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Gary J. Buehler, R.Ph.
Director, Office of Generic Drugs (HFD-600)
Food and Drug Administration
Center for Drug Evaluation and Research
Room 286, Metro Park North 2 Bldg.
7500 Standish Place
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Dear Mr. Buehler:

On behalf of our client, Lupin Pharmaceuticals, Inc. ("Lupin"), we write to request immediate approval for ANDA No. 77-626, for ramipril capsules.

Factual Background

King Pharmaceuticals, Inc. ("King") is the holder of NDA No. 019901 for ramipril 1.25mg, 2.5mg, 5mg, and 10mg capsules, which are marketed under the name Altace®. Two patents are listed as claiming the drug, U.S. patent No. 5,061,722 ("the '722 patent") and a method of use patent, U.S. Patent No. 5,403,856 ("the '856 patent"). Aventis Pharma Deutschland Gmbh ("Aventis") is the owner of the '722 patent and has licensed the rights to sell ramipril drug products in the United States to King.

On March 18, 2005, Lupin submitted ANDA No. 77-626 referencing King's ramipril capsules. Lupin's ANDA contained a paragraph IV certification to the '722 patent and a section viii statement indicating it would carve out the '856 patent. King received Lupin's notice of the paragraph IV certification June 8, 2005.

King sued Lupin on July 19, 2005 for patent infringement in the United States District Court for the Eastern District of Virginia. The District Court entered a judgment against Lupin on infringement and invalidity, which Lupin appealed. After years of litigation, on September 11, 2007, the Court of Appeals for the Federal Circuit ruled in Lupin's favor, holding that the '722 patent is invalid. A copy of the decision of the court of appeals is attached as Exh. 1.

Other ANDAs seeking approval to market ramipril capsules have been submitted to FDA. It appears that the first ANDA referencing King's ramipril capsules that contained a paragraph IV

certification to the '722 patent was submitted by Cobalt Pharmaceuticals, Inc. ("Cobalt"),[1] an affiliate of Arrow International Limited ("Arrow"). Cobalt provided notice to King of its paragraph IV certification on February 5, 2003, and on March 14, 2003, Aventis and King sued Cobalt for infringement of the '722 patent.[2]

In the course of the litigation, Cobalt stipulated to infringement, but not to the validity and enforceability of the '722 patent. Instead, the parties settled the patent infringement case, avoiding a holding on the merits.[3]

The settlement between Cobalt and King appears to involve a series of transactions and agreements between King and Cobalt and other Cobalt affiliates, including Arrow, Robin Hood Holdings Limited, and Selamine Limited ("Selamine").[4] The exact nature of these transactions and agreements is difficult to ascertain because not all the terms are public. It appears these transactions include a Ramipril Patent License Agreement, under which Selamine receives $10 million from King in exchange for a license to its ramipril patents; a Ramipril Application License Agreement, under which King licenses a ramipril NDA from Arrow and obtains an option to buy the NDA upon approval in exchange for an amount between $75-100 million; and a Product Supply Agreement, giving Selamine certain rights to supply ramipril tablets to King.[5] King also granted Cobalt the right to market generic capsules at some undisclosed date under another agreement.[6]

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1. Aventis Pharma Deutschland Gmbh and King Pharmaceuticals, Inc. v. Cobalt Pharmaceuticals, Inc., Civil Action No. 03-10492 JLT, (D. Mass. Complaint filed Mar. 14, 2003) ("Cobalt Complaint") at ¶ 6. A copy of the Cobalt complaint is attached as Exh. 2.

2. Id.

3. A copy of the stipulation voluntarily dismissing the case without prejudice is attached as Exh. 3.

4. King Pharmaceuticals Inc., Quarterly Report (Form 10-Q), at 10 (Aug. 7, 2007) ("King 10-Q"), available at http://www.sec.gov/Archives/edgar/data/1047699/000095014407007396/g08394e10vq.htm/; Exhibits to King Pharmaceuticals, Inc., Quarterly Report (Form 10-Q) (May 10, 2006), available at http://www.sec.gov/Archives/edgar/data/1047699/000095014406004699/g00994e10vq.htm

