United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued November 8, 2004 Decided November 30, 2004

No. 04-5296

MYLAN LABORATORIES, INC., *ET AL.*,
APPELLANTS

v.

TOMMY G. THOMPSON, SECRETARY,
UNITED STATES DEPARTMENT OF HEALTH AND
HUMAN SERVICES, *ET AL.*,
APPELLEES

Appeal from the United States District Court
for the District of Columbia
(No. 04cv01049)

E. Anthony Figg argued the cause for the appellants. *Thomas C. Goldstein* was on brief.

Paul F. Brinkman, *Amy S. Manning* and *Thomas J. Parker* were on brief for *amicus curiae* Generic Pharmaceutical Association in support of appellants.

Bills of costs must be filed within 14 days after entry of judgment. The court looks with disfavor upon motions to file bills of costs out of time.

Howard S. Scher, Attorney, United States Department of Justice, argued the cause for the appellees. *Peter D. Keisler*, Assistant Attorney General, *Kenneth L. Wainstein*, United States Attorney, *Douglas N. Letter*, Counsel, United States Department of Justice, and *Alex M. Azar, II*, General Counsel, *Daniel E. Troy*, Chief Counsel, and *Eric M. Blumberg*, Deputy Chief Counsel, United States Department of Health & Human Services, were on brief for federal appellees. *Andrew E. Clark* and *Karen E. Schifter*, Attorneys, United States Department of Justice, entered appearances.

Anthony Herman, *Peter O. Safir*, *Carolyn F. Corwin* and *Kelly M. Jaske* were on brief for appellees Alza Corporation and Janssen Pharmaceutica, Inc.

Bruce N. Kuhlik, *David E. Korn* and *Donald O. Beers* were on brief for *amicus curiae* Pharmaceutical Research and Manufacturers of America in support of the appellees.

Gary W. Brown was on brief for *amicus curiae* Candlelighters Childhood Cancer Foundation National Office in support of the appellees.

Before: EDWARDS and HENDERSON, *Circuit Judges*, and WILLIAMS, *Senior Circuit Judge*.

Opinion for the court filed by *Circuit Judge* HENDERSON.

KAREN LECRAFT HENDERSON, *Circuit Judge*: Appellants Mylan Laboratories, Inc. Mylan Technologies, Inc. and Mylan Pharmaceuticals, Inc (Mylan) appeal the district court's summary judgment upholding the decision of appellee Food and Drug Administration (FDA). The FDA decision granted appellees ALZA Corp. and Janssen Pharmaceutica, Inc, both subsidiaries of Johnson and Johnson, (collectively, ALZA) a six-month period of pediatric marketing exclusivity, pursuant to 21 U.S.C. § 355a, following expiration of the final patent for ALZA's brand name transdermal fentanyl system, the Duragesic patch, which releases fentanyl, a narcotic analgesic, through the skin to treat chronic pain. Mylan contends the FDA's final approval of Mylan's Abbreviated New Drug Applications (ANDA) to market a generic version of the Duragesic patch, granted before the FDA issued the decision

challenged here, entitled Mylan to market its generic product immediately upon expiration of the patent pursuant to 21 U.S.C. § 355(j), without regard to pediatric exclusivity. For the reasons set out below, we affirm the district court's judgment upholding the FDA's decision.

I.

This appeal requires that the court consider three separate statutory provisions: (1) 21 U.S.C. § 355(j), a provision of the 1984 Hatch–Waxman Amendments to the Federal Food, Drug, and Cosmetic Act (FDCA), which authorizes a drug manufacturer to submit an ANDA to the FDA to obtain approval of a generic version of a previously approved drug; (2) 21 U.S.C. § 355a, a 1997 amendment to the FDCA, which authorizes an extra six-month "pediatric exclusivity" period following expiration of a drug patent for a patent holder that has satisfactorily conducted pediatric testing of its drug upon the FDA's request; and (3) 35 U.S.C. § 271(e)(4), a patent statute, also enacted in the Hatch–Waxman Amendments, which sets out the exclusive remedies available in a patent infringement action. We begin with a summary of these three provisions.

