

United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued September 17, 1999 Decided February 11, 2000

No. 99-5048

Warner-Lambert Company,  
Appellant

v.

Donna E. Shalala, Secretary of Health  
and Human Services, et al.,  
Appellees

Appeal from the United States District Court  
for the District of Columbia  
(No. 99cv00093)

Bruce N. Kuhlik argued the cause for appellant. With him on the briefs were Herbert Dym, Michael S. Labson, and Michael A. Listgarten.

Jeffrey B. Chasnow, Attorney, U.S. Department of Justice, argued the cause for appellees Donna E. Shalala, et al. With

him on the brief was David W. Ogden, Acting Assistant Attorney General.

E. Anthony Figg argued the cause for appellee Mylan Pharmaceuticals, Inc. With him on the brief was Bart G. Newland. Steven M. Lieberman entered an appearance.

Before: Williams, Rogers and Garland, Circuit Judges.\*

Opinion for the Court filed by Circuit Judge Williams.

Williams, Circuit Judge: When is a pill a capsule rather than a tablet? Plaintiff Warner-Lambert's entitlement to relief against the Food and Drug Administration turns on this point. Warner-Lambert believes that an anti-epilepsy drug made by Mylan Pharmaceuticals--having the interior form of a tablet but placed inside a capsule--cannot properly be viewed as a capsule. The Mylan product therefore has, according to Warner-Lambert, a different "dosage form" from that of Warner-Lambert's anti-epilepsy drug "Dilantin."<sup>1</sup> If Warner-Lambert is right, then the FDA should not have found the Mylan product "therapeutically equivalent" to Dilantin and (without putting Mylan's product through additional hoops) should not have approved Mylan's "abbreviated new drug application." And, again if Warner-Lambert is right, it would likely be entitled to the district court injunction that it sought, forcing the FDA to withdraw its finding of equivalence and to rescind its approval of the Mylan product. Because Warner-Lambert has not convinced us of any legal error in the FDA's decision on the capsule-tablet issue, we affirm the denial of the preliminary injunction.

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\* Circuit Judge Garland was originally a member of the panel but did not participate in the opinion in this case.

1. Dilantin is the brand name of a family of anti-epilepsy drugs manufactured by Warner-Lambert's Parke-Davis division. The drug at issue here is the largest-selling of the Dilantin line, the 100 mg strength of extended phenytoin sodium capsules marketed as Dilantin Kapseals. For simplicity, we adopt Warner-Lambert's terminology and refer to the Dilantin Kapseals product simply as "Dilantin."

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The FDA must find a new drug to be safe and effective for its intended use before any person may introduce it into interstate commerce. See 21 U.S.C. s 355(a) (1994). The first, or "pioneer," applicant for a given drug must submit a new drug application ("NDA"), which includes "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use." Id. s 355(b). Once the FDA approves the application for the pioneer drug, it becomes a "listed drug," id. s 355(j)(7), and generic copies may be approved using the far simpler, abbreviated new drug application ("ANDA"), id. s 355(j)(2)(A)(ii)-(iv).

An ANDA will be approved if the applicant demonstrates that the generic drug is bioequivalent to the listed drug and has the same active ingredients, route of administration, strength, and dosage form. See id. s 355(j)(2)(A)(ii)-(iv), (j)(4); see also 21 CFR s 314.92(a)(1) (1999) (indicating the categories of drug products for which ANDAs may be filed). If the drug is different in any of these four respects, a generic manufacturer may use an abbreviated application only if it first files a "suitability petition" and the FDA grants it permission to file an ANDA. 21 U.S.C. s 355(j)(2)(C); 21 CFR s 314.93. The petition must be granted unless the FDA finds that the difference calls the safety and effectiveness of the drug into doubt. See 21 U.S.C. s 355(j)(2)(C). But drugs that require a suitability petition cannot be considered "therapeutically equivalent"<sup>2</sup> to the pioneer drug, and therefore cannot take advantage of state pharmacy laws that deem such products substitutable. See *Serono Labs. v. Shalala*, 158 F.3d 1313, 1317 (D.C. Cir. 1998). Substitutability is competitively important. When a doctor prescribes a drug by brand name, the pharmacist may (and in some states must)

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2. Therapeutic equivalence turns on "pharmaceutical equivalence" which is based in part upon identity of dosage form. Pharmaceutical equivalence is defined in FDA regulations, see 21 CFR s 320.1(c), and an FDA publication known as the Orange Book, available on the FDA's web site, see <<http://www.fda.gov/cder/ob>>.

dispense a therapeutically equivalent generic alternative unless the doctor requires that the prescription be dispensed as written. See, e.g., N.Y. Educ. Law s 6816-a (McKinney 1999) (requiring generic drug substitution unless the doctor indicates otherwise).