5. Id.

6. King 10-Q.

Once FDA approved Cobalt's NDA for ramipril tablets on Feb. 27, 2007,[7] King acquired the rights to the tablet NDA from Arrow.[8] King has announced that, notwithstanding the approval of the tablet NDA, it will not launch ramipril tablets until the last quarter in 2007, or the first quarter in 2008.[9] In a filing with the SEC, King has revealed that its settlement with Cobalt is under investigation by the Federal Trade Commission (FTC). King has received a civil investigative demand (CID) from the FTC seeking information related to the dismissal without prejudice of the patent litigation and King's collaboration with Arrow.[10]

Cobalt has never marketed ramipril capsules. While Cobalt's ANDA was approved Oct. 24, 2005, its ramipril capsules appear in the Discontinued Section of the Orange Book.[11] To date, Cobalt has not announced that it expects ever to do so. Cobalt's parking of its 180-day exclusivity period allows King to delay launch of the ramipril tablets until its status as sole marketer of the capsules is close to its end, and then convert the market to tablets.

Other generic companies have submitted ANDAs for ramipril capsules. Teva's ANDA No. 077470, Purepac's ANDA No. 077513, Sandoz's ANDA No. 077514, Roxanne's ANDA No. 077900 and Dr. Reddy's ANDA No. 078191, all have received tentative approval.[12] Had Lupin not pursued its patent litigation to a successful conclusion, Cobalt could have continued to park its exclusivity until the '722 patent expired in October 2008, thereby precluding any generic competition.

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7. Letter from Norman Stockbridge, M.D., Ph.D., to Cobalt Pharmaceuticals Inc. (Feb. 27, 2007), available at http://www.fda.gov/cder/foi/appletter/2007/022021s001tr.pdf.

8. King 10-Q.

9. Id.

10. King 10-Q at 18.

11. Approved drug products are added to the Discontinued Section when the drug is not being marketed. Orange Book, § 1.11 (27th edition), available at www.fda.gov/cder/orange/obannual.pdf (last visited Sept. 21, 2007).

12. Lupin assumes that these ANDAs contained paragraph III certifications as none was sued for patent infringement by King or Aventis and King's 10-Q filing, King 10-Q at 18, identifies only Cobalt and Lupin as having filed paragraph IV certifications to the '722 patent.

Discussion

King has followed a not unfamiliar strategy seeking to protect its ramipril monopoly. King entered into an agreement with Cobalt, the first applicant with an ANDA containing a paragraph IV certification, before the courts could decide King's patent infringement case. As a result of the agreement, although Cobalt has received final approval, it did not launch, allowing its exclusivity to act as a barrier to entry for other generics. The strategy could have served to perpetuate King's monopoly until patent expiration, but for Lupin's decision to pursue its patent litigation to a successful conclusion.

In Mova Pharm. Corp. v. Shalala, the court observed that "the problem of the meritorious second applicant is a real one," but concluded that the successful defense requirement was too blunt an instrument to solve it.[13] The court was careful to observe that it did not "of course, foreclose the FDA from attempting to address the problem of the meritorious second applicant in some narrower way, as long as that solution conforms to the statute."[14]

Lupin is the meritorious second applicant whose successful challenge to the King patent opens the door to generic competition. The statute manifests a clear intent to encourage ANDA applicants to challenge listed patents and open up markets to generic competition. FDA should conclude that Cobalt is no longer entitled to 180-day exclusivity. In the alternative, FDA should recognize an exception to the usual certification practice for the meritorious second applicant, particularly where the first applicant frustrates the intent of the statute. Under either approach, Lupin is entitled to immediate approval of its ANDA.

I. Cobalt is No Longer Entitled to 180-Day Exclusivity

To entitle an ANDA applicant to 180-day exclusivity, its ANDA must "contain" a paragraph IV certification.[15] Cobalt's ANDA no longer contains a valid certification.

Cobalt's entitlement to 180-day exclusivity is grounded in the paragraph IV certification to the '722 patent "contained" in its ANDA. In order to make that certification, Cobalt manifested its opinion that the '722 patent was invalid or not infringed by the Cobalt drug.[16]

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13. Mova Pharm. Corp. v. Shalala, 140 F.3d 1060, 1074 (D.C. Cir. 1998).

14. Id.

15. 21 U.S.C. § 355(j)(5)(B)(iv).

16. 21 U.S.C. § 355(j)(2).

