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**BY HAND DELIVERY**

Gary J. Buehler
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Document Control Room, Metro Park North II
7500 Standish Place, Room 150
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**RE: FDA NO. 2007-0382: 180-DAY EXCLUSIVITY FOR GENERIC RAMIPRIL ORAL CAPSULES**

Dear Dr. Buehler:

We are writing on behalf of a client that has filed an ANDA for generic ramipril oral capsules, and in reference to the above-listed docket regarding 180-day generic drug exclusivity for those drug products. This letter addresses the issues raised in the September 25, 2007 submissions from Hyman, Phelps & McNamara, P.C. and Lupin Pharmaceuticals, Inc. (collectively, the "Petitioners").

We believe that those submissions are unpersuasive, and that Cobalt Pharmaceuticals, Inc. ("Cobalt") remains eligible for 180-day exclusivity for ramipril oral capsules. Petitioners' arguments (1) are inconsistent with the text and structure of the Hatch-Waxman Act, as elucidated in authoritative D.C. Circuit precedent, and (2) would essentially render superfluous or otherwise rewrite the forfeiture triggers added to the statute by Title XI of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (the "MMA"), Pub. L. No. 108-173, 117 Stat. 2066 (Dec. 8, 2003).

It is well-settled that the Agency may not condition the first applicant's eligibility for exclusivity on the *initiation* of patent infringement litigation. *See Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120 (D.C. Cir. 2006); *Purepac Pharm. Co. v. Friedman*, 162 F.3d 1201 (D.C. Cir. 1998); *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060 (D.C. Cir. 1998). As a result, it is beyond question that the Agency may not condition eligibility for exclusivity on the *maintenance* of such litigation to a final court decision. That is precisely what Petitioners have asked FDA to hold in this case, and the Agency should reject that approach to 180-day exclusivity.

It is no answer that Cobalt somehow "abandoned" its paragraph IV certification by conceding infringement when it stipulated to the dismissal of patent litigation initiated by

Aventis Pharma Deutschland GmbH ("Aventis") and King Pharmaceuticals, Inc. ("King"). Beyond the fact that Cobalt obtained a license as part of the settlement—which is itself sufficient to preserve Cobalt's paragraph IV certification, *see* 21 C.F.R. § 314.94(a)(12)(v)—each of Cobalt's admissions of infringement was accompanied by an express reservation that Cobalt was maintaining its paragraph IV challenges to both the validity and enforceability of U.S. Patent No. 5,061,722 (the "'722 patent"). *See* Stipulation, *Aventis v. Cobalt*, No. 03-10492 (D. Mass. Mar. 2, 2004) [the "Stipulation"] at ¶¶ 2, 3, 4, 5 (attached as Exh. 1 to the Hyman Phelps Letter). Paragraph IV certifications need not challenge a patent on *every* conceivable ground; the statute is clear that *any* ground will suffice. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (exclusivity-qualifying paragraph IV certification states "that [the] patent is invalid *or* will not be infringed") (emphasis added); 21 C.F.R. § 314.52(a) ("patent is invalid, unenforceable, *or* will not be infringed") (emphasis added).

In addition, the positions taken by Petitioners would essentially write the MMA's forfeiture triggers out of the statute. Those amendments make clear that Congress knew applicants were settling patent infringement cases and that Congress well understood that such settlements did not affect eligibility for exclusivity under the prior statute. That is why Congress *amended* the Act to provide—for the first time—that a court decision invalidating a patent settlement on antitrust grounds would result in a forfeiture of exclusivity, *see* 21 U.S.C. § 355(j)(5)(D)(i)(V), and that the first applicant's failure to market could result in forfeiture under certain circumstances. *Id.* § 355(j)(5)(D)(i)(I). More recent legislation proposes to build on those provisions. *See, e.g.*, H.R. 1902, 107th Cong. (2007).

