

United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued September 17, 2001 Decided November 6, 2001

No. 01-5125

American Bioscience, Inc.,
Appellant

v.

Tommy G. Thompson,
Secretary of Health and Human Services, et al.,
Appellees

Appeal from the United States District Court
for the District of Columbia
(00cv02247)

Jacqueline H. Eagle argued the cause for appellant. With her on the briefs were Joseph F. Coyne, Jr., Carlton A. Varner, Arthur Y. Tsien, David F. Weeda, and Robert F. Green.

Howard S. Scher, Attorney, United States Department of Justice, argued the cause for appellee. With him on the brief were Kenneth L. Wainstein, United States Attorney, Douglas N. Letter, Litigation Counsel, Michael M. Landa, Acting Chief Counsel, Food & Drug Administration, and AnnaMarie Kempic, Associate Chief Counsel.

Richard M. Cooper argued the cause for appellees Baker Norton Pharmaceuticals, Inc. and IVAX Pharmaceuticals, Inc. With him on the brief was Philip A. Sechler.

Before: Tatel, Circuit Judge; Silberman and Williams,* Senior Circuit Judges.

Opinion for the Court filed by Senior Circuit Judge Silberman.

Silberman, Senior Circuit Judge: American Bioscience, Inc., appeals from the district court's denial of its request for preliminary injunctive relief. Appellant argues that the Food and Drug Administration's decision to approve intervenor-defendant Baker Norton Pharmaceutical's Abbreviated New Drug Application (ANDA) for a generic version of the cancer treatment Taxol was arbitrary and capricious. We agree and vacate that approval.

I.

This case is here for the second time. See *American Bioscience, Inc. v. Thompson*, 243 F.3d 579 (D.C. Cir. 2001). American Bioscience is a pharmaceutical research firm that has developed a patented process for delivering safer and more effective dosage forms of Taxol. Bristol-Myers Squibb Company holds the patent on and FDA approval of Taxol itself, a drug that has generated billions of dollars in sales. Bristol-Myers intervened in the district court proceeding for the limited purpose of providing information. Appellees Baker Norton Pharmaceuticals, Inc. (BNP) and Zenith Goldline Pharmaceuticals, Inc., who are corporate affiliates and hold

* Senior Judge Williams was in regular active service at the time of oral argument.

ANDAs for generic versions of Taxol, intervened as defendants.

This dispute arises out of the complex relationship between the FDA's approval process for generic drugs and patent law. A company wishing to market a new (or "pioneer") drug must seek FDA approval, usually by completing a New Drug Application. The NDA is expensive and time-consuming, requiring data from tests showing the drug's safety and effectiveness. Prior to 1984, a firm that wished to make a generic version of an approved drug was required to file a new NDA, complete with new safety and effectiveness studies. In 1984, Congress enacted the Hatch-Waxman Amendments,¹ which introduced the Abbreviated NDA and allowed a generic drug ANDA to rely on the pioneer NDA's safety and effectiveness studies. These amendments also provide that a competitor may use and manufacture an approved and patented drug, for the purpose of developing a generic version, without infringing that patent.

The Hatch-Waxman Amendments also sought to afford an NDA holder some patent protection, to lower the risk to innovation posed by the simplified ANDA process. NDAs are required to contain a list of any patents which claim the drug or which claim a method of using such a drug and with respect to which a claim of patent infringement could reasonably be asserted--but that includes patents held by those other than the NDA holder. The FDA publishes all patent listings in the Approved Drug Products With Therapeutic Equivalence (the "Orange Book"). For "each patent which claims" the pioneer drug, an ANDA must certify: (1) that no patent has been filed with the FDA; (2) that the patent has expired; (3) that the patent has not expired, but will expire on a particular date; or (4) that the patent is either invalid or the generic drug will not infringe it (a "Paragraph IV certification"). When an ANDA applicant files a Paragraph IV certification, it must also certify to the FDA that it will give notice to the patent holder. That notice must include a

¹ The Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984).

detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed and must be given at the same time the certification is submitted to the FDA. Filing a Paragraph IV certification can constitute patent infringement. Upon receipt of notice of a Paragraph IV certification, the patent holder has 45 days in which to file an infringement suit. If the patent holder does not file within that time period, the FDA may immediately approve an otherwise conforming ANDA. If, on the other hand, the patent holder does sue within 45 days, the FDA may not approve the ANDA for 30 months, or until the patent dispute has been resolved, whichever is sooner. The first ANDA filed and approved gets a 180-day period of market exclusivity.

