United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued September 12, 2006 Decided November 14, 2006

No. 06-5154

RANBAXY LABORATORIES LIMITED, ET AL.,
APPELLEES

v.

MICHAEL O. LEAVITT, SECRETARY OF HEALTH AND HUMAN SERVICES, ET AL.,
APPELLANTS

Appeal from the United States District Court
for the District of Columbia
(No. 05cv01838)

Howard S. Scher, Attorney, U.S. Department of Justice, argued the cause for appellants. With him on the briefs were *Peter D. Keisler*, Assistant Attorney General, *Kenneth L. Wainstein*, U.S. Attorney, *Douglas N. Letter*, Attorney, and *Eric M. Blumberg*, Deputy Chief Counsel, U.S. Department of Health and Human Services. *Drake S. Cutini*, Attorney, U.S. Department of Justice, entered an appearance.

Simon E. Dance was on the brief for *amicus curiae* Blue Cross & Blue Shield Association, Inc. in support of appellants.

Carmen M. Shepard argued the cause for appellees

Ranbaxy Laboratories Limited, *et al.* With her on the brief were *Kate C. Beardsley* and *William B. Schultz*.

Jay P. Lefkowitz argued the cause for appellee Teva Pharmaceuticals, USA, Inc. With him on the brief were *John C. O'Quinn* and *Michael D. Shumsky*.

Theodore Case Whitehouse was on the brief for *amicus curiae* Generic Pharmaceutical Association in support of appellees.

Before: GINSBURG, *Chief Judge*, and GRIFFITH and KAVANAUGH, *Circuit Judges*.

Opinion for the Court filed by *Chief Judge* GINSBURG.

GINSBURG, *Chief Judge*: The Hatch-Waxman Amendments to the Food, Drug, & Cosmetic Act provide a period of marketing exclusivity to the first drug manufacturer that either successfully challenges a patent listed by the Food and Drug Administration for an approved, branded drug and markets an approved generic version of that drug or prevails in litigation establishing that the patent is valid or not infringed. Ranbaxy Laboratories Limited and Ivax Pharmaceuticals, Inc., the latter since acquired by Teva Pharmaceuticals, USA, Inc., applied for approval of drugs to compete with an approved drug manufactured by Merck & Co. and challenged two patents covering it. Thereafter, at Merck's request, the FDA removed the challenged patents from the "Orange Book," its listing of patents covering approved drugs, thereby depriving the generic manufacturers of an opportunity to have a period of marketing exclusivity.

Ranbaxy and Teva each filed a "citizen petition" asking the FDA to relist the two patents. The FDA denied the petitions

because Merck had not sued Ranbaxy or Teva for patent infringement. Ranbaxy and Teva then repaired to the district court, which entered a summary judgment for the plaintiffs, and the FDA appealed.

We hold the FDA's requirement that a generic manufacturer's patent challenge give rise to litigation as a condition of retaining exclusivity when a patent is delisted is inconsistent with the Act, which provides that the first generic manufacturer to file an approved application is entitled to exclusivity when it either begins commercially to market its generic drug or is successful in patent litigation. Accordingly, we affirm the judgment of the district court.

I. Background

Before marketing a new "branded" drug, the manufacturer must file with the FDA a New Drug Application (NDA), including evidence the drug is safe and effective, and the identifying number and expiration date of any patent or patents covering the drug. 21 U.S.C. § 355(a)-(b)(1). When it approves the NDA, the FDA must publish the patent information, *id.* § 355(b)(1), (c)(2), which it does in *Approved Drug Products with Therapeutic Equivalence Evaluations*, better known as the Orange Book.

Before marketing a "generic drug," which is bioequivalent to a branded drug previously approved pursuant to an NDA, the manufacturer may submit an Abbreviated New Drug Application (ANDA). Unlike an NDA, an ANDA need not contain evidence of the drug's safety or efficacy. *See* 21 U.S.C. § 355(j)(2). Each ANDA, however, must contain:

> a certification ... with respect to each patent which claims [a drug or a method of using a drug listed in the

> Orange Book] for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) of this section—
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> > (I) that such patent information has not been filed,
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> > (II) that such patent has expired,
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> > (III) [that] such patent will expire [on a specified date], 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[.]

