United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued March 21, 2013 Decided April 26, 2013

No. 12-5227

ASTRAZENECA PHARMACEUTICALS LP,
APPELLANT

v.

FOOD & DRUG ADMINISTRATION, ET AL.,
APPELLEES

Appeal from the United States District Court
for the District of Columbia
(No. 1:12-cv-00472)

Robert A. Long Jr. argued the cause for appellant. With him on the briefs were *Timothy C. Hester*, *Benjamin C. Block*, and *Matthew J. Berns*.

Gerald C. Kell, Senior Trial Counsel, U.S. Department of Justice, argued the cause for appellees. With him on the brief were *Stuart F. Delery*, Principal Deputy Assistant Attorney General, *Maame Ewusi-Mensah Frimpong*, Deputy Assistant Attorney General, *William B. Schultz*, Acting General Counsel, U.S. Department of Health and Human Services, and *Eric M. Blumberg*, Deputy Chief Counsel, Litigation.

Before: ROGERS and TATEL, *Circuit Judges*, and SENTELLE, *Senior Circuit Judge*.

Opinion for the Court filed by *Senior Circuit Judge* SENTELLE.

SENTELLE, *Senior Circuit Judge*: AstraZeneca Pharmaceuticals LP, a manufacturer of pharmaceutical products, appeals from the district court's grant of summary judgment in an action praying a declaratory judgment that the Food and Drug Administration ("FDA") could not approve generic versions of its Seroquel product and seeking to restrain the FDA from approving abbreviated new drug applications ("ANDAs") for such competing products until the expiration of a period of exclusivity. The district court granted summary judgment in favor of the FDA, and AstraZeneca appealed. For the reasons set forth below, we agree with the district court that the FDA reasonably determined that AstraZeneca was not entitled to such period of exclusivity. We therefore affirm the grant of summary judgment.

I. BACKGROUND

A. Statutory Framework

The Federal Food, Drug, and Cosmetic Act ("FDCA") governs the drug approval process for new and generic drugs. *See* 21 U.S.C. §§ 301–99. A drug manufacturer, such as AstraZeneca, seeking to introduce a new, or pioneer, drug must file a new drug application ("NDA") with the FDA. *Id.* § 355(b)(1). If the FDA approves the application, the statute entitles the manufacturer to a period of marketing exclusivity during which the FDA cannot approve bioequivalent generic

drugs. *See id.* § 355(j)(5)(F). Once the exclusivity period has expired, the FDA can approve generic drugs bioequivalent to the pioneer drug through an abbreviated new drug application. *See id.* § 355(j). ANDAs need not include new clinical studies demonstrating the generic drug's safety or efficacy, but must propose the same basic labeling as approved for the pioneer drug. *See id.* § 355(j)(2)(A)(v); *see also* 21 C.F.R. § 314.94(a)(8)(iv).

The FDCA provides for additional periods of exclusivity for pioneer drugs based on medical studies completed after the initial approval process if such studies support new indications of the drugs, which typically means that the drugs can be used in new patient populations or to treat different conditions. 21 U.S.C. § 355(j)(5)(F); *see AstraZeneca Pharm. LP v. FDA*, 872 F. Supp. 2d 60, 64 (D.D.C. 2012). Drug manufacturers can apply for this additional exclusivity through a supplemental new drug application ("sNDA"). The statutory provision governing such sNDAs provides:

> If a supplement to an application . . . contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement . . . .

21 U.S.C. § 355(j)(5)(F)(iv). Therefore, as provided in FDA regulations, the FDA cannot approve an ANDA for three years following the approval of an sNDA if the ANDA "relies on . . . information supporting a change approved in the

supplemental new drug application." 21 C.F.R. § 314.108(b)(5)(ii). An amendment makes this exclusivity period "three years and six months rather than three years" in some circumstances where the manufacturer provides pediatric studies that the FDA requests. 21 U.S.C. § 355a(c)(1)(A)(i)(II). The statute leaves the word "supplement," along with many of its other terms, undefined. The FDA has promulgated extensive regulations setting forth the application process and defining the statutory terms. *See* 21 C.F.R. §§ 314.3, 314.50, 314.60, 314.70.

