any subsequent ANDA sponsor that is otherwise eligible for final approval should receive final approval.

FDA reached this conclusion six years ago in a matter concerning 30mg nifedipine extended release tablets. There, the agency concluded that the ANDA sponsor entitled to 180-day exclusivity (Mylan Pharmaceuticals, Inc. (Mylan)) had "effectively changed" its Paragraph IV certification to a Paragraph III certification by settling patent infringement litigation and

agreeing to distribute an "authorized generic." FDA has never renounced that 2001 interpretation and so should continue to follow it. FDA should apply the same reasoning to ramipril capsules (and other similarly situated drugs, as appropriate).[1]

FDA should act to prevent Cobalt from "parking" its 180-day exclusivity indefinitely. Allowing Cobalt to block the entire market for generic ramipril capsules is definitely at odds with the intent of the Hatch-Waxman Amendments: "Congress sought to get generic drugs into the hands of patients at reasonable prices – fast." *In Re: Barr Laboratories, Inc.*, 930 F.2d 72, 76 (D.C. Cir. 1991). It also works to the disadvantage of a subsequent ANDA sponsor that has succeeded in clearing the patent-related hurdles but nevertheless finds itself blocked by the first sponsor's 180-day exclusivity. Here, Apotex understands that Lupin Pharmaceuticals, Inc.

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[1] Mylan challenged FDA's decision in a West Virginia federal district court. In ruling on Mylan's motion for preliminary injunction, the district court rejected FDA's interpretation as unreasonable. *Mylan Pharmaceuticals, Inc. v. Thompson*, 207 F. Supp.2d 476 (N.D. W. Va. 2001). The court's decision was based on a number of factors, including the court's view that FDA did not have either statutory or regulatory authority to change Mylan's patent certification. 207 F. Supp.2d at 487. Despite the rejection of the agency's decision on this issue, FDA prevailed before the West Virginia district court on other grounds (207 F. Supp.2d at 488); thus, FDA had no basis to appeal.

In the ensuing six years, the U.S. Court of Appeals for the D.C. Circuit has had two occasions to consider very similar issues. In both cases, the D.C. Circuit held that FDA does have the authority to convert patent certifications by operation of law, even though there is no specific provision in the Federal Food, Drug, and Cosmetic Act or in FDA's regulations that addresses this issue. *See Mylan Laboratories, Inc. v. Thompson*, 389 F.3d 1272 (D.C. Cir. 2004) (concerning fentanyl transdermal drug product); *Ranbaxy Laboratories, Inc. v. Food and Drug Administration*, 96 Fed. Appx. 1 (D.C. Cir. 2004), affirming 307 F. Supp.2d 15 (D.D.C. 2004) (concerning fluconazole drug product). Thus, Apotex believes that a court confronted with the same issue today would uphold FDA's decision.

For these reasons, this 2001 West Virginia district court decision does not necessitate any change in the agency's interpretation, that the abandonment of patent infringement litigation effectively converts the ANDA sponsor's Paragraph IV certification to a Paragraph III certification.

(Lupin) is a subsequent ANDA sponsor that recently succeeded in obtaining a decision from the U.S. Court of Appeals for the Federal Circuit that all asserted claims of the patent that forms the basis for Cobalt's 180-day exclusivity are invalid. Despite having cleared the patent hurdle for itself – and for all other ANDA sponsors – Lupin finds itself blocked by Cobalt's "parked" 180 day exclusivity. This result is perverse.

FDA must strike a proper balance on implementing the 180-day exclusivity provisions of the statute. On the one hand, FDA must preserve the 180-day exclusivity "reward" to encourage ANDA sponsors to challenge *Orange Book* patents that would otherwise delay generic competition, often for many years. Apotex understands and values the short term and long term benefits of the 180-day exclusivity "head start." That "head start" serves as a very important incentive that encourages ANDA sponsors to expend the resources to, as appropriate, design non-infringing drug products and to challenge the validity or enforceability of questionable *Orange Book* patents. On the other hand, FDA must ensure that generic competition is not unduly blocked, particularly with regard to a subsequent sponsor that is the first to clear patent hurdles and is otherwise eligible for final approval. To prevent blocking the generic market, the 180-day exclusivity award should only be available to the first filer if that sponsor continues to pursue Paragraph IV patent litigation and final approval, actively and in good faith.

The situation where a subsequent Paragraph IV ANDA sponsor is the first to clear patent hurdles but finds itself blocked by the first filer's 180-day exclusivity is an important issue that merits FDA's attention. Particularly in circumstances (such as here) that are not governed by the 180-day exclusivity forfeiture provisions added by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), Pub. L. No. 108-173, FDA needs to find

ways to carry out the intent of Congress. FDA correctly decided in 2001 that a first filer that abandons its defense of patent infringement litigation should lose its eligibility for 180-day exclusivity. That reasoning remains sound today, and should be applied by FDA with regard to ramipril capsules, as well as to any other pre-MMA situation with similar facts.

In closing, FDA should conclude that, by settling its patent litigation and entering into an "authorized generic" distribution agreement, Cobalt effectively abandoned its Paragraph IV patent challenge. As a result, Cobalt's Paragraph IV certification should be deemed to have been converted to a Paragraph III certification by operation of law, resulting in the loss of Cobalt's 180-day exclusivity. Such a conclusion would clear the path for any subsequent ANDA sponsor that is otherwise eligible for final approval to receive final approval. Allowing Cobalt to maintain its 180-day exclusivity would be counter to good public policy as Cobalt's actions have not resulted in opening the generic marketplace; if anything, they will continue to delay generic competition.

Apotex appreciates the opportunity to comment.

Sincerely yours,

Steve Giuli

Director of Government Affairs &
Public Policy