If a qualifying patent issues at a later date--after the NDA is approved--the NDA holder must inform the FDA within 30 days of the patent's issuance. See 21 U.S.C. s 355(c)(2). But if the NDA holder fails to so notify the FDA, an ANDA applicant is excused, according to the FDA's late-listing regulation, from amending its patent certification to reflect the new patent so long as the ANDA had an "appropriate" patent certification on file. As shall be apparent, however, only the NDA holder has the obligation (and the right) to list the new patent--not the patent holder if it is another company. In this case, if Bristol-Myers listed American Bioscience's patent within 30 days of its issuance, BNP was required to certify to that patent, potentially leading to a patent infringement suit and 30-month stay.²

In the event a person disputes the accuracy or relevance of patent information published by the FDA in the Orange Book, he must first notify the agency, in writing, stating the grounds for disagreement. The FDA will then request that the applicable NDA holder confirm the correctness of the patent information or omission of patent information. Unless the NDA holder withdraws or amends its patent information

² BNP argues that the statute does not allow for consecutive 30-month stays, even if there are subsequent Paragraph IV certifications. The FDA did not adopt this reading.

in response to the FDA's request, the agency will not change the patent information in the list. And if the NDA holder does not change the patent information, an ANDA must, despite any disagreement as to the correctness of the patent information, contain an appropriate certification for each listed patent. The FDA, pursuant to longstanding practice and its own regulations, and based on its acknowledged lack of expertise and resources, has refused to become involved in patent listing disputes, accepting at face value the accuracy of NDA holders' patent declarations and following their listing instructions.

The FDA approved Bristol-Myers' NDA to manufacture and distribute Taxol, an anti-cancer drug with the active ingredient paclitaxel, in 1992. Five years later, BNP submitted an ANDA for a generic version of Taxol. Bristol-Myers instituted patent infringement proceedings against BNP within the 45-day statutory window, triggering the 30-month stay, which expired in June 2000. The record does not reveal, and counsel for the FDA could not explain, why the FDA did not approve BNP's ANDA promptly upon expiration of the stay. But on August 1, 2000, American Bioscience received U.S. Patent Number 6,906,331 for a new process that purported to permit a patient to receive higher doses of Taxol with fewer side effects. Bristol-Myers did not immediately list the new patent.³ Ten days after the patent issued, American Bioscience sued Bristol-Myers in the United States District Court for the Central District of California requesting a TRO compelling Bristol-Myers to submit the '331 patent for listing in the Orange Book, which the court granted, ordering Bristol-Myers to "immediately take all steps under its control to cause the FDA to list in its 'Orange Book' [American Bioscience's] Taxol Patent, subject to the proviso that, unless Plaintiff carries its burden of proof on the [Order to Show Cause], [Bristol-Myers] shall then take all steps

³ We are told that correspondence between American Bioscience and Bristol-Myers indicates that Bristol-Myers refused to list the patent without a court order, but that is not part of the administrative record.

under its control to cause the de-listing of the Taxol Patent from the FDA's Orange Book." That same day, Bristol-Myers sent a letter to the FDA, stating that it was submitting the '331 patent for listing "pursuant to" the August 11 court order and "in accordance with" the voluntary listing provision. Bristol-Myers also submitted a patent declaration with the listing.

On August 14, 2000, BNP filed a Paragraph IV certification for the '331 patent but contrary to the statute it did not notify either Bristol-Myers or American Bioscience. One week later, the California court held a hearing at which Bristol-Myers, American Bioscience and BNP (as a proposed intervenor) were present.⁴ American Bioscience then learned for the first time of BNP's Paragraph IV certification. On August 28, 2000, the FDA tentatively approved BNP's ANDA, subject to resolution of the '331 patent issues. Meanwhile, after two hearings, the California court determined that it lacked "jurisdiction" over American Bioscience's suit because the Food Drug and Cosmetic Act did not provide American Bioscience a private right of action. On September 7, 2000, the California court dissolved the TRO and ordered Bristol-Myers "[p]ursuant to the condition in the TRO and in order to restore the status quo ... [to] use its best efforts to cause the delisting of [American Bioscience's] '331 Patent from the Orange Book." It recommended to the FDA that it toll the amount of time the TRO was in place and stayed its order until September 13, 2000.