A. Applicable Statutory Provisions

The ANDA provision, 21 U.S.C. § 355(j), creates an approval short-cut for applicants seeking to market generic versions of approved drugs. Under this provision the generic applicant need not conduct its own clinical trials if the ANDA certifies that the generic version is bioequivalent to an approved drug. In addition, the ANDA must include one of four statutory "certifications" regarding the approved drug's patent status:

> (I) that such patent information has not been filed,
>
> (II) that such patent has expired,
>
> (III) . . . 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; . . . .

21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV) (paragraphs I-IV). If the ANDA contains a paragraph IV certification, the applicant must, within 20 days of the ANDA filing, send a notice to the patent holder stating it has submitted an ANDA with the paragraph IV certification and setting out the factual and legal bases for believing the patent is invalid or will not be infringed. 21 U.S.C. § 355(j)(2)(B).

The ANDA provision also establishes the effective date for approval of the ANDA, depending on the particular certification made.

If the applicant makes a certification under paragraph I or II, "the approval may be made effective immediately." 21 U.S.C. § 355(j)(5)(B)(i).

If the certification is under paragraph III, "the approval may be made effective on the date certified under [paragraph III]." 21 U.S.C. § 355(j)(5)(B)(ii).

If the certification is under paragraph IV, "the approval shall be made effective immediately" unless the patent holder files an infringement action in the district court within 45 days of receiving the notice, in which event "the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice," unless the district court rules on the infringement claim within the 30-month period. *See* 21 U.S.C. § 355(j)(5)(B)(iii). If the district court issues a ruling during the 30-month stay period, the ANDA approval date is determined by the decision of the district court, or the appellate court if appealed.[1]

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[1] If the district court decides within the stay period that the patent is invalid or not infringed, "the approval shall be made effective on" the date of entry of judgment or of a settlement order or consent decree. 21 U.S.C. § 355(j)(5)(B)(iii)(I). If the district court decides the patent is infringed and the judgment is not appealed or is affirmed, "the approval shall be made effective on the date specified by the district court in a court order under section

The pediatric exclusivity provision, 21 U.S.C. § 355a, provides an incentive for a drug patent holder to conduct pediatric studies of a drug which the FDA believes may have beneficial pediatric use. Under the statute, the FDA must first request that the drug patent holder conduct pediatric studies; if the requested studies are satisfactorily completed and submitted within the FDA-prescribed time frame, the patent holder is eligible to receive a six-month period of market exclusivity for the drug beyond the patent expiration date. 21 U.S.C. § 355a(c). The pediatric exclusivity provision expressly addresses the effect of a grant of pediatric exclusivity, depending on the particular certification included in the ANDA:

> (2)(A) if the drug is the subject of–
>
> > (i) a listed patent for which a certification has been submitted under [paragraph II] and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or
> >
> > (ii) a listed patent for which a certification has been submitted under [paragraph III],
>
> the period during which an application may not be approved under . . . section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions); or
>
> (B) if the drug is the subject of a listed patent for which a certification has been submitted under [paragraph IV], and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under

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271(e)(4)(A)." *Id.* § 355(j)(5)(B)(iii)(II)(bb). In turn, if the infringement judgment is appealed, "the approval shall be made effective on" either "the date on which the court of appeals decides that the patent is invalid or not infringed" or "the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed." *Id.* § 355(j)(5)(B)(iii)(II)(aa).

> . . . section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions).

21 U.S.C. § 355a(c)(2)(A)-(B).[2]

Finally, 35 U.S.C. § 271, a patent statute provision, authorizes the following remedies in a patent infringement action:

> (4) For an act of infringement described in paragraph (2)—
>
> (A) the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed,
>
> (B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug or veterinary biological product, and
>
> (C) damages or other monetary relief may be awarded against an infringer only if there has been commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug or veterinary biological product.
>
> The remedies prescribed by subparagraphs (A), (B), and (C) are the only remedies which may be granted by a court for an act of infringement described in paragraph

[2] If the district court in the patent infringement litigation determines the patent is invalid or will not be infringed, ANDA approval is effective upon the date of the court order so stating under 21 U.S.C. § 355(j)(5)(B)(iii) and the patent holder is entitled to no exclusivity thereafter. *See, e.g., Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998).

(2), except that a court may award attorney fees under section 285.

35 U.S.C. § 271(e)(4).

B. This Proceeding

Appellee ALZA owned U.S. Patent No. 4,588,580 ('580 patent) for Duragesic. By its terms the '580 patent expired on July 23, 2004.