Id. § 355(j)(2)(A)(vii). The Act rewards the first manufacturer to file an approved ANDA containing the certification in paragraph IV by giving it a 180-day period of marketing exclusivity, which begins with the earlier of the applicant's first commercial marketing of the generic drug or when the applicant prevails in a suit over infringement or the validity of the patents covering the branded drug. *Id.* § 355(j)(5)(B)(iii)-(iv).[*]

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[*] If the [ANDA] contains a certification described in [paragraph] (IV) ... and is for a drug for which a previous [ANDA] has been submitted under this subsection [containing] such a certification, the [ANDA] shall be made effective not earlier than one hundred and eighty days after—

> (I) the date the Secretary receives notice from the applicant under the previous [ANDA] of the first

When a patent is removed from the Orange Book (or, in the parlance of the agency is "delisted"), the FDA by regulation requires the sponsor of the corresponding ANDA to delete its paragraph IV certification with respect to the delisted patent. 21 C.F.R. § 314.94(a)(12)(viii)(B).* If no patent covering the

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> commercial marketing of the drug under the previous [ANDA], or
>
> (II) the date of a decision of a court in an action ... holding the patent which is the subject of the certification to be invalid or not infringed,
>
> whichever is earlier.

Id. § 355(j)(5)(B)(iv).

This provision was amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), Pub. L. No. 108-173, tit. XI, § 1102(a)(2)(D)(i)(I)(bb)(CC), (a)(2)(D)(ii), 117 Stat. 2066, 2457-59 (Dec. 8, 2003) (codified at 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC), (j)(5)(D)(ii) (2003)). The decisions of the FDA and of the district court were made pursuant to the Act as it stood before the MMA and, because the MMA was not made retroactive, § 1102(b)(1), 117 Stat. at 2460, this decision is also geared to the Act pre-MMA.

* If a patent is removed from the [Orange Book], any applicant ... who has made a certification with respect to such patent shall amend its certification. The applicant shall certify ... that no patents [required to be listed in the Orange Book] claim the drug or, if other relevant patents claim the drug, shall amend the certification to refer only to those relevant patents .... Once an amendment ... has been submitted, the application will no longer be considered to be one containing a [paragraph IV certification].

branded drug remains listed, then the generic applicant must file a paragraph I certification, and the FDA treats the ANDA as though it had never contained a paragraph IV certification. As a result, the generic applicant that was first to file an approved application does not get the 180-day period of exclusivity. *See id.*

Merck, which marketed simvastatin under the brand name Zocor®, submitted to the FDA information with respect to three patents covering the drug: U.S. Patent Nos. 4,444,784 (the 784 Patent), RE 36,481 (the 481 Patent), and RE 36,520 (the 520 Patent). Teva and Ranbaxy each filed an ANDA to market generic simvastatin. The two ANDAs — both of which were eligible for a 180-day period of marketing exclusivity because they involved different dosages — each contained a paragraph IV certification with respect to the 481 and 520 Patents. With respect to the 784 Patent, Ranbaxy and Teva each filed a paragraph III certification that it would expire in December 2005.

Merck, however, did not sue Ranbaxy or Teva for patent infringement based upon their paragraph IV certifications. Instead, before their ANDAs were approved, Merck asked the FDA to delist the 481 and 520 Patents from the Orange Book, which the agency did in 2004. Consequently, under 21 C.F.R. § 314.94(a)(12)(viii)(B), Ranbaxy and Teva were required to delete the paragraph IV certifications from their ANDAs and thereby lost their eligibility for a period of marketing exclusivity. Ranbaxy and Teva accordingly petitioned the FDA to relist the 481 and 520 Patents in the Orange Book, restore their period of exclusivity, and refrain from approving any other manufacturer's ANDA for generic simvastatin until their period of exclusivity expired.

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21 C.F.R. § 314.94(a)(12)(viii)(B).

In a letter ruling denying the petitions, the FDA said it had considered three possible methods of handling the request of a manufacturer with an approved NDA to delist a patent. First, the FDA could always delist the patent, but that could unfairly deny a period of marketing exclusivity to the generic manufacturer that would later be the first to file an approved ANDA by depriving it of the opportunity to prevail in patent litigation. Second, it could refuse to delist the patent only if a generic manufacturer had filed an ANDA containing a paragraph IV certification with respect to the patent, but the agency rejected that possibility on the ground that "eligibility for exclusivity does not vest with a patent challenge," that is, upon the filing of a paragraph IV certification. Finally, the FDA could delist a patent only if a generic manufacturer had filed an ANDA containing a paragraph IV certification with respect to the patent *and* the NDA holder had not filed a lawsuit to contest the certification. The FDA chose the last option on the ground that it best balanced, on the one hand, the pro-competitive effect of the incentive for a generic drug manufacturer to be the first to challenge a patent listed in the Orange Book and thereby introduce generic competition to a branded drug and, on the other, the loss of competition among generic manufacturers caused by the 180-day period of marketing exclusivity for the first to file an approved ANDA containing a paragraph IV certification.