Since Cobalt made its certification, the facts have changed dramatically. Cobalt has stipulated that its drug infringes the '722 patent. A copy of this stipulation, filed in the litigation between King and Cobalt, is attached as Exh. 4. Cobalt settled the case and ceased asserting that the patent is invalid. Similarly, it has been unwilling to stand behind its initial opinion by marketing its ramipril product. In short, Cobalt has long since given up its challenge to the '722 patent, and its ANDA no longer contains a valid paragraph IV certification.

Rewarding Cobalt with exclusivity when it has declined to defend its position in litigation is directly contrary to the purpose of 180-day exclusivity. As many courts have noted, 180-day exclusivity was intended to reward the first ANDA applicant to file a paragraph IV certification and risk litigation. But Cobalt eliminated any risk by settling the litigation and failing to market. FDA should be guided by the design of the statute as a whole, and the statute's object and policy.[17]

FDA faced a similar situation in 2001 with respect to nifedipine. There, Mylan, the first paragraph IV filer, was sued by the innovator, Pfizer. Eventually, the companies settled and, as here, even though its drug was approved, Mylan did not market. When Teva argued that Mylan had no exclusivity, FDA agreed. Because Mylan had settled the suit and failed to market, FDA presumed that Mylan believed that its product might infringe the relevant patent and that Mylan was waiting for patent expiration to market its generic product. Thus, Mylan had effectively converted its paragraph IV certification to a paragraph III.[18] When Mylan sued FDA, the West Virginia District Court concluded that FDA could not deem Mylan's certification a paragraph III because neither the statute nor the regulations provided for doing so, and because the agency's presumption was inadequately supported.[19]

FDA had no opportunity to appeal the District Court's decision on this issue because it prevailed in the litigation on other grounds. But FDA has never acquiesced in the decision. Moreover, the West Virginia District Court's rationale conflicts with current readings of the statute and regulations. Since that 2001 decision, it has been well-established that, despite the absence of a specific provision in the statute or regulations, FDA may deem certifications changed in appropriate circumstances, and there is ample precedent for doing so.[20] Whether the

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17. See Kelly v. Robinson, 479 U.S. 36, 43 (1986); Mylan v. Henney, 94 F. Supp. 2d at 50.

18. Letter from Janet Woodcock, M.D. to Deborah Jaskot, Docket 00P-1446/PAV1 (February 6, 2001).

19. Mylan v. Thompson, 207 F. Supp. 2d. 476, 486-87 (N.D. W.Va. 2001).

20. See Mylan Labs, Inc. v. Thompson, 332 F. Supp. 2d 106, 124 (D.D.C. 2004), aff'd, 389 F.3d 1272 (D.C. Cir. 2004); Ranbaxy Labs, Ltd. v. FDA, 307 F. Supp. 2d 15 (D.D.C. 2004), aff'd, 2004 U.S. App. LEXIS 8311 (D.C. Cir. Apr. 26, 2004); Dr. Reddy's Laboratories, Inc. v.

presumption was adequately reached with respect to Mylan is a factual judgment that will vary with the circumstances of the particular case. In light of the subsequent case law, FDA should not follow the rationale of the Mylan opinion. Instead, FDA should follow its own prior precedent by concluding that Cobalt paragraph IV certification is no longer valid, thereby extinguishing Cobalt's entitlement to 180-day exclusivity.

Lupin does not suggest that any agreement to settle patent litigation or failure to market should extinguish 180-day exclusivity. Whether a first filer retains its exclusivity necessarily involves consideration of the facts. In this situation, however, there can be no doubt that allowing Cobalt to retain exclusivity would be contrary to the intent of the statute.

II. Lupin Should Be Permitted to Amend Its ANDA to Remove the Paragraph IV Certification

Because Lupin was not the first applicant to file a paragraph IV certification for ramipril, Lupin's approval will be delayed if it is required to maintain a paragraph IV certification and Cobalt has 180-day exclusivity.[21] The FDCA and FDA's regulations provide for changes in certification when circumstances change. In this case, the circumstances have changed and Lupin should be permitted to amend its certification so that its approval is not affected by Cobalt's exclusivity.

Section 505(j)(2)(vii) provides that an ANDA shall contain:

> a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug ... for which the applicant is seeking approval ... and for which information is required to be filed...
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> (I) that such patent information has not been filed,
>
> (II) that such patent has expired,
>
> (III) of the date on which such patent will expire, or
>
> (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted...[22]

Thompson, 302 F. Supp. 2d 340 (D.N.J. 2003).