In July 1999 the FDA wrote ALZA requesting that it perform pediatric studies of Duragesic pursuant to 21 U.S.C. § 355a(c). ALZA submitted the requested studies in November 2002. On January 29, 2003 the FDA granted ALZA a six-month pediatric exclusivity period.

Meanwhile, in October 2001 Mylan filed with the FDA an ANDA to market its generic fentanyl transdermal system pursuant to 21 U.S.C. § 355(j) with a paragraph IV certification that ALZA's '580 patent was invalid or would not be infringed by Mylan's martketing of its generic product. As required under 21 U.S.C. § 355(j)(2)(B), on December 6, 2001 Mylan sent ALZA notice of its ANDA application and certification which ALZA received on December 10, 2001. On January 25, 2002, the forty-sixth day after notice was received, ALZA filed a patent infringement action against Mylan in the United States District Court for the District of Vermont. Because the action was not brought within the statutory 45-day window following notice receipt, there was no automatic 30-month stay and, under 21 U.S.C. § 355(j)(5)(B)(iii), Mylan's ANDA was to "be made effective immediately." Accordingly, on November 21, 2003, the FDA granted final approval of Mylan's ANDA.

On March 24, 2004 the Vermont District Court issued a decision holding that "[t]he '580 patent is not invalid" and "Mylan's ANDA filing for a generic version of Duragesic ® infringe[s] . . . the '580 patent." *ALZA v. Mylan,* 310 F. Supp. 2d 610, 637 (D. Vt. 2004). The court therefore enjoined Mylan from "making, using, offering to sell, selling within the United States or importing into the United States" its generic

fentanyl transdermal system. 310 F. Supp. 2d at 637. Regarding Mylan's ANDA approval, the court stated simply that "the effective date of any approval of Mylan's ANDA product shall be no earlier than the date of expiration of the '580 patent family." *Id.* Mylan appealed the decision to the Federal Circuit where it remains pending.

In the meantime, both Mylan and ALZA sought a determination from the FDA on whether Mylan could lawfully market its generic fentanyl transdermal system when the '580 patent expired or whether Mylan was required to wait until the six-month pediatric exclusivity period expired. In two letters dated June 22, 2004, the FDA issued its administrative decision.

In the first letter (Letter 1), addressed to counsel for both parties, the FDA concluded that "ALZA's pediatric exclusivity for fentanyl will attach, and thus delay effective approval of Mylan's ANDA," so that "[u]nless Mylan were to win its patent case on appeal, Mylan's ANDA would be eligible for final effective approval no earlier than six months after the '580 patent expires on July 23, 2004." Letter 1 at 11. The FDA rested its decision on two key determinations.

First, the FDA concluded that the Vermont district court's order that "the effective date of any approval of Mylan's ANDA product shall be no earlier than the date of expiration of the '580 patent family," 310 F. Supp. 2d at 637, transformed Mylan's ANDA approval into "an approval with a delayed effective date," which "is a tentative approval that cannot be made effective until FDA issues a letter granting final effective approval." Letter 1 at 11 (citing 21 C.F.R. § 314.107(b)(3)(v);[3] *Barr Labs. v. Thompson*, 238 F. Supp. 2d 236, 245-50 (D.D.C. 2002)).

[3] This regulation provides:

> In order for an approval to be made effective under paragraph (b)(3) of this section, the applicant must receive an approval letter from the agency indicating that the application has received final approval. Tentative approval of an application

Second, the FDA concluded that, when ALZA's patent expired, Mylan's paragraph IV certification would no longer be accurate and Mylan would be required to amend it or, "[i]f Mylan refuses to amend its application to change its certification after the patent expires, FDA can treat that certification as automatically amended to contain a paragraph II certification (because there is no other proper certification upon expiry)." Letter 1 at 12 (citing *Ranbaxy Labs. v. FDA*, 307 F. Supp. 2d 15, 19, 21 (D.D.C. 2004), *aff'd*, 96 Fed. App. 1 (D.C. Cir 2004)). Then, once Mylan's certification converted to paragraph II, "pediatric exclusivity attaches under 355a(c)(2)(A)(i)," Letter 1 at 12 (citing *Ranbaxy*, 307 F. Supp. 2d at 20, 21), so that " 'the period during which an [ANDA] may not be approved . . . shall be extended by a period of six months after the date the patent expires,' "*id.* (quoting 21 U.S.C. § 355a(c)(2)(A)(i)).