Ranbaxy and Teva then brought this action in the district court, which held the FDA's delisting policy was inconsistent with the Act because, by requiring the first generic manufacturer that filed a paragraph IV certification to remove that certification before its ANDA could be approved, it deprived the generic applicant of the opportunity to obtain a period of exclusivity pursuant to 21 U.S.C. § 355(j)(5)(B)(iv)(I) by commercially marketing its drug. The court entered judgment for Ranbaxy and Teva and the FDA appealed.

II. Analysis

We review the FDA's interpretation of the Act it administers under the two-step analysis in *Chevron, U.S.A. Inc. v. NRDC*, 467 U.S. 837 (1984). *See Teva Pharm. Indus. Ltd. v. Crawford*, 410 F.3d 51, 53 (D.C. Cir. 2005) (reviewing under *Chevron* FDA ruling on citizen petition). First, we ask whether the "Congress has directly spoken to the precise question at issue." *Chevron*, 467 U.S. at 842. "If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Id.* at 842-43. If, however, "the statute is silent or ambiguous with respect to the specific issue, the question ... is whether the agency's answer is based on a permissible construction of the statute." *Id.* at 843.

Ranbaxy and Teva claim this case can be resolved at *Chevron* step one. Ranbaxy argues that 21 U.S.C. § 355(j)(5)(B)(iv) on its face entitles the company to a period of marketing exclusivity, and Teva contends the FDA's distinction between filers of paragraph IV certifications that are sued and those that are not has no basis in the Act.

Under the rubric of *Chevron* step two, Ranbaxy and Teva argue the FDA's policy of delisting a patent in the absence of litigation is unreasonable for a variety of reasons. Upon examination, however, we believe their arguments are better considered at *Chevron* step one. More specifically, Teva contends the requirement of litigation is inconsistent with the text and structure of the statute and with its purpose, as elucidated in circuit precedent. Here it refers in particular to *Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060, 1069 (D.C. Cir. 1998), in which we held 21 U.S.C. § 355(j)(5)(B)(iv) precludes the FDA from conditioning marketing exclusivity upon the first to file an ANDA prevailing in patent litigation,

and to *Purepac Pharmaceutical Co. v. Friedman*, 162 F.3d 1201, 1204-05 (D.C. Cir. 1998), in which we held the FDA reasonably gave a period of marketing exclusivity to the first generic drug manufacturer to file a paragraph IV certification even though it never litigated the infringement or validity of the patent. Based upon these cases, Teva argues that the Act precludes the FDA from predicating exclusivity upon a patent infringement suit being brought by the NDA holder. Ranbaxy suggests the FDA's policy is inconsistent with the Act for two other reasons: first, the policy diminishes the incentive the Congress provided for a generic manufacturer to challenge a patent by reducing the certainty of its getting a period of marketing exclusivity; and second, by balancing anew the costs and benefits of the exclusivity provided by the Congress, the policy exceeds the authority of the agency.

In response, the FDA argues that its regulation requiring the filer of an ANDA to amend its certification when a patent is delisted, 21 C.F.R. § 314.94(a)(12)(viii)(B), is not inconsistent with the Act because 21 U.S.C. § 355(j)(5) is silent with regard to the withdrawal of patent information previously submitted for listing in the Orange Book. The FDA points out that a generic applicant's exclusivity does not vest upon the filing of a paragraph IV certification; otherwise, it asserts, the filer's eligibility for exclusivity would not be lost when, for example, the patent subject to the paragraph IV certification expires, *see Dr. Reddy's Labs., Inc. v. Thompson*, 302 F. Supp. 2d 340, 354-55 (D.N.J. 2003) (holding FDA reasonably interpreted 21 U.S.C. § 355(j)(5)(B)(iv) not to extend exclusivity to ANDA approved after patent had expired), or the generic applicant loses in patent litigation, *see Mylan Labs., Inc. v. Thompson*, 389 F.3d 1272, 1282-84, 1283 n.10 (D.C. Cir. 2004).