B. Factual and Procedural Background

AstraZeneca has marketed Seroquel, an atypical antipsychotic medication used to treat disorders such as schizophrenia, since 1997, largely without generic competition. Based on various sNDAs, the FDA has given supplemental exclusivity to AstraZeneca when it added indications to Seroquel. AstraZeneca has made other label changes which did not add indications to Seroquel, but only added safety information. With respect to these safety-related label changes, the FDA has not granted any additional period of exclusivity. *AstraZeneca*, 872 F. Supp. 2d at 67.

One side effect of drugs like Seroquel is hyperglycemia, or high blood sugar. The FDA has added information about observed changes in blood sugar levels to labeling on all antipsychotic drugs. On June 26, 2008, in response to a request from the FDA, AstraZeneca submitted metabolic data regarding observed changes in blood sugar levels among patients taking Seroquel or Seroquel XR, an extended release version of Seroquel. The data came from fifteen clinical trials, all conducted for reasons other than generating this particular data and none conducted on pediatric patients.

Separately, AstraZeneca submitted two sNDAs in support of new pediatric indications of Seroquel on October 28, 2008, requesting three years of exclusivity for the new indications. The FDA considered those sNDAs while it was continuing review of the blood sugar labeling question. Correspondence between AstraZeneca and the FDA establishes that they discussed those two subjects and others in the same letters. On October 16, 2009, the FDA asked for a table summarizing the previously submitted glucose data, which AstraZeneca supplied, along with other labeling changes. This table, referred to as Table 2, is the basis of the current litigation.

On December 2, 2009, the FDA approved the pediatric sNDAs as well as the proposed labeling changes, including Table 2. The FDA sent AstraZeneca a single letter reflecting these approvals.

On September 2, 2011, AstraZeneca filed two citizen petitions with the FDA requesting exclusivity for Table 2 based on the clinical trials that provided the relevant data. The FDA denied the petitions without responding to AstraZeneca's request by, as the district court put it, "conveniently" ignoring the legal question regarding Table 2's eligibility for exclusivity. *AstraZeneca*, 872 F. Supp. 2d at 74. AstraZeneca filed suit and moved for a preliminary injunction. The district court dismissed that action as unripe and denied the motion for a preliminary injunction because the FDA had not yet decided whether to grant ANDAs that included Table 2 in the labeling for generic versions of Seroquel and Seroquel XR. *See AstraZeneca Pharm. LP v. FDA*, 850 F. Supp. 2d 230, 249–51 (D.D.C. 2012). Four days after the district court's decision, on March 27, 2012, the FDA approved ANDAs for generic versions of Seroquel with Table 2 included as part of the labeling.

The FDA issued a letter to AstraZeneca on the same day explaining its decision that Table 2 was not entitled to a period of exclusivity. The letter points out that "changes in labeling that involve the addition of warnings or other similar risk information are generally not entitled to 3-year exclusivity." Public Joint Appendix 304. It goes on to explain that Table 2 contains only "generally applicable safety information" and thus is not protected by any exclusivity. *Id.* In addition, the letter states that Table 2 does not include data from any indications for which Seroquel still had exclusivity, including the pediatric indications. *Id.* at 306. Finally, according to the letter, it was purely "coincidental" that the FDA approved Table 2 "in the course of approving" the pediatric sNDAs. The FDA's letter explicitly stated that "there is no relationship between the exclusivity for pediatric indications . . . and the data in Table 2." *Id.*

AstraZeneca again filed suit, seeking a temporary restraining order and further relief. The district court denied the motion for a temporary restraining order and later granted summary judgment in favor of the FDA, holding that the statute is ambiguous and the FDA's interpretation is reasonable. AstraZeneca filed this appeal.