In the second letter (Letter 2), addressed to Mylan only, the FDA informed Mylan that, "in light of [the Vermont district court's] decision, the Agency hereby rescinds the final approval of ANDA 76–258 issued on November 21, 2003, and regards ANDA 76–258 as tentatively approved." Letter 2 at 1. The letter again noted that, after the Vermont district court's order, Mylan's ANDA approval had "a delayed effective date," which, by FDA regulation, constitutes "tentative," rather than "final," approval. *Id.* (citing 21 C.F.R. § 314.105(a)).[4] Accordingly, the FDA informed Mylan: "Final Approval cannot be granted earlier than the date of a court decision finding the patents invalid, not infringed or unenforceable, or the expiration date of the patent and any period of pediatric exclusivity granted to the NDA holder."

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does not constitute "approval" of an application and cannot, absent a final approval letter from the agency, result in an effective approval under paragraph (b)(3) of this section.

[4] This regulation provides: "An approval becomes effective on the date of the issuance of the approval letter, except with regard to an approval under section 505(b)(2) of the act with a delayed effective date. An approval with a delayed effective date is tentative and does not become final until the effective date."

Id. at 1-2 & n.2 (noting that Mylan's ANDA was "subject to ALZA's pediatric exclusivity for fentanyl transdermal system").

On June 24, 2000 Mylan filed this action in the district court seeking a determination that the FDA's "revocation" of Mylan's final ANDA approval was unlawful and an injunction prohibiting the FDA "from revoking the final approval of Mylan's ANDA and from applying [ALZA's] pediatric exclusivity to Mylan's ANDA." *Mylan v. Thompson*, 332 F. Supp. 2d 106, 114 (D.C.C. 2004). In a decision filed August 17, 2004 the district court granted summary judgment in the FDA's favor, concluding that the agency "did not improperly revoke or reclassify its final approval of Mylan's ANDA for a generic version of a fentanyl transdermal system to a tentative approval and did not improperly apply ALZA pediatric exclusivity to Mylan's ANDA." 332 F. Supp. 2d at 124. Mylan appealed the district court's summary judgment.

II.

"The court reviews the district court's summary judgment decision *de novo* and 'we may affirm only if "there is no genuine issue as to any material fact [and] the moving party is entitled to judgment as a matter of law." ' " *Trans Union LLC v. Fed. Trade Comm'n*, 295 F.3d 42, 48 (D.C. Cir. 2002) (quoting *Gilvin v. Fire,* 259 F.3d 749, 756 (D.C. Cir 2001) (quoting *Anderson v. Liberty Lobby, Inc.,* 477 U.S. 242, 250 (1986) (quoting Fed. R. Civ. P. 56(C)))). We review the FDA's decision under the Administrative Procedure Act, 5 U.S.C. § 706(2)(A). *Serono Labs. v. Shalala*, 158 F.3d 1313, 1327 (D.C. Cir. 1998) (citing *Troy Corp. v. Browner,* 120 F.3d 277, 283 (D.C. Cir. 1997); *Schering Corp v. FDA,* 51 F.3d 390, 399 (3d Cir. 1995)). Accordingly, we must uphold the FDA's decision unless it is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2). We conclude that the FDA's decision was none of these.

At issue is the FDA's application of the statutory provisions summarized above. "Ordinarily we review an agency's inter-

pretation of a statute it is charged with implementing under the familiar and deferential two-part framework of *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 104 S.Ct. 2778, 81 L.Ed.2d 694 (1984)." *Pharm. Research & Mfrs. of Am. v. Thompson*, 362 F.3d 817, 821 (D.C. Cir. 2004). Mylan contends, however, that only minimal deference is owed to the FDA's interpretation of the FDCA because it was expressed in letters to the parties and "is not embodied in any regulation, much less a regulation that was subject to notice and comment rulemaking." Appellants' Br. at 19-20. The FDA's letter decisions, Mylan maintains, are "analogous to 'opinion letters,' " *id.* at 20 (quoting *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944)), and therefore "do not warrant *Chevron*-style deference" but are entitled only " ' "to respect" ' " and even then " 'only to the extent that those interpretations have the power "to persuade," ' " *Christensen v. Harris County*, 529 U.S. 576, 587 (2000) (quoting *Skidmore*, 323 U.S. at 140; other citations omitted)). We are not persuaded by Mylan's argument and conclude, as did the district court, that the FDA's decision is entitled to *Chevron* deference.[5]