Those changes would not have been necessary if the statute already provided for forfeiture upon settlement—as Petitioners all but concede. *See* Hyman Phelps Letter at 2 n.1 ("[I]f this were a post-MMA case, Cobalt would almost certainly have forfeited its 180-day exclusivity."); *id.* at 5 n.5 (acknowledging that "Congress did not, however, make most of the [MMA] changes retroactive"); Lupin Letter at 9 (discussing recent congressional hearings on patent settlements). Indeed, because the MMA's settlement-based forfeiture trigger applies retroactively, *see* MMA § 1102(b), Petitioners effectively are asking the Agency to rewrite current law, by expanding the otherwise limited list of forfeiture conditions to include *any* patent settlement—regardless of whether (as Congress required) such a settlement is held to violate the antitrust laws. At bottom, the MMA speaks directly to these issues; there are no gaps or ambiguities for the Agency to fill; and the Agency may neither read the failure-to-market forfeiture trigger into the pre-MMA Act nor rewrite the settlement forfeiture trigger to apply in these circumstances.

## ARGUMENT

Petitioners basically argue that Cobalt "abandoned" its paragraph IV certification and thereby forfeited its eligibility for 180-day exclusivity by admitting that its ramipril capsules would infringe the '722 patent in the course of settling its litigation with King and Aventis. *See, e.g.*, Hyman Phelps Letter at 6 n.5 ("The relevant issue is whether Cobalt's ANDA still contains a paragraph IV certification to the '722 patent given the company's abandonment of patent

infringement litigation."); *id.* at 10 ("Cobalt abandoned patent infringement litigation and entered into a stipulation acknowledging that the company's products 'would infringe' the '722 patent."); *id.* at 11 ("Cobalt is no longer challenging the '722 patent and is therefore no longer participating in litigation intended to prove that its product will not infringe the listed patent.") (quotation omitted); Lupin Letter at 5 ("Cobalt settled the case and ceased asserting that the patent is in[fringed]."); *id.* ("Rewarding Cobalt with exclusivity when it has declined to defend its position in litigation is directly contrary to the purpose of 180-day exclusivity."); *id.* ("Cobalt eliminated any risk by settling the litigation."). That argument is unpersuasive.

### A. Cobalt Maintained Its Paragraph IV Challenge To The '722 Patent When It Settled With King and Aventis.

As a factual matter, Cobalt plainly *did* maintain its paragraph IV challenge to the '722 patent. Though Cobalt admitted that its product "would infringe" various claims of the '722 patent, the parties' stipulation also expressly reserved Cobalt's paragraph IV claims that the '722 patent is invalid and unenforceable. Indeed, each of Cobalt's admissions that it "would infringe" a particular claim of the '722 patent was followed by an express reservation that Cobalt was maintaining its "allegations that [that] claim [of the patent] is invalid and unenforceable." Stipulation ¶¶ 2, 3, 4, 5; *see also* Lupin Letter at 2 ("Cobalt stipulated to infringement, but *not* to the validity and enforceability of the '722 patent.") (emphasis added).

Nothing else was necessary for Cobalt to maintain a valid paragraph IV certification. Neither the statute nor FDA's implementing regulations require an applicant to challenge a listed patent on every possible ground in order to secure eligibility for 180-day exclusivity. To the contrary, the statute and regulations provide that a paragraph IV certification merely requires the applicant to certify that the challenged "patent is invalid, unenforceable, *or* will not be infringed" by the proposed new drug. 21 C.F.R. § 314.52(a) (emphasis added); *see also* 21 U.S.C. § 355(j)(2)(A)(vii)(IV). "Or" simply does not mean "and," and it is by now well-settled that an applicant need not maintain its paragraph IV challenge on every possible ground in order to maintain a valid certification. After all, applicants routinely concede validity or infringement in the course of patent litigation and thereafter focus their defense (or declaratory claims) on one or both of the remaining paragraph IV grounds. *See, e.g.*, *Impax Labs., Inc. v. Aventis Pharms. Inc.*, 468 F.3d 1366, 1373 (Fed. Cir. 2006); *Valley Drug Co. v. Geneva Pharms., Inc.*, 344 F.3d 1294, 1299 (11th Cir. 2003); *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1564 (4th Cir. 1997); *Sanofi-Synthelabo v. Apotex Inc.*, 488 F. Supp. 2d 317, 326 (S.D.N.Y. 2006); *Janssen Pharmaceutica N.V. v. Mylan Pharmaceuticals, Inc.*, 456 F. Supp. 2d 644, 647 (D.N.J. 2006); *In re Terazosin HCl Antitrust Litig.*, 335 F. Supp. 2d 1336, 1353 (S.D. Fla. 2004).