Also on September 7, 2000, American Bioscience sued BNP for patent infringement and informed the FDA the next day but the FDA did not grant a stay. On September 11, 2000, Bristol-Myers wrote the FDA a letter stating that it was listing the '331 patent "pursuant to" the voluntary listing provision. Then three days later, on September 14, 2000, Bristol-Myers wrote the FDA another letter, which stated

⁴ BNP repeatedly refers to the transcript of this hearing in support of its allegation that Bristol-Myers and American Bioscience colluded to obtain temporary injunctive relief. This transcript is not a part of the administrative record.

that it was de-listing the '331 patent to the extent it was listed pursuant to the California court's TRO, but that it did not mean to affect the continued and continuous listing of the patent. That same day, after receiving a phone call from the FDA, BNP withdrew its Paragraph IV certification.⁵ And the next day, the FDA approved BNP's ANDA. In its approval letter, the FDA referenced BNP's September 8 and September 14 amendments, but did not otherwise discuss the '331 patent.

American Bioscience then brought this action, claiming that the FDA's actions were contrary to the Administrative Procedure Act. Specifically, it asserted that the '331 patent was timely and continuously listed from August 11, 2000, therefore the FDA's refusal to grant a stay and its approval of BNP's ANDA were contrary to law; that the FDA's decision not to toll the 30-day listing window was arbitrary and capricious; that BNP could not benefit from the late-listing regulation because a certification could not be "appropriate" without the required notice; and that the FDA exceeded its regulatory authority in promulgating the late-listing regulation. Appellant requested a declaration that approval be stayed; injunctive relief ordering the FDA to rescind the approval; attorney fees and costs; and any other just and proper relief. The district court granted BNP's motion to intervene and allowed Bristol-Myers to intervene to provide additional information.

The FDA defended on the ground that Bristol-Myers had not "timely" listed the '331 patent and therefore BNP did not have to certify to it. The agency had not previously disclosed the basis for its approval, nor did it provide a certified administrative record. After oral argument, the district court issued a written memorandum and opinion denying American Bioscience's requested relief on the ground that it had failed to show that it was likely to prevail on the merits because the FDA's interpretation and application of the late-listing regu-

⁵ Between August 14, 2000 and September 14, 2000, the FDA had at least seven telephone conversations with BNP.

lation was not plainly erroneous or inconsistent with the regulation, which was itself valid.

American Bioscience appealed and we vacated the district court's decision and remanded because "there [was] nothing in the FDA's approval letter to indicate how it interpreted [the late-listing] regulation." *American Bioscience*, 243 F.3d at 582. We did not know whether the FDA approved the application because it considered the '331 patent to have been de-listed; whether it considered the court-ordered listing ineffective for purposes of the Hatch-Waxman Act; whether it treated the application as one covered by the late-listing regulation; or, if it did, why it thought the regulation applied, observing that, for all we knew, the FDA made a "clerical error" in approving the application even though it thought that the '331 patent had been continually listed. We held that the district court, "before assessing American Bioscience's probability of success on the merits, should have required the FDA to file the administrative record and should have determined the grounds on which the FDA granted [BNP]'s application." *Id.* We left to the district court the determination of how best to proceed on remand in light of what the administrative record revealed.

On April 6, 2001, the FDA certified the administrative record which included a declaration by Gary J. Buehler, the acting director of the FDA's Office of Generic Drugs, Center for Drug Evaluation and Research. Buehler focused on the court orders in his explanation of the agency's rationale. In his view, the September 7 order compelled Bristol-Myers to de-list the '331 patent "to restore the status quo." He concluded that because the court order directing Bristol-Myers to submit the patent to the FDA was dissolved, and Bristol-Myers withdrew the original submission, the August 11 listing was "without effect." Accordingly, because Bristol-Myers had failed to timely list the patent, BNP was entitled to the benefit of the late-listing regulation. The FDA did not follow the court's recommendation that it toll the period in which Bristol-Myers could timely list because the FDA was not a party to the California litigation; he was not sure that the FDA had the authority to toll the statutory time limit;

tolling would set an undesirable precedent; and he saw no reason why Bristol-Myers could not have "voluntarily" listed the '331 patent during the 30-day statutory period.