" '[T]he want of' notice and comment 'does not decide the case' " against *Chevron* deference. *Barnhart v. Walton*, 535 U.S. 212, 222 (2002) (quoting *United States v. Mead Corp.*, 533 U.S. 218, 230-31 (2001)). "Indeed, *Mead* pointed to instances in which the Court has applied *Chevron* deference to agency interpretations that did not emerge out of notice-and-comment rulemaking," *Id.* (citing *United States v. Mead Corp.*, 533 U.S. at 230-31 (citing *NationsBank of N. C., N.A. v. Variable Annuity Life Ins. Co.*, 513 U.S. 251, 256-57

[5] Mylan also asserts, correctly, that the court owes no deference to the FDA's interpretation of 35 U.S.C. § 271(e)(4)(A), a patent statute provision which the FDA is not charged with administering, *see Scheduled Airlines Traffic Offices, Inc. v. Dep't of Defense*, 87 F.3d 1356, 1361 (D.C. Cir. 1996); or of the decision of the Vermont district court, *see American Bioscience v. Thompson*, 269 F.3d 1077, 1085 (D.C. Cir. 2001). Neither the statute nor the court decision, however, presented any ambiguity for the FDA to interpret.

(1995))). "[W]hether a court should give such deference depends in significant part upon the interpretive method used and the nature of the question at issue." *Id.* (citing *Mead*, 533 U.S. at 229-31). In *Barnhardt* the Court concluded that "the interstitial nature of the legal question, the related expertise of the Agency, the importance of the question to administration of the statute, the complexity of that administration, and the careful consideration the Agency has given the question over a long period of time all indicate that *Chevron* provides the appropriate legal lens through which to view the legality of the Agency interpretation here at issue." *Id.* We reach the same conclusion here.

There is no denying the complexity of the statutory regime under which the FDA operates, the FDA's expertise or the careful craft of the scheme it devised to reconcile the various statutory provisions. Further, the FDA's decision made no great legal leap but relied in large part on its previous determination of the same or similar issues and on its own regulations. *See* Letter 1 at 11-12 (citing 21 C.F.R. § 314.107(b)(3)(v), *Barr* and *Ranbaxy*); Letter 2 at 1 (citing 21 C.F.R. § 314.105(a)). We therefore accord *Chevron* deference to the FDA's letter decision here, as we have previously done on at least one other occasion. *See Abbott Labs. v. Young,* 920 F.2d 984, 986-89 (D.C. Cir. 1990), *cert. denied,* 502 U.S. 819 (1991) (reviewing under *Chevron* letter decision construing term "active ingredient" in ANDA provision, 21 U.S.C. § 355(j)(4)(D)(i), (v)); *id.* at 992–96 (Edwards, J., dissenting) (applying *Chevron*); *see also Barr Labs. v. Thompson*, 238 F. Supp. 2d 236, 245-50 (D.D.C. 2002) (applying *Chevron* to FDA letter ruling).[6]

"Under the *Chevron* framework, '[i]f . . . "Congress has directly spoken to the precise question at issue," we must give effect to Congress's "unambiguously expressed intent" ' but

[6] Even were the FDA's decision subject only to *Skidmore* deference, the result would likely be the same. *See Ranbaxy Labs. v. FDA,* 96 Fed. App. 1, 1 (D.C. Cir. 2004) ("Regardless whether the [FDA's] decision is reviewed under *[Skidmore* or *Chevron*], the district court properly affirmed the FDA's determination. . . .").

'[i]f "the statute is silent or ambiguous with respect to the specific issue," we ask whether the agency's position rests on a "permissible construction of the statute." ' " *Pharm. Research & Mfrs.,* 362 F.3d at 823–24 (quoting *Beverly Health & Rehab. Servs. v. NLRB,* 317 F.3d 316, 321 (D.C. Cir. 2003) (quoting *Chevron*, 467 U.S. at 842–43). In applying the FDCA provisions to the particular facts here, the FDA found two ambiguities.