No one has ever suggested that this common approach to ANDA litigation would result in the effective abandonment of an applicant's paragraph IV certification, and given the thoroughly destabilizing effect that such a decision would have on the law, it is no surprise that

neither Petitioner seriously defends such a claim. There is therefore no basis for concluding that Cobalt somehow abandoned its paragraph IV challenge to the '722 patent.[1]

### B. The Mere Act Of Settling Patent Infringement Litigation Is Not Sufficient To Divest The First Applicant Of Its Exclusivity.

The only remaining question, then, is whether Cobalt's mere agreement to settle its litigation with King and Aventis is sufficient to divest Cobalt of 180-day exclusivity. *See, e.g.*, Hyman Phelps Letter at 6 n.5 ("The relevant issue is whether Cobalt's ANDA still contains a paragraph IV certification to the '722 patent given the company's abandonment of patent infringement litigation."); Lupin Letter at 5 ("Rewarding Cobalt with exclusivity when it has declined to defend its position in litigation is directly contrary to the purpose of 180-day exclusivity."). Given the long line of cases holding that eligibility for exclusivity cannot be conditioned on the maintenance of patent litigation, the Agency should reject Petitioners' efforts to revive such an approach.

That line of cases began in 1994, when the Agency promulgated a "successful defense requirement" that sought to prevent "first applicants who are not sued or who lose their suits from benefiting from the exclusivity period," and to that end "permit[ted] later applications to be approved ... simply because the first applicant's litigation *has not yet come to a successful conclusion*." *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1069 (D.C. Cir. 1998) (emphasis added); *see also Abbreviated New Drug Application Regulations*, 59 Fed. Reg. 50,338, 50,367 (1994) (then-codified at 21 C.F.R. § 314.107(c)(1)). The D.C. Circuit invalidated that rule, holding that it was "inconsistent with the unambiguously expressed intent of Congress [and] gravely inconsistent with the text and structure of the statute," because "its practical effect [was] to write the commercial-marketing trigger out of the statute," *id.* at 1069, and because "Congress may have intended to reward the first ... applicant for his enterprise whether or not he is later sued." *Id.* at 1071 n.11. The court therefore sent the Agency "back to the drawing board." *Purepac Pharm. Co. v. Friedman*, 162 F.3d 1201, 1205 (D.C. Cir. 1998).

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[1] The Agency need not address the point here, but even if Cobalt had conceded infringement, validity, *and* enforceability of the '722 patent, a strong case could be made that Cobalt would retain 180-day exclusivity based on the fact that it obtained a license to the '722 patent—at least so long as Cobalt did not simultaneously agree to abstain from entering the market until after the '722 patent expires. Paragraph IV certifications manifest an applicant's intention to market the generic drug product prior to patent expiry, and FDA thus has recognized that receipt of a license authorizing early market entry permits the applicant to maintain its paragraph IV certification. *See* 21 C.F.R. § 314.94(a)(12)(v). Without regard to any concessions or reservations contained in a given patent settlement, and provided that the applicant maintains its intention to enter the market at some point before the patent expires, the Agency thus cannot lawfully deprive the first-filer of its exclusivity simply because it settled litigation in exchange for license. After all, paragraph IV certifications are intended to enable early market entry, and once the first applicant secures what its paragraph IV certification was intended to secure—a right to enter the market before patent expiry—the only possible basis for depriving it of exclusivity is where the applicant agrees not to exercise that right.

On remand, the Agency not only excised the "successful defense" requirement from its regulation, but eliminated the antecedent requirement that a first applicant even be sued in the first place to obtain eligibility for exclusivity. *See id.* at 1204. Purepac challenged the Agency's revisions, arguing (as the D.C. Circuit later noted) that "[w]ithout a lawsuit there would be no judicial decision [trigger, and i]f the applicant never begins marketing its product, the 180 days would never run [because there would be no commercial marketing trigger]." *Id.* at 1205. In a footnote that anticipated the precise claims now raised by Petitioners, the D.C. Circuit observed that "this could happen if, for instance, the suit is dropped *or settled*." *Id.* at 1205 n.6 (emphasis added).