21. 21 U.S.C. § 355(j)(5)(B)(4).

22. 21 U.S.C. § 355(j)(2)(vii).

When Lupin submitted its ANDA in 2005, it included a paragraph IV certification to the '722 patent because it believed that the '722 patent was invalid. At that time, the patent, duly issued by the Patent and Trademark Office, was presumed valid. Therefore, Lupin could not certify that the '722 patent did not claim the listed drug, and was required to submit a paragraph IV certification.

Those circumstances have now changed. As between King and Lupin, the decision of the Federal Circuit in Aventis v. Lupin,[23] held that the patent is invalid. There is no longer any valid claim arising from the '722 patent that can be asserted against Lupin by King/Aventis. King is precluded by principles of res judicata from pursuing any claim against Lupin.[24] Thus, the '722 patent cannot in any real sense be said to be a "patent which claims the drug referred to" in Lupin's ramipril ANDA, and Lupin's ANDA need not contain any certification to that patent. For this reason, the appropriate certification for Lupin is that there are no relevant patents that claim the drug, a certification provided for in 21 C.F.R. § 314.94(a)(12)(ii).

FDA's regulations provide that certifications may be "changed at any time before the effective date of the approval of the application."[25] Although the regulations identify narrowly circumscribed situations in which certifications may not be changed, none are applicable to Lupin's planned change.

Interpreting the statute and regulations as Lupin has done yields a result that furthers the intent of Hatch Waxman and the policies that it was designed to promote and is just. Hatch Waxman was intended to strike a balance between promoting generic competition and protecting innovator investment.[26] 180-day exclusivity was intended to encourage generic applicants to challenge brand company patents to remove barriers to approval.[27] Lupin has challenged the patent successfully, so that generic ramipril can be brought to market. Cobalt has done just the reverse. No generic ramipril is now marketed, and Aventis, King and Cobalt clearly had no incentive to bring one to market absent Lupin's successful challenge. Aventis, King, and Cobalt have prevented generic competition for almost two years beyond when generic competition should have been available. "Hatch-Waxman intended to provide an incentive for drug

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23. Aventis v. Lupin, 2007 U.S. App. LEXIS 21753 (Fed. Cir. Sept. 11, 2007).

24. Hart Steel Co. v. Railroad Supply Co., 244 U.S. 294, 297-98 (1917).

25. 21 C.F.R. § 314.94(a)(viii).

26. See Serono Labs. Inc. v. Shalala, 158 F.3d 1313, 1326 (D.C. Cir.1998); Andrx Pharm., Inc. v. Biovail Corp. Int'l, 256 F.3d 799, 809 (D.C. Cir. 2001).

27. Letter from Gary Buehler to ANDA Applicant/Holder for Amlodipine Besylate Tablets, (Apr. 15, 2007) ("Amlodipine Letter"), p.8; Mova v. Shalala, 140 F.3d 1060.

companies to explore new drugs, not a market 'windfall' for crafty, albeit industrious market players,"[28] and statutes should not be interpreted to create anticompetitive effects.[29] Interpreting the statute so as to prevent Lupin's entry would be both anticompetitive and directly contrary to the policies that underlie Hatch Waxman.

It would also be just to adopt Lupin's interpretation. Lupin, a relatively small company that did not even enter the U.S. market until 2003, bore the expense of litigating the '722 patent's validity, and Lupin was successful in invalidating the patent. Cobalt, on the other hand, gave up its patent challenge, and chose instead to halt all generic competition. As a relatively new entrant in the U.S. generic pharmaceutical market without a large base of marketed products, Lupin will be severely harmed if it is forced to wait another six to nine months before marketing its generic ramipril. Lupin is ready to market now and should be allowed to do so. The public also will be harmed if it must continue to pay the high prices now charged for ramipril. Justice requires that Lupin be allowed to market its generic ramipril.