First, application of the various statutory provisions results in conflicting effective dates for Mylan's ANDA. The patent infringement remedy statute, 35 U.S.C. § 271(e)(4)(A), directs that the court deciding the infringement action "shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed," which is precisely what the Vermont district court did here, directing that "the effective date of any approval of Mylan's ANDA product shall be no earlier than the date of expiration of the '580 patent family," 310 F. Supp. 2d at 637; yet under 21 U.S.C. § 355(j)(5)(B)(iii), approval of the paragraph IV ANDA was to "be made effective immediately" after the 45-day window closed without an infringement action filed by the patent holder, so that the FDA was required to (and did) grant final approval of Mylan's ANDA, immediately effective, notwithstanding the pending infringement action. As a result, at the time of the FDA letter decision, Mylan's ANDA was subject to two conflicting approval effective dates: the date of the FDA's approval decision (November 21, 2003) and, pursuant to the Vermont district court's order, a date "no earlier than the date of expiration of the '580 patent family" (i.e., July 23, 2004).

Second, after the Vermont district court's finding of patent validity, Mylan's paragraph IV ANDA certification was at variance with the legal reality. Because the '580 patent was then valid and infringed as a matter of law, ANDA's certification that the '580 patent "is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted" was no longer accurate. Further,

section 355a(c)(2), which governs the consequences for pediatric exclusivity under each of the alternative patent certifications, provided no mechanism to resolve this discrepancy because, at least as construed in the administrative proceeding, this section applies to a paragraph IV certification only if an infringement action has been filed within the 45-day window so as to trigger the 30–month stay period.[7] Because the infringement action here was filed outside the 45-day window, the FDA was left with a statutory gap to fill.

In deciding the exclusivity issue submitted by Mylan and ALZA, the FDA was called upon to construe the statutes so as to resolve these two conflicts. We conclude the FDA did so in a way that reflects a permissible construction of the applicable FDCA provisions and therefore satisfies *Chevron*. *See Western Coal Traffic League v. Surface Transp. Bd.*, 216 F.3d 1168, 1173 (D.C. Cir. 2000) (reviewing under *Chevron* agency resolution of "unanticipated conflict" arising from application of statute).

A. Conversion of Approval from "Final" to "Tentative"

First, the FDA concluded that, as a consequence of the Vermont district court's determination under 35 U.S.C. § 271(e)(4)(A) that "the effective date of any approval of Mylan's ANDA product shall be no earlier than the date of expiration of the '580 patent family," the FDA's approval of Mylan's ANDA was no longer "immediately effective"—its effective date had changed, as the Congress had contemplated it would under such circumstances when it enacted 35 U.S.C. § 271. *See* H.R. Rep. No. 98-857, pt. 1, at 46 (1984) ("In the case where an ANDA had been approved, the order would mandate a change in the effective date."). The FDA

[7] On appeal the appellees argue alternatively that section 355a(c)(2)(B) can be read to cover the situation when the action is filed after the 45-day window as well as before (obviating the need for certification conversion). This may well be a permissible construction of the provision but it is not the reading the FDA applied during the administrative proceeding nor the one before us on review of the FDA's decision.

next determined, logically enough, that the effective date was then "delayed" and therefore "tentative," rather than "immediate" and "final," under the FDA's own regulation which provides that "[a]n approval with a delayed effective date is tentative and does not become final until the effective date." 21 C.F.R. § 314.105(a); *see Barr Labs. v. Thompson*, 238 F. Supp. 2d 236, 245-50 (D.D.C. 2002) (upholding FDA determination under 21 C.F.R. § 314.105(a) that ANDA approval before patent expiration was tentative, not final).

Mylan contends the FDA lacked authority to revoke Mylan's final ANDA approval granted on November 21, 2003 because its authority to revoke a final approval is limited to those specific circumstances set out in 21 U.S.C. § 355(e), none of which exists here. Mylan's characterization of section 355(e) is off the mark. As the FDA indicates in its decision, Letter 1 at 12 n.10, section 355(e) simply sets out specific, not necessarily exclusive, circumstances under which the FDA must withdraw any ANDA approval (whether final or otherwise) after notice and hearing. But the provision does not prohibit the FDA from withdrawing approval under other circumstances—or, more precisely, does not prohibit the FDA from changing a final into a tentative approval under circumstances different from those named in section 355(e).[8] Moreover, the patent remedy statute directs that upon a finding of infringement the district court establish a new effective date for approval which is "not earlier than the date of the expiration of the patent which has been infringed." 35 U.S.C. § 271(e)(4)(A), and the FDA was bound under the district court's order to treat the status of Mylan's ANDA under the FDCA "the same as that of other ANDAs blocked from final approval by patent or exclusivity rights." Letter 1 at 12 n.10.