Notwithstanding those concerns, the D.C. Circuit flatly rejected Purepac's assertion that eligibility for 180-day exclusivity could be conditioned on the initiation or maintenance of patent litigation, observing that "[s]ection 355(j)(5)(B)(iv) does not, on its face, require the first applicant to be sued in order to benefit from market exclusivity," and holding that "Purepac's real objection is to the words Congress used, not the FDA's revision of its regulation." *Id.* at 1204-05.

Together, those precedents precluded the Agency from conditioning an applicant's exclusivity on a successful litigation outcome (*Mova*), or even on the initiation of litigation in the first instance (*Purepac*). Nonetheless, the Agency continued to draw a litigation/non-litigation distinction in cases where a patentee or NDA holder requested the delisting of a claimed patent—effectively permitting NDA holders and patentees to deprive the first-filer of 180-day exclusivity where the NDA holder or patentee had not initiated suit, but preserving the first-filer's exclusivity in those cases where the NDA holder or patentee had done so. *See Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120, 123 (D.C. Cir. 2006). That regulation likewise was challenged, and the D.C. Circuit invalidated that approach as well. As the court explained, "the statute [does] not require litigation to preserve a generic applicant's eligibility for exclusivity, as those precedents make clear; such a requirement is inconsistent with the structure of the statute." *Id.* at 125.

Despite this unbroken line of authority, Petitioners insist that Cobalt's agreement to settle its litigation with King and Aventis—as Lupin puts it, to "decline[] to defend its position in litigation," Lupin Letter at 5—somehow operates to divest Cobalt of its entitlement to 180-day exclusivity. That position, in short, all but expressly seeks to revive the very successful defense requirement that the D.C. Circuit rejected in *Mova*, *Purepac*, and *Ranbaxy*. But as those decisions repeatedly explained, such a requirement essentially writes the commercial marketing trigger out of the statute, because it would force a sued first applicant to keep litigation alive until the entry of a final judicial decision in order to maintain its eligibility for 180-day exclusivity. *Ranbaxy*, 469 F.3d at 125; *Purepac*, 162 F.3d at 1204-05; *Mova*, 159 F.3d at 1069.

If these cases stand for nothing else, it is that the Agency cannot, consistent with the statute, force first applicants to obtain—or even to seek—a final court decision in order to preserve their eligibility for exclusivity. To the contrary, these cases recognize that the pathway to early market entry is a paragraph IV certification, and that the first paragraph IV filer is

entitled to a 180-day period of exclusivity regardless of whether they are sued in the first instance, and regardless of whether they maintain litigation (if any) to a final court decision. The positions advocated by Petitioners cannot be reconciled with this unbroken line of authority, and the Agency should reject their invitation to reversal.

Indeed, Petitioners' approach not only lacks any basis in the text or structure of the statute, it undermines the statute's incentive structure. In many cases, sued applicants are able secure favorable settlement terms from the patentee or NDA holder—including a license that would permit market entry prior to the expiration of the challenged patent—precisely because their legal defense of a paragraph IV certification is so strong. In such cases, the applicant has not only assumed the very litigation risk that 180-day exclusivity is designed to reward, *see, e.g.*, *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 879 (D.C. Cir. 2004); *Sandoz, Inc. v. FDA*, 439 F. Supp. 2d 26, 29 (D.D.C. 2006), but has accomplished precisely what 180-day exclusivity is intended to achieve—the possibility of market entry prior to the expiration of a blocking patent. Stripping a first applicant of its exclusivity in these circumstances thus not only contravenes the text and structure of the Act; it subverts the scheme by "diminish[ing] the incentive for a manufacturer of generic drugs to challenge a patent listed in the Orange Book in the hope of bringing to market a generic competitor for an approved drug without waiting for the patent to expire." *Ranbaxy*, 469 F.3d at 126.

### C. Petitioners' Remaining Arguments Are Inconsistent With The MMA.

To be sure, not all applicants will enter the market immediately following a patent settlement, and Petitioners each make much of the fact that Cobalt does not yet appear to have entered the market pursuant to its settlement-derived ramipril license (to its credit, Hyman Phelps does concede that the point is all but moot here, given the Federal Circuit's recent decision in Lupin's patent infringement case, *see* Hyman Phelps Letter at 6 n.5). However meritorious those concerns may be as a general matter, however, they do not authorize the Agency to rewrite the Hatch-Waxman Act—and not least of all because Congress already did.