Buehler quoted the passage from the September 14 letter in which Bristol-Myers stated that it was "[t]hereby withdrawing" the August 11 listing to the extent that listing was compelled by the TRO, but did not address the significance of Bristol-Myers' statement that it had not intended to affect the continued and continuous listing of the patent. Buehler also said that the FDA received letters pertaining to "this issue" (presumably the issue of approving a generic version of Taxol), and that he had been made aware of the concerns of the Federal Trade Commission and some members of the public about the potential for the aggressive use of patent listings to delay generic competition.⁶ The administrative record consists in large part of the tentative and final approval letters for BNP's ANDA; the August 11, 2000 TRO and the September 7, 2000 order; the August 11, 2000, September 11, 2000, and September 14, 2000 letters from Bristol-Myers to the FDA; correspondence from BNP to the FDA outlining BNP's concerns about the '331 patent, certifying to the '331 patent, and withdrawing the certification to the '331 patent; the Federal Trade Commission's amicus brief in the California case; records of telephone conversations between the FDA and BNP; and letters from the National Organization for Women Foundation, the Generic Pharmaceutical Association, and Senator Kennedy expressing their concerns about delay in the availability of generic drugs. The administrative record does not contain either the transcripts of the hearings in the California court, or any correspondence between Bristol-Myers and American Bioscience.

⁶ After American Bioscience filed suit and before the FDA filed a certified administrative record, the FDA approved a second potentially infringing ANDA for Zenith Goldline and granted "tentative" approval to a third. BNP apparently waived its 180-day statutory market exclusivity as to its corporate affiliate Zenith Goldline, but not with respect to the third ANDA.

Shortly after the FDA certified the administrative record, American Bioscience renewed its request for preliminary injunctive relief, which the district court denied. The court held that American Bioscience failed to show that it would suffer irreparable harm and was not substantially likely to prevail on the merits. It acknowledged that the administrative record did not include any "overt reference to the decisions at issue," but concluded that the record implicitly supported the FDA's version of events (as set forth by counsel) and that the FDA's decision to approve BNP's ANDA was supported by "inferences" that could be drawn from the administrative record.

II.

Appellant makes two basic arguments. The FDA acted contrary to law by approving BNP's application in light of Bristol-Myers' listing of the '331 patent. It was arbitrary and capricious for the agency to have concluded that Bristol-Myers' September 14 letter revoked the August 11 listing. Secondly, American Bioscience argues that even if the September 11 listing were legitimately thought to be Bristol-Myers' first listing, BNP could not benefit by the late-listing regulation since it did not have an "appropriate" patent certification filed (as it had never given notice). We need not reach appellant's second argument because we think it is clearly correct on its first.

Before discussing the merits we must dispose of the government's argument as to appellant's asserted lack of irreparable injury. Normally when a party seeks a preliminary injunction in district court the district judge properly balances the likelihood of the plaintiff prevailing on the merits against the severity of the injury the plaintiff will suffer if relief is denied. But that procedure assumes that the district judge will be obliged to make a decision before the complete case is presented--before all the evidence is submitted.

As we have repeatedly recognized, however, when a party seeks review of agency action under the APA, the district

judge sits as an appellate tribunal.⁷ The "entire case" on review is a question of law. See, e.g., *Marshall County Health Care Auth. v. Shalala*, 988 F.2d 1221, 1226 (D.C. Cir. 1993) (holding that in agency review context there was no real distinction between questions presented in Rule 12(b)(6) motion to dismiss and motion for summary judgment); *University Medical Center of S. Nevada v. Shalala*, 173 F.3d 438, 440 n.3 (D.C. Cir. 1999) (explaining that when reviewing agency action the question of whether the agency acted in an arbitrary and capricious manner is a legal one which the district court can resolve on the agency record, regardless of whether it is presented in the context of a motion for judgment on the pleadings or in a motion for summary judgment); *James Madison Ltd. v. Ludwig*, 82 F.3d 1085, 1096 (D.C. Cir. 1996), cert. denied, 519 U.S. 1077 (1997) (holding that issues that appellant argued were issues of fact precluding summary judgment were issues of law in the context of agency review); *County of Los Angeles v. Shalala*, 192 F.3d 1005, 1011 (D.C. Cir. 1999), cert. denied, 530 U.S. 1204 (2000) (holding that rule of finality does not apply to bar appellate review of the district court's finding that the agency action was arbitrary and capricious even though that court had not yet resolved the issue of remedy). Absent very unusual circumstances the district court does not take testimony. See, e.g., *Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402 (1971); *James Madison*, 82 F.3d at 1096.