II. DISCUSSION

A. Mootness

The FDA first argues that we should dismiss this case as moot. Article III of the Constitution gives federal courts jurisdiction to decide cases and controversies. This provides federal courts jurisdiction to decide only "actual, ongoing controversies." *See, e.g.*, *Honig v. Doe*, 484 U.S. 305, 317 (1988). "Even where litigation poses a live controversy when filed, the mootness doctrine requires a federal court to refrain

from deciding it if events have so transpired that the decision will neither presently affect the parties' rights nor have a more-than-speculative chance of affecting them in the future." *LaRoque v. Holder*, 679 F.3d 905, 907 (D.C. Cir. 2012) (quoting *Clarke v. United States*, 915 F.2d 699, 701 (D.C. Cir. 1990) (en banc)). According to the FDA, this case is now moot because any period of exclusivity attached to Table 2 would have expired by December 2, 2012, three years after the FDA approved the addition of Table 2 to Seroquel's labeling. *See* 21 U.S.C. § 355(j)(5)(F)(iv).

However, the FDA is not correct that the possibility of relief has been extinguished. As we noted above, the period of exclusivity can be extended beyond three years for an additional six months if the FDA requests and receives pediatric studies from the manufacturer. *See id.* § 355a(c)(1)(A)(i)(II). If applicable in this case, the longer period of exclusivity would not expire until June 2, 2013. The FDA argues that AstraZeneca waived this claim of longer exclusivity by failing to specifically argue it below. This is not, however, dispositive on the particular facts of this case. As the FDA concedes, it would have to consider the pediatric exclusivity period "if AstraZeneca prevails in its request for three-year exclusivity for Table 2." Appellees' Br. at 48. Because AstraZeneca has submitted some pediatric studies regarding Seroquel, if AstraZeneca were to prevail on the merits of its claim, exclusivity through June 2, 2013, might be available. *See AstraZeneca*, 872 F. Supp. 2d at 65 n.4. Therefore, our decision will affect AstraZeneca's actual rights, and the case is not moot. Thus, we must determine the merits of the summary judgment.

B. Summary Judgment

Under the Federal Rules of Civil Procedure, grant of summary judgment is appropriate where "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). Our review of the district court's grant of summary judgment is *de novo*. *See, e.g.*, *Calhoun v. Johnson*, 632 F.3d 1259, 1261 (D.C. Cir. 2011). We therefore undertake the same examination as the district court to determine the presence or absence of genuine disputes of material fact and legal entitlement to judgment of the movant, in this case the FDA. *Sherley v. Sebelius*, 689 F.3d 776, 780 (D.C. Cir. 2012). When summary judgment is at issue in a case of administrative review under the APA, we, like the district court, are required to "hold unlawful and set aside agency action, findings, and conclusions found to be . . . arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). Under the applicable standard the district court, and now this court, must allow summary judgment for the agency (in this case, the FDA), unless the appellants can demonstrate by record evidence that "a genuine dispute" exists as to some material fact supporting the proposition that the FDA's actions under review were "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." *See Sherley*, 689 F.3d at 780.

There being no genuine dispute as to the facts of record, *see id.*, our analysis is limited to the validity of the FDA's interpretation and application of the statute. Since the determinative issue is one of an agency's interpretation of a statute, we apply the familiar test of *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). *See Mylan Labs., Inc. v. Thompson*, 389 F.3d 1272,

1279–80 (D.C. Cir. 2004) (applying *Chevron* to FDA decision letters). "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." *Chevron*, 467 U.S. at 842–43. If the statute is ambiguous, "the question for the court is whether the agency's answer is based on a permissible construction of the statute." *Id.* at 843.

AstraZeneca contends that it should prevail at the first step of the *Chevron* test. That is, it contends that the statute *clearly* provides the exclusivity it seeks based on Table 2. AstraZeneca relies on the statutory language that provides for exclusivity where a supplement "contains reports of new clinical investigations . . . essential to the approval of the supplement." 21 U.S.C. § 355(j)(5)(F)(iv).

AstraZeneca argues that the statute clearly entitles Table 2 to exclusivity on two grounds. First, Table 2 was "a change approved in" the pediatric supplements, and the supplements included "reports of new clinical investigations . . . essential to the approval of the supplement[s]." *Id.* Second, some of the clinical studies that provided the data for Table 2 were "new clinical investigations" "essential to the approval" of the labeling changes so as to independently warrant exclusivity. Either way, AstraZeneca claims, Table 2 is entitled to exclusivity, so the FDA's approval of ANDAs incorporating Table 2 prior to June 2, 2013, was contrary to the statute. Because we disagree that the statute mandates exclusivity in these circumstances, and because we consider the FDA's interpretation reasonable, we affirm the district court's grant of summary judgment.