[8] We are skeptical whether the parties properly characterize the FDA's action as "withdrawal" or "revocation" of approval. It seems to us that Mylan's ANDA approval was never in fact "withdrawn" or "revoked" but remained continuously in effect based on the FDA's review of the ANDA described in the November 21, 2003 final approval letter. The approval merely underwent a change of

Mylan also claims the approval conversion is "contrary to past Agency practice." Appellants' Br. 43 (citing *Mead Johnson Pharm. Group v. Bowen*, 838 F.2d 1332, 1334 (D.C. Cir. 1988), and *Unimed, Inc. v. Quigg*, 888 F.2d 826, 827 (Fed. Cir. 1989)). Each cited case, however, involved not an ANDA but a New Drug Application, a different animal entirely because the latter is generally not subject to a delayed effective date, and each application was subject to an approval letter authorizing *immediate* marketing without any delayed effective date. *See Mead Johnson*, 838 F.2d at 1336 (noting applicant could have marketed its product on day of approval by filing required supplemental labeling); *Unimed*, 888 F.2d at 828 (FDA letter noting product could not be marketed until it was "rescheduled" by DEA simply "*reminded* Unimed that DEA rescheduling was necessary before the drug could be marketed" and "was not a condition on FDA approval") (emphasis original).[9]

B. Conversion of Paragraph IV to Paragraph II Certification

The FDA next addressed the problem of Mylan's inaccurate ANDA certification and resolved it relying on *Ranbaxy Labs. v. FDA*, 307 F. Supp. 2d 15 (D.D.C. 2004), *aff'd*, 96 Fed. App. 1 (D.C. Cir 2004). The FDA concluded that under *Ranbaxy* when the '580 patent expired, Mylan's paragraph IV certification would convert to a paragraph II certification and ALZA would be entitled to pediatric exclusivity for six months following the expiration. The FDA reasoned that

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status or classification from final to tentative after the Vermont district court delayed its effective date.

[9] Nor do we see any force in Mylan's citation to the FDA's 1994 rulemaking, in which the FDA declined to extend by rule the statutory 45-day window. Appellants' Br. at 42 (quoting 59 Fed. Reg. at 50,353). The FDA simply explained there that if the window were to be extended (which it was not), the FDA would retain authority during the extension to grant final effective ANDA approval, notwithstanding the patent holder might *subsequently* file a successful infringement action.

once the certification became inaccurate, Mylan was under a duty to amend its ANDA to change the certification to paragraph II, *see* 21 C.F.R. § 314.94(a)(12)(viii)(C)(i) (providing "an applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate"); and if Mylan failed to do so, the FDA could "treat that certification as automatically amended to contain a paragraph II certification." Letter 1 at 12. Once the certification changed to paragraph II—whether *de facto* or *de jure*—pediatric exclusivity attached under 21 U.S.C. § 355a(c)(2)(A)(i) ("[I]f the drug is the subject of– . . . a listed patent for which a certification has been submitted under [paragraph II] and for which pediatric studies were submitted prior to the expiration of the patent; . . . the period during which an application may not be approved under . . . section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires."). We find the FDA's application of the statutory provisions both reasonable and supported by *Ranbaxy*.

In *Ranbaxy* the FDA also converted an ANDA classification from a paragraph IV to a paragraph II certification under similar circumstances. The patent holder in *Ranbaxy* filed an infringement action within forty-five days after receiving the required paragraph IV certification notice. Upon learning the district court would be unable to decide the case before the patent expiration date, the parties signed a stipulation to dismiss the action as of the expiration date. The day before expiration, the FDA informed the ANDA applicant that its ANDA would be subject to a six-month pediatric exclusivity period for the patented drug. There, as here, 21 U.S.C. § 355a(c)(2)(B) did not apply (there, because there was no finding of a valid patent or infringement) and the FDA concluded that upon the patent expiry the paragraph IV certification converted to a paragraph II certification and pediatric exclusivity attached under 21 U.S.C. § 355a(c)(2)(A)(i). The district court agreed with the FDA's statutory construction and on appeal we concluded:

> [T]he district court properly affirmed the FDA's determination that, under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301, *et seq.,* final approval of Ranbaxy's Abbreviated New Drug Applications ("ANDAs") did not automatically occur upon the dismissal of the underlying patent litigation, the expiration of the patent, and the termination of the thirty-month statutory stay. The district court also properly affirmed the FDA's conclusion that, upon the expiration of Pfizer's patent on January 29, 2004, Ranbaxy's "Paragraph IV" certifications became invalid, and the applicable pediatric exclusivity provision became 21 U.S.C. § 355a(c)(2)(A), the provision pertaining to "Paragraph II" certifications. *Id.* Under that provision, approval of Ranbaxy's ANDAs is delayed six months. . . . *See* 21 U.S.C. § 355a(c)(2)(A).

96 Fed. App. at 1. For the same reasons, the district court here acted properly in upholding the FDA's certification conversion.

Mylan contends that one of the FDA's own regulations weighs against this rationale, namely, 21 C.F.R. § 314.94(a)(12)(viii)(A), which requires that an ANDA applicant amend its application to recertify under paragraph III ("that the patent will expire on a particular date") if a finding of validity/infringement is made in a lawsuit *that has been filed within the statutory 45-day window.* Mylan asserts the "necessary implication" of this language is that "if the applicant is not sued within the forty-five-day-period, 21 U.S.C. § 355(j)(5)(B)(iii) requires that approval of an ANDA shall be 'effective immediately' and certifications are no longer relevant." Appellants' Br. at 42. Mylan reads too much into the regulation. That the FDA has expressly required recertification when an action is filed within the 45-day window does not "necessarily" mean an applicant need not amend its application to change the patent certification to reflect changed circumstances if the action is not filed within the window. To the extent that the cited regulation is relevant here, it supports the FDA's rationale in requiring a generic drug appli-

cant to amend its ANDA to include an accurate certification.[10]

Mylan also contends the FDA's construction "would read [section 355a(c)(2)(B)] entirely out of the statute" because, if it "does not govern the availability of pediatric exclusivity in cases like this one involving Paragraph IV certifications in which infringement is found, the statute serves no purpose at all." Appellants' Br. at 22-23. Not so. Under the FDA's interpretation, section 355a(c)(2)(B) applies when—and only when—all three of its express conditions are met: "a certification has been submitted under [paragraph IV]," there is "patent infringement litigation resulting from the certification" and in the litigation "the court determines that the patent is valid and would be infringed." It is only because one of these requirements was missing in *Ranbaxy* (a valid patent finding) and in this case (an infringement action filed within the 45-day window) that the FDA, prevented from applying its reading of section 355a(c)(2)(B), was required to fill the statutory gap by deeming the patent certification changed.

* * *

We affirm the district court's judgment because the FDA's decision reasonably resolves the ambiguity in applying the relevant statutes to a factual situation not fully foreseen or provided for by the Congress when it enacted the statutes or the FDA when it promulgated regulations. The Vermont district court's finding of patent validity and consequent injunction changed the factual and legal landscape and the agency's response to the court's decision is both reasonable and consistent with the statutory language. The FDA's

[10] The FDA might well have concluded that in this situation too, as ALZA suggested in the administrative proceeding, *see* Letter 1 at 11, the paragraph IV certification should have changed to a paragraph III certification immediately upon the district court's finding of validity/infringement, consistent with the directive of 21 C.F.R. § 314.94(a)(12)(viii)(C)(1)(i) that "an applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate."

solution effects the policies of both the generic ANDA provision, by eliminating the need for Mylan to conduct clinical trials of its generic product, and the pediatric exclusivity provision, by granting ALZA a six-month exclusivity period in return for the pediatric studies it performed, the adequacy of which Mylan does not dispute. At the same time, it maintains the incentive under 21 U.S.C. § 355(j)(5)(B)(iii) for a patent holder to promptly file an infringement action when its patent is challenged because, if the patent holder fails to do so within forty-five days, it will lose the benefit of the 30-month stay period and possibly, for a time, market exclusivity it should rightfully enjoy.[11]

So ordered.

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[11] In a case such as this, for example, if the district court found the patent invalid, without the 30–month stay the ANDA applicant would obtain immediate approval under the court's decision to market its generic product notwithstanding the patent holder might subsequently successfully appeal the district court's decision.