FDA faced a somewhat similar situation in deciding when to issue approvals for amlodipine. In issuing effective approvals on amlodipine, FDA distinguished the position of an ANDA applicant that had invalidated relevant claims of the patent from those that had not. FDA decided that Apotex, which had succeeded in invalidating the relevant claims of the patent, could be approved despite the brand manufacturer's pediatric exclusivity, whereas Teva and others could not. Both the D.C. District Court and D.C. Court of Appeals rejected challenges to FDA's decision.[30] In the amlodipine situation, FDA was interpreting the pediatric exclusivity statutory provisions, rather than 180-day exclusivity provisions. But the logic of recognizing an exception for a meritorious applicant is very similar. In that case, FDA created an "exception to the application of the Hatch-Waxman certification provisions" in order to further the clear "Congressional intent."[31]

Like the situation in amlodipine, FDA has not previously, to our knowledge, permitted an applicant to remove its paragraph IV certification from its ANDA. For the same reasons articulated in the amlodipine decision – the fact that the statute does not address this situation and the Congress' intent is so clear – FDA should create an exception here, allowing a change in certification permitting immediate approval of an applicant that has invalidated a patent when the

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28. Mylan Pharm. Inc. v. Henney, 94 F. Supp. 2d 36, 53 (D.D.C. 2000), vacated as moot, Pharmachemie B.V. v. Barr Labs., Inc., 284 F.3d 125 (D.C. Cir. 2002).

29. Id., citing Two Pesos, Inc. v. Taco Cabana, Inc., 505 U.S. 763 (1992).

30. Mylan v. Leavitt, 483 F. Supp. 2d (D.D.C. 2007); Mylan v. Leavitt, 2007 U.S. App. LEXIS 12462 (D.C. Cir. May 23, 2007) (denying injunction pending appeal).

31. Amlodipine Letter, at p.9.

first applicant has abandoned its effort to do so, and particularly where the first applicant has participated in blocking generic competition.[32]

There are strong public policy reasons for adopting this exception. FDA, along with the FTC and others, have long been concerned with arrangements between a brand name company and the first ANDA applicant to file a paragraph IV certification that can be of considerable financial benefit to the parties, but delay competition by forestalling the beginning of 180-day exclusivity.[33] Some settlements result in early entry of generics and benefit to consumers. Others, however, serve to protect the brand company's monopoly by compensating a generic challenger for its agreement to a later entry date than the generic firm would otherwise have chosen.[34] According to the FTC, features of such settlements may include provisions to defer entry by others, and compensation to the generic – directly or conveyed through other products and side deals. This exemption to the certification practice will function as an incentive for subsequent filers to litigate a patent infringement case to its conclusion and serve to spur competition and diminish the effects of anticompetitive settlements.

In summary, FDA should not allow Cobalt to prevent Lupin, which has litigated for years at great cost, from marketing the generic ramipril now. It need not do so. The statute plainly provides for a fair result, and FDA should construe the statute accordingly. Lupin is prepared to amend its certification immediately if FDA will permit it to do so.

III. The Clear Language Of The Statute Entitles Lupin To Immediate Approval

When a district court judgment in favor of the patent holder is overturned on appeal (and no 180-day exclusivity delays the approval), the clear statutory language directs FDA to approve the ANDA on "the date on which the court of appeals decides that the patent is invalid or not

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32. Lupin does not intend that all generic applicants be able to change their certifications. As FDA decided with respect to amlodipine, Lupin proposes that only those applicants that succeed in invalidating the patent where a first applicant has failed or given up the attempt should change certifications.

33. E.g., 180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications, 64 Fed. Reg. 42873, 42874 (proposed Aug. 6, 1999) (to be codified at 21 C.F.R. pt. 314).

34. Protecting Consumer Access to Generic Drugs: The Benefits of a Legislative Solution to Anticompetitive Patent Settlements in the Pharmaceutical Industry: Hearing Before the Subcomm. on Commerce, Trade, and Consumer Protection of the H. Comm. on Energy and Commerce, 110th Cong. 18 (2007) (statement of Jon Leibowitz, Comm'r of the Federal Trade Commission).

infringed."[35] The date on which the court of appeals decided that the '722 patent is invalid is September 11, 2007. Lupin, therefore, is entitled to approval now.