The FDA then argues its policy is reasonable because it allows an NDA holder to eliminate the patent as a barrier to

approval of an ANDA when that patent does not cover the drug or method of use for which it was listed in the Orange Book. At the same time the policy preserves the ministerial nature of the FDA's role in maintaining the patent listings in the Orange Book because, when an NDA holder asks it to delist a patent, the agency need not determine whether the NDA holder is acting strategically to deny the generic applicant a period of marketing exclusivity or the patent actually does not cover the drug for which it was submitted — the interpretation of patent listings being outside the agency's expertise.

The "precise question at issue" at *Chevron* step one is, in our view, whether the FDA may delist a patent upon the request of the NDA holder after a generic manufacturer has filed an ANDA containing a paragraph IV certification so that the effect of delisting is to deprive the applicant of a period of marketing exclusivity. The Congress unquestionably provided two ways in which a generic drug manufacturer may begin a 180-day period of exclusivity: (1) by marketing its drug commercially, or (2) by convincing a court that the patent subject to its paragraph IV certification is either invalid or not infringed. 21 U.S.C. § 355(j)(5)(B)(iv). When the NDA holder asks the FDA to delist the patent, however, the FDA's policy of acquiescence prevents the generic manufacturer that has filed an ANDA containing a paragraph IV certification from beginning its period of exclusivity.

We have previously rejected at *Chevron* step one the FDA's attempt to add to the statutory requirements for exclusivity by making it contingent upon success in litigation. In *Mova* we held the "successful defense" rule, which afforded exclusivity only to the generic applicant that both filed the first approved ANDA with a paragraph IV certification and successfully defended an infringement suit, was inconsistent with the text and structure of the Act because it permitted the FDA to approve a

later ANDA before either the first to file began to market its drug commercially or a court held the subject patent invalid or not infringed; the rule thereby "[wrote] the commercial-marketing trigger out of the statute." 140 F.3d at 1069-70. Later we upheld as reasonable at *Chevron* step two the FDA's decision to grant a generic applicant a period of marketing exclusivity even though its paragraph IV certification did not result in litigation precisely because the FDA's approach "basically duplicat[ed] the statute." *Purepac*, 162 F.3d at 1204-05.

Not only does the statute 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 because, if the patent is delisted before a pending ANDA is approved, then the generic manufacturer may not initiate a period of marketing exclusivity. The FDA's observation that the generic applicant's right to a period of marketing exclusivity does not vest upon its filing a paragraph IV certification is beside the point, which is that the Act makes the generic applicant eligible for exclusivity while the FDA's policy makes it ineligible for exclusivity.[*]

In addition, the FDA's policy allows an NDA holder, by delisting its patent, to deprive the generic applicant of a period of marketing exclusivity. By thus reducing the certainty of receiving a period of marketing exclusivity, the FDA's delisting

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[*] We need not address the question of patent expiration in this case. We note, however, as Ranbaxy and Teva acknowledged at oral argument, the text and structure of the statute suggest a distinction between expiration and delisting such that the first generic applicant may no longer retain exclusivity when the patent has expired. *See* 21 U.S.C. § 355(j)(5)(B)(i); *see also Dr. Reddy's Labs.*, 302 F. Supp. 2d at 354-55.

policy diminishes 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. The FDA may not, however, change the incentive structure adopted by the Congress, for the agency is bound "not only by the ultimate purposes Congress has selected, but by the means it has deemed appropriate, and prescribed, for the pursuit of those purposes." *MCI Telecomms. Corp. v. AT & T Co.*, 512 U.S. 218, 231 n.4 (1994). Therefore, we hold unlawful the FDA's policy requiring that the first filer of a paragraph IV certification be sued in order to preserve its statutory exclusivity when the NDA holder seeks to delist the patent rather than to litigate.

III. Conclusion

In sum, the FDA's policy conditioning a generic applicant's period of marketing exclusivity upon the generic applicant being sued for patent infringement by the NDA holder is inconsistent with the text and structure of the Act and, because it diminishes the incentive the Congress gave manufacturers of generic drugs, is inconsistent with the purpose of the Act. Therefore, we conclude the FDA improperly denied Ranbaxy and Teva a period of marketing exclusivity by delisting Merck's patents. For the foregoing reasons, the judgment of the district court is

Affirmed.