Mylan Pharmaceuticals, Inc. filed an ANDA for its 100 milligram phenytoin sodium product, which it said satisfied the criteria for approval as a generic version of Dilantin. The FDA issued an approval letter on December 28, 1998, finding the product therapeutically equivalent to Dilantin. In so holding, it necessarily found that Mylan's product had the same dosage form as Dilantin, i.e., was in the form of a capsule.

Because the ANDA process is not public, the approval letter was Warner-Lambert's first notice of Mylan's application. But Warner-Lambert rose quickly to the challenge. Two weeks later it filed a complaint and request for preliminary injunction in the district court. All its claims rested on the argument that Mylan's product is properly classified as a tablet rather than a capsule. More specifically, however, Warner-Lambert argued that the FDA violated the statute by failing to apply the definitions of the United States Pharmacopoeia ("USP") for particular dosage forms as required by the Food, Drug and Cosmetic Act (under which, Warner-Lambert urges, Mylan's product would be a tablet), and acted arbitrarily and capriciously by classifying Mylan's product as a capsule when it has previously classified indistinguishable products as tablets.

The district court disagreed and denied Warner-Lambert's preliminary injunction request on January 29, 1999, in a ruling from the bench. Warner-Lambert filed a timely notice of appeal.

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It is commonly said that we review a district court's decision to deny a preliminary injunction under the deferential "clear error" or "abuse of discretion" standards, due to the "latitude the district court properly enjoys in balancing

the four factors that traditionally constitute the preliminary injunction calculus." *City of Las Vegas v. Lujan*, 891 F.2d 927, 931-32 (D.C. Cir. 1989). And of course we always accord deference to the district court's findings of fact. See *id.* at 931. Here, however, the case can be resolved by reference to purely legal claims about the FDA's decision, legal claims that require deference not to the district court but to the agency. See *Novicki v. Cook*, 946 F.2d 938, 941 (D.C. Cir. 1991).

Warner-Lambert's statutory claim is that the dosage form definitions in the USP are binding upon the FDA under the Food, Drug and Cosmetic Act and that under the USP's definition, Mylan's product is a tablet. We assume in Warner-Lambert's favor that the USP definitions in question are indeed binding on the FDA, but we do not see that the FDA ruling here violates the key definition--that of capsules. The USP defines them as "solid dosage forms in which the drug is enclosed within either a hard or soft soluble container or 'shell.'" *United States Pharmacopeia 1942* (1995). Warner-Lambert identifies no characteristic of the Mylan product that is inconsistent with this definition on its face. Rather it relies on the declarations of two eminently distinguished members of the USP's Committee on Revisions, in which both argue that when read properly the USP definition precludes such a finding. But as Warner-Lambert conceded at oral argument, we owe these experts' interpretation no deference. See *Tr. of Oral Argument* at 16. Of course the absence of an administrative record explaining how the FDA applied the terms "dosage form," "capsule," or "tablet" in this case also deprives it of the deference that would ordinarily be due such reasoning. See *City of Kansas City v. HUD*, 923 F.2d 188, 192 (D.C. Cir. 1991). But where the agency ruling seems entirely congruent with the (allegedly) binding legal language, the existence of a conflicting interpretation by others, no matter how distinguished or well-informed about the background of the language, is an inadequate basis to overturn the agency's ruling. Of course the opinions of Warner-Lambert's experts would bolster Warner-Lambert's position if it had a convincing claim that inconsistencies with earlier FDA deter-

minations rendered the FDA's decision arbitrary and capricious under the Administrative Procedure Act, 5 U.S.C. s 706(2)(A). But, as we shall see, that is not the case.

The core of Warner-Lambert's inconsistency claim is that the FDA has irrationally distinguished between virtually identical products, "classifying Mylan's capsule-shaped tablet in a gelatin shell as a 'capsule' while classifying gelatin-coated capsule-shaped tablets as 'tablets.'" Appellant's Initial Br. at 19. Warner-Lambert does not claim that the FDA has ever treated a capsule-shaped tablet in a gelatin shell as a tablet. That is, it makes no claim of direct self-contradiction.