Section 505(j)(5)(B)(iii) provides, in pertinent part, that:

> If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification . . . . If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order . . . except that –
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> * * *
>
> (II) if before the expiration of such period the district court decides that the patent has been infringed –
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> (aa) if the judgment of the district court is appealed, the approval shall be made effective on –
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> (AA) the date on which the court of appeals decides that the patent is invalid or not infringed . . . .[36]

There is no ambiguity to the phrase "the date on which the court of appeals decides." The term "decides" is clear. "Decide" means to arrive at a choice or solution concerning which ends uncertainty.[37] "Decides" can be a synonym for "determines," though while "determine" may imply that considerations and judgments are decisive, "decide" simply means to come to a

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35. Id.

36. 21 U.S.C. § 355(j)(5)(B)(iii) (2007). This section was amended in 2003 as part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Public Law 108-173) ("MMA"). The amendment applies to any proceeding under section 505 of the FDCA that is pending on or after the date of enactment of the MMA. Pub. Law 108-173, Sec. 1101(c), 117 Stat. 2456.

37. Webster's Third New International Dictionary, p. 585 (2002).

conclusion.[38] As commonly understood, a "decision" can, but need not, finally resolve a case.[39] When Congress has directly spoken to the precise question at issue, as it has here, "the agency must give effect to the unambiguously expressed intent of Congress."[40] The court of appeals decided that King's patent was invalid on September 11, 2007, and Lupin has been entitled to approval since then, regardless of when the mandate issues.

In the context of pediatric exclusivity, FDA recently interpreted the term "court determined," to require issuance of the mandate.[41] As explained below, that interpretation of the pediatric exclusivity provisions does not compel imposition of the same requirement on the approval provisions of Hatch Waxman.

First, as a matter of statutory construction, the use of different terms generally signifies that different meanings were intended.[42] Conversely, different terms within a statute generally may not be construed to have the same meaning.[43] The language used by Congress for pediatric exclusivity, "the court determines that the patent is invalid and would be infringed," 21 U.S.C. § 355a(c)(2)(B), is different than the language used by Congress to trigger approval, "the date on which the court of appeals decides that the patent is invalid or not infringed." As a matter of statutory construction, the two different terms should not be construed to have the same meaning.

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38. Id.

39. Teva Pharms. v. United States, 182 F.3d 1003, 1007-08 (D.C. Cir 1999) (holding that "[a] 'decision' can take several forms, including final judgment after a full trial, summary judgment or partial summary judgment, or even a dismissal for failure to state a cause of action").

40. Chevron, U.S.A. Inc. v. NRDC, 467 U.S. 837, 842-43 (1984).

41. Amlodipine Letter at pp.5-7; Mylan v. Leavitt, 484 F. Supp. 2d 109 (D.D.C. 2007).

42. Sutherland, Statutory Construction 193-94 § 46:06 (2000).

43. Id. See also Sosa v. Alvarez-Machain, 542 U.S. 692, 712 (2004) quoting 2 A. N. Singer, Statutes and Statutory Construction § 46:06, p. 194 (6th Ed. 2000) (relying on "the usual rule that 'when the legislature uses certain language in one part of the statute and different languages in another, the court assumes different meanings were intended,"); Doe v. Chao, 540 U.S. 614, 630 (2004), quoting Rusello v. United States, 464 U.S. 16, 23 (1983) ("we refrain from concluding here that the differing language in the two subsections has the same meaning in each."); INS v. Cardoza-Fonseca, 480 U.S. 421, 432 (1987); International Union v. Dole, 919 F.2d 753 (D.C. Cir 1990), citing to Persinger v. Islamic Republic of Iran, 729 F.2d 835, 843 (D.C. Cir 1984) ("the use of different language in different parts of the same statute creates a strong inference that different meanings are intended").

Congress already decided what degree of finality is necessary for approval. For a district court decision, the statute provides that when no appeal is taken approval is triggered not by a decision, but by a judgment.[44] When a judgment is appealed, however, the statute provides that the decision of the court of appeals provides the necessary assurance of finality, without requiring a mandate, which is roughly the appellate analogue to a district court judgment. By doing so, Congress intended to eliminate any delay arising from a petition for certiorari to the Supreme Court, or from a petition for rehearing or rehearing en banc or from the issuance of the mandate.

As a practical matter, awaiting for the mandate adds no more meaningful certainty of finality. The Federal Circuit grants petitions for rehearing, and rehearing en banc very rarely. From January 1, 2003, to May 15, 2004, of 400 petitions for rehearing and rehearing en banc, the court granted 7. In other years, the percentage has ranged between 3% to 1%.[45] Thus, the likelihood that a court of appeals will even consider rehearing is extremely low, and the likelihood that any rehearing will result in reversal necessarily is even more minute. Congress did not intend that this extremely low threshold of uncertainty delay approval.