If an appellant has standing--which is undeniable here--and prevails on its APA claim, it is entitled to relief under that statute, which normally will be a vacatur of the agency's order. See, e.g., *Association of Battery Recyclers, Inc. v. EPA*, 208 F.3d 1047, 1061 (D.C. Cir. 2000). Cf. *Canadian Pacific Railway Co. v. Surface Transp. Bd.*, 197 F.3d 1165 (D.C. Cir. 1999). To be sure, although appellant based its cause of action on the APA, it introduced a good deal of

⁷ Which is not to say that a motion for preliminary injunction against an agency is never appropriate. See, e.g., *CityFed Financial Corp. v. Office of Thrift Supervision*, 58 F.3d 738 (D.C. Cir. 1995) (involving Office of Thrift Supervision's decision to issue a temporary cease and desist order against appellant freezing virtually all of its assets).

confusion by seeking an injunction (as well as other appropriate relief). But, whether or not appellant has suffered irreparable injury, if it makes out its case under the APA it is entitled to a remedy.⁸

We implicitly recognized this point before when we ordered the remand of the case for the agency to produce a record without consideration as to whether appellant's injury was irreparable. See *American Bioscience*, 243 F.3d 579. The challenged action is an "informal adjudication" which is the administrative law term for agency action that is neither the product of formal adjudication or a rulemaking. See, e.g., *id.* at 582; *United States v. Mead Corp.*, 121 S. Ct. 2164, 2178 n.1 (2001) (Scalia, J., dissenting). Ever since *Overton Park and Camp v. Pitts*, 411 U.S. 138 (1973), government agencies which issue orders subject to appeal under the APA typically include some explanation--however short--that will provide a record on appeal. After examining the Buehler declaration, which purports to explain the FDA's action in this case, it is perhaps not surprising that the agency took the action it did originally without explanation. For assuming that that declaration satisfies our demand for the record before the agency, we find it sadly inadequate to sustain the agency's action.

As we noted, and the parties agree, the FDA has a longstanding policy not to get involved in patent disputes. It administers the Hatch-Waxman Amendments in a ministerial fashion simply following the intent of the parties that list patents. In this case, however, Buehler appears to have relied on his reading of the district court order--to which the agency was not a party--to trump Bristol-Myers' stated intention.⁹ His declaration notes that the district court on September 7 "dissolved the TRO, dismissed [American Bioscience's] complaint and ordered [Bristol-Myers] to delist the

⁸ Since under 28 U.S.C. s 1657(a) the granting or denying of a preliminary injunction is the basis for an expedited appeal the district courts should be careful--in such a case as this--not to do so.

⁹ Paradoxically, in rejecting the district court's tolling recommendation Buehler emphasizes the California district court had no jurisdiction and the FDA was not a party.

'331 patent from the Orange Book to restore the status quo." And then "on September 14, 2000 [Bristol-Myers] submitted a letter to FDA to comply with the court order to delist the patent. The letter states '[Bristol-Myers] hereby withdraws the Original Listing to the extent that listing was compelled by the TRO.' " Because of that sequence, the "FDA considered [Bristol-Myers'] first submission of the patent on August 11, 2000 to be without effect."

But Buehler omits reference to much of the September 14 letter which clearly indicates that Bristol-Myers' original filing of August 11 had a bifurcated purpose--to comply with the court order and to voluntarily list the '331 patent and accordingly it was abrogating the first but not the second.