With Congress's passage of the MMA, the statute now specifically requires parties to submit patent settlements like the one at issue here to the FTC and Attorney General for review, *see* 21 U.S.C. § 355 note (FTC Review), and expressly provides for the forfeiture of 180-day exclusivity in the event the FTC obtains a final court decision that the agreement violates the antitrust laws. *See* 21 U.S.C. §§ 355(j)(5)(D)(i)(V)-(j)(5)(D)(ii). Notably, that provision of the Act was made effective "without regard to when the first [paragraph IV] certification ... for the listed drug was made." MMA § 1102(b).

Thus, while Petitioners emphasize that the FTC initiated an investigation into the Cobalt-King-Aventis ramipril settlement after receiving notice from the parties, *e.g.*, Hyman Phelps Letter at 3 n.4; Lupin Letter at 3, that point actually undermines their position in this case. That Congress now has *amended the statute* to provide for a forfeiture where FTC obtains a final decision holding that the parties' settlement was anticompetitive shows that Congress well understood that settlement agreements had no impact on the applicant's eligibility for exclusivity

under the pre-MMA scheme. That fundamentally undermines any claim that the mere settlement of infringement litigation operates to divest the first applicant of 180-day exclusivity. Congress is ordinarily presumed not "to pass vain or meaningless legislation," *International Ass'n of Machinists & Aerospace Workers v. BF Goodrich Aerospace Aerostructures Group*, 387 F.3d 1046, 1057 (9th Cir. 2004) (citation and quotation omitted), and the addition of this forfeiture trigger would not have been necessary if the prior statute already mandated forfeiture whenever an applicant fails to successfully defend a patent infringement suit through the entry of a final court decision.

Far more important, the fact that Congress made this provision of the statute retroactive—and that it thus applies in this case—eliminates any leeway the Agency otherwise may have had to adopt the position advocated by Petitioners. In short, this forfeiture trigger speaks directly to the issue of patent settlements, and it leaves no gap for the Agency to fill. The FTC's investigation of the parties' settlement shows that the statute is working precisely as Congress intended, and Petitioners thus are effectively asking this Court rewrite the MMA, by expanding the otherwise limited list of forfeiture conditions to include *any* patent settlement—regardless of whether, as Congress provided, such a settlement is finally determined to violate the antitrust laws. That turns the ordinary rules of statutory construction upside down; it generally is presumed that Congress's expression of one thing manifests its intent to exclude others, *e.g.*, *O'Melveny & Myers v. FDIC*, 512 U.S. 79, 86 (1994), and there is no sound basis for departing from that rule here.

By the same token, another set of MMA forfeiture provisions now addresses the concern that eligible applicants might indefinitely deprive the public of market competition by failing to diligently pursue market entry. Indeed, the post-MMA statute provides that exclusivity is forfeited in the event an applicant fails to obtain tentative approval within 30 months of submitting its exclusivity-qualifying paragraph IV certification, *see* 21 U.S.C. § 355(j)(5)(D)(i)(IV), and, in certain cases, where the applicant fails to commence commercial marketing within 75 days of the date that "a court signs a settlement order or consent decree that enters a final judgment that includes a finding that [each exclusivity-qualifying] patent is invalid or not infringed." 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(BB).

These amendments likewise would have been unnecessary if the pre-MMA scheme already contained such restrictions, but the key point here is that Congress did *not* make those provisions of the statute retroactive. *See* Hyman Phelps Letter at 5 n.5 ("Congress did not ... make ... these changes retroactive."). There is no basis for "carry[ing] out Congress' intent in creating [these provisions] in pre-MMA cases involving 'parked' exclusivity." *Cf.* Hyman Phelps Letter at 5 n.5. Congress's manifest intent was *not* to make those changes to the statute retroactive, and the Agency has no authority to impose retroactively what Congress chose to impose prospectively.

## CONCLUSION

For the foregoing reasons, the Agency should hold that Cobalt remains eligible for 180-day exclusivity despite conceding infringement in its settlement with King and Aventis. If you have any questions or require additional information regarding this matter, please contact me by telephone (202-879-5228) or fax (202-654-9628).

Sincerely,
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