In contrast, the harm to an ANDA applicant from awaiting for a mandate to issue before approval usually will be, as it is in this case, immediate, severe, and irreparable. In this instance, Lupin's competitors avoided litigation by filing paragraph III certifications. Presumably many, if not all, have amended their certifications to paragraph IV certifications. Assuming King does not delist the '722 patent, their approval must, at a minimum, wait until 45 days after notice. Thus, Lupin, whose litigation efforts have permitted generic competition, ought to have at least weeks of head start over its competitors – unless FDA delays approval to await issuance of the mandate. Delaying approval until the mandate issues erodes Lupin's hard-earned head start.

Lupin's competitors in the ramipril capsule market include some of the largest generic drug companies in the world. Lupin will be able to offset some of their advantage if it is able to enter the market ahead of them, even if only slightly. The loss of this head start will permanently disadvantage Lupin in the market for ramipril.

Given the slim likelihood that rehearing will be granted by the Federal Circuit, one would not expect many petitions for rehearing. But delaying approval until the mandate issues gives rise to a strong incentive to ask for rehearing. According to King, sales of ramipril capsules in

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44. 21 U.S.C. § 355(j)(5)(B)(iii)(I)(aa).

45. George Quillin & Jacqueline Wright, Rare Success Upon Filing Petitions for Rehearing by the Panel or En Banc at the Federal Circuit v. Certiorari at the Supreme Court, Corporate Counsel (July 2004), at A6, available at http://www.foley.com/files/tbl_s31Publications/FileUpload137/2090/Quillin%20-%20Wright%20FINAL.pdf.

2006 exceeded $650 million.[46] Each month of delay insulates over $50 million in sales from generic competition. That is incentive for King, or any other losing patent holder, to file a petition for rehearing, regardless of the merits, and delay the issuance of a mandate. Such a petition, however, results in real harm to Lupin and the public.

The harm to Lupin far exceeds the sales foregone while awaiting the mandate, because of the loss of intangible benefits that go along with being the first generic on the market, such as the opportunity to become the most visible generic entrant, forge early relationships with customers and acquire market share.[47] Delay in approval already has harmed Lupin. Further delay will cause additional imminent, serious, and irreparable harm to Lupin.

The public also will lose by having to pay higher prices than it would if Lupin were able to market its lower-priced generic ramipril capsules during any delay. Hatch Waxman was intended to "get generics into the hands of patients at reasonable prices – fast."[48] Delaying approval even after the court of appeals has decided is not in the public interest.

Conclusion

The plain language of Section 505(j)(5)(B)(iv) entitles Lupin to approval immediately upon the issuance of the Federal Circuit's decision and nothing in that section or elsewhere authorizes delay in approval. Accordingly, FDA should immediately approve Lupin's ANDA for ramipril.

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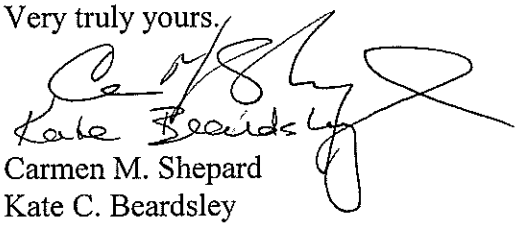
46. King Pharmaceuticals, 2006 Annual Report, at 9 (2007), available at www.kingpharm.com/kingpharm/uploads/2006_KPI_AnnualReport.pdf (last visited Sept. 23, 2007).

47. See, e.g., Mova v. Shalala, 955 F. Supp. 128, 128-131 (D.D.C. 1997), aff'd, 140 F.3d 1060 (D.C. Cir. 1998) ("the earliest generic drug manufacturer in a specific market has a distinct advantage over later entrants.").

48. Andrx Pharms., Inc. v. Biovail Corp. Int'l, 256 F.3d at 809.

We appreciate your willingness to consider these issues on an expedited basis. In the event FDA decides to deny Lupin immediate approval, we request that Lupin be promptly informed.

Very truly yours,



Carmen M. Shepard
Kate C. Beardsley

cc: Elizabeth H. Dickinson, Esq.