Thus, Bristol-Myers' counsel stated:

Although that submission (the "Original Listing") (Attachment A) was made in accordance with a Temporary Restraining Order ("TRO") entered on that date by the United States District Court for the Central District of California, it was also timely filed in full compliance with all governing statutory and regulatory requirements for voluntary patent listing. It contained all required listing information, was presented in the format recommended by the agency for voluntary listings, and was supported by a declaration signed by Steven Reiter, counsel for the patent owner, using the precise language required by regulations set forth at 21 C.F.R. 314.53(c)(2).

And at the end of the letter, after the sentence Buehler quoted, counsel states: "This action does not affect the continued and continuous listing of the patent ...," which unequivocally indicates what Bristol-Myers meant when it limited its withdrawal of the listing only "to the extent that listing was compelled by the TRO ..." As such Buehler, speaking for the FDA, seems to wholly ignore Bristol-Myers' stated intent. He gives no forthright justification for such a blatantly artificial reading of its letters.¹⁰

¹⁰ The government contends that Bristol-Myers' letter of September 11 again listing the '331 patent suggests that it realized the

He seems to implicitly suggest that Bristol-Myers' stated intent is somehow inconsistent with the California district court's order and on appeal the government boldly contends that that intent--to continue its listing on a voluntary basis--is "unacceptable" without explaining why that should be so. But there is nothing in the California district court's original order that prevented Bristol-Myers from changing its mind and deciding to list voluntarily in addition to complying with the court order. Nor is there anything in the order directing the return to the status quo that would extend to requiring Bristol-Myers to abrogate such voluntary action. We, of course, owe no deference to an agency's reading of judicial orders or decisions, see, e.g., *United States Dep't of Justice v. FLRA*, No. 00-1433, 2001 WL 1180726, *2 (D.C. Cir. Oct. 9, 2001); *New York v. Shalala*, 119 F.3d 175, 180 (2d Cir. 1997), but even if we did we would not accept the reading the government urges upon us because it is unreasonable. Indeed, it is not at all clear to us that the FDA, under its regulations, would be authorized to reject the obvious intent of an NDA holder even if it acted directly contrary to a court order. Certainly, the FDA points us to no authority upon which it could rely to do so.

Intervenor BNP in its brief (and its letters to the FDA) would have us believe that appellant and Bristol-Myers are in cahoots, that the California lawsuit was a Kabuki play and that they have a common objective to frustrate the introduction of generic versions of Taxol. The difficulty with these assertions--besides being not proven--is that the FDA (Buehler) did not rely on this rationale. Nor is it clear that the FDA, as opposed to a district court in an antitrust or patent infringement case, could adjudicate such a claim.

district court order would result in the elimination of the August 11 listing. But the FDA (Buehler) did not offer that reasoning. In any event, it seems obvious to us that Bristol-Myers' September 11 letter was simply an effort to add a belt to suspenders and is even a greater indication that it never intended to completely de-list the '331 patent.

To be sure, Buehler hints in his declaration that he has dark suspicions by saying that he "was also made aware of the concerns of the Federal Trade Commission and some members of the public of the potential for the aggressive use of patent listings to delay generic competition." But such hints are hardly the stuff of reasoned decisionmaking. We therefore do not see how we can give any weight to BNP's allegations nor the letter from other members of the public opposing appellant's position.

Which brings us to the remedy. We have already directed the district court to remand this case once to compile a record. See *American Bioscience*, 243 F.3d at 582-83. That is consistent with our practice of remanding without vacating when we are unsure of the grounds the agency asserts to defend its action (and, perhaps, where we perceive that a ground poorly articulated might be sufficient to sustain the action). See, e.g., *Checkosky v. SEC*, 23 F.3d 452, 454 (D.C. Cir. 1992); *City of Los Angeles*, 192 F.3d at 1023; *Radio-Television News Directors Assoc. v. FCC*, 184 F.3d 872, 887-88 (D.C. Cir. 1999). But at this point we think the only appropriate course is to vacate the action appellant challenges--the FDA's approval of BNP's ANDA. We frankly do not know what recourse is left to the FDA or other government agencies to take any steps that would affect the marketing of generic versions of Taxol. But we are convinced that the FDA's order, in this case, was arbitrary and capricious and must be vacated.

* * * *

Accordingly, the district court is directed to vacate the FDA's order and remand to the agency.

ordered.

So