At the core of this dispute is the statutory language that limits exclusivity to "a change approved in the supplement" and requires that "the supplement contain[] reports of new

clinical investigations . . . essential to the approval of the supplement." 21 U.S.C. § 355(j)(5)(F)(iv). This language is permeated by ambiguities that, under *Chevron*, leave discretion in the FDA to adopt reasonable interpretations of the application process outlined by the statute.

The statute leaves to the FDA the interpretation of a "supplement" to a drug application. Under the statute, the FDA has power to implement the entire application and approval process, which necessarily gives the FDA discretion to determine the requirements of "applications" and "supplements" and how to handle changes that are not contained in such applications or supplements. Because the statute includes these ambiguities, the language "constitutes an implicit delegation from Congress to the agency to fill in the statutory gaps." *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 159 (2000).

The fundamental problem with both of AstraZeneca's arguments is that the FDA has maintained that Table 2 was not "a change approved" in any supplement, and only changes approved in a supplement are entitled to a statutory period of exclusivity. *See* Public Joint Appendix 306; 21 U.S.C. § 355(j)(5)(F)(iv). The FDA has exhaustive regulations detailing the parameters of the application process, including how to amend pending supplements and applications. *See* 21 C.F.R. §§ 314.50, 314.60, 314.70. AstraZeneca makes no attempt to show that these procedures are contrary to the statute. Nor has AstraZeneca shown that the FDA's application of the law to the relevant facts was arbitrary or capricious.

The supplements here dealt with new pediatric indications of Seroquel. AstraZeneca submitted the data for Table 2 in letters coded as general correspondence (not

supplements) prior to even filing those supplemental applications. *See* Public Joint Appendix 298. Further, no data for Table 2 was derived from the pediatric studies at issue in the supplements, and AstraZeneca cited only the pediatric studies in support of its request for exclusivity. Table 2 is only contained in the "Adult" section of Seroquel's labeling. Finally, though AstraZeneca makes much of the fact that the FDA approved the pediatric supplements and Table 2 at the same time, the FDA explained that the "this timing was only coincidental, and there is no relationship between the exclusivity for the pediatric indications earned on December 2, 2009, and the data in Table 2." *Id.* at 306. We see nothing arbitrary or capricious about the FDA's reasoned explanation for its actions.

We have examined the remainder of the administrative record and find nothing that contradicts the FDA's position that it considered Table 2 as separate from the pediatric supplements. As the district court explained, "the administrative record shows that the pediatric supplements were approved on their own merits based upon clinical investigations unrelated to the Table 2 labeling change, which standing alone does not entitle AstraZeneca to exclusivity." *AstraZeneca*, 872 F. Supp. 2d at 83. The fact that AstraZeneca titled its eventual submission of Table 2 an "Amendment to a Pending Application" does not require the FDA to consider that submission an actual amendment to a completely unrelated supplemental application.

Therefore, the labeling changes in Table 2 were neither "a change approved" in the pediatric supplements nor submitted as a separate supplement. AstraZeneca states that Table 2 could have been submitted as a separate efficacy supplement, but AstraZeneca does not claim it ever was.

Because the statute only provides exclusivity for changes approved as part of a supplement, AstraZeneca's claims fail.

AstraZeneca attempts to establish that the FDA was arbitrary or capricious by directing us to prior grants of exclusivity to label changes approved in supplements. *See* Public Joint Appendix 119–22. However, the FDA's explanation that it considered Table 2 independently of a supplemental application sufficiently distinguishes this case to defeat that claim. The consistency of the FDA's denial of exclusivity in this case with prior FDA actions is strikingly underscored by the fact that the agency did not extend exclusivity in seven other recent labeling changes for drugs in Seroquel's class. *See AstraZeneca*, 872 F. Supp. 2d at 86.

Because the FDA reasonably considered Table 2 as separate from the pediatric supplements, Table 2 was not "a change approved in the supplement," and therefore the statute does not entitle AstraZeneca to exclusivity for Table 2.

III. CONCLUSION

For the foregoing reasons, the decision of the district court is

Affirmed.