ANDA applications are not treated as adversary proceedings, and evidently no one in the process formally posed Warner-Lambert's question as to why these superficially rather similar things should be differently classified. As a result the Mylan application file contains no explicit answer to the question. In the preliminary injunction proceeding, however, the FDA offered materials as to prior decisions that shed some light on the subject. For example, an FDA response to a citizen petition filed on behalf of Novartis Pharmaceuticals stated its position that "dosage form is the way of identifying the drug in its physical form, which is linked both to physical appearance of the drug product and to the way it is administered." FDA Docket No. 96P-0459, Nov. 2, 1998, Response to Petition filed by Novartis, Inc., at 12 (Nov. 2, 1998), Joint Appendix ("J.A.") 102, 113 (quoting FDA Docket No. 93P-0421, Aug. 12, 1997, Response to Petition filed by Pfizer, Inc., at 4). Similarly FDA responded to such a petition by Zenith Goldline Pharmaceuticals, Inc.: "The contents of a capsule do not change the fact that the product is a capsule.... Compressed tablets with a gelatin coating are considered by the Agency to be tablets." FDA Docket No. OGD 98-045, Mar. 31, 1998, Response to Petition filed by Zenith Goldline Pharmaceuticals, Inc., at 1, J.A. at 121.

These opinions support two inferences. First, they state the general criteria that FDA says are properly applied in making the "dosage form" determination--namely, that it is a

matter of looking to a drug's (1) physical appearance and (2) the way it is administered. Second, those general criteria are consistent with the FDA's conduct here: Both products (Dilantin and the Mylan product) are administered orally,<sup>3</sup> and their physical appearance--a capsule shell with some contents--is the same. Warner-Lambert has not undertaken to show that the Mylan product looks "more" like a gelatin-coated tablet than it looks like what it is, a capsule with a tablet inside.

Warner-Lambert argues that these rulings were not part of the administrative record. True enough--but that hardly renders them immaterial as evidence that the FDA has formulated a principle and that its individual case decisions have stuck to it. Indeed, at that level Warner-Lambert really has no complaint.

Its real complaint, then, is that the line the FDA has drawn is rather formalistic; so much so as to be in effect arbitrary and capricious. Obviously drawing distinctions without a difference may be arbitrary. See *Independent Petroleum Ass'n of Am. v. Babbitt*, 92 F.3d 1248, 1258-60 (D.C. Cir. 1996); *Green Country Mobilephone, Inc. v. FCC*, 765 F.2d 235, 238 (D.C. Cir. 1985). But consider Warner-Lambert's basic position. It rests on the statutory requirement that an ANDA can be approved only if the new drug is identical in "dosage form." Its attack on the FDA's line-drawing can be framed in three ways: It may be saying that any line between capsules and tablets is silly or pointless, in which case the two dosage forms should be collapsed. If so, Warner-Lambert cannot have been harmed here, as the dosage form would plainly have been identical for both products under the alter-

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3. The scope of the "administration" part of the dosage form definition remains unclear. FDA acknowledges that "method of administration" is more subtle than simply distinguishing between the manner in which the drug is introduced into the patient, such as orally, topically, or via injection. But we have no occasion to probe the contours of "method of administration" in this case because there is no allegation that Dilantin and Mylan's product have different methods of administration.

native rule. Or Warner-Lambert may be saying that while there should be a line between capsules and tablets, the FDA's line is incapable of consistent application because there is no method for separating a gelatin coating from a capsule shell. But Warner-Lambert has provided no reason to believe that the FDA is unable to distinguish consistently between the two. Finally, Warner-Lambert may be saying the FDA has drawn the line in the wrong place, that capsules containing tablets belong with tablets rather than with capsules. Yet it offers virtually no reason to think that there is anything irrational about the FDA's choice of exactly where in these shadowlands it should locate this border (a necessary border, under this last assumption).

The exception (the reason the previous sentence says "virtually no reason") is a claim tucked away in the section of Warner-Lambert's brief devoted to USP definitions. It asserts that the way in which the body absorbs a garden-variety capsule is different from the way it absorbs a tablet in a capsule, so that the FDA's capsule classification of the Mylan product may lead to inaccurate inferences about its absorption.

There are at least three difficulties with this claim. First, Warner-Lambert made no attack on the FDA's bioequivalence finding. Bioequivalence requires an FDA finding that "the rate and extent of absorption of the [new] drug do not show a significant difference from the rate and extent of absorption of the listed drug." 21 U.S.C. s 355(j)(8)(B). Thus, contrary to what Warner-Lambert proposes here, we must assume that rate and extent of absorption are the same. Second, Warner-Lambert's argument would place limits on the capsule dosage form that have no statutory or regulatory basis. As Warner-Lambert acknowledges, Reply Br. at 9, multiple tablets encapsulated in a shell are treated as capsules. Warner-Lambert evidently accepts this as sound practice. But under Warner-Lambert's conception of dosage form, a liquid-filled capsule (which Warner-Lambert agrees is properly deemed a capsule) that sought to gain approval as a generic equivalent of this tablet-filled capsule would have the added hurdle of showing that the liquid would perform the

same way as the tablets independent of a showing of bioequivalence. The FDA has not required such a showing. Third, contrary to Warner-Lambert's assertion that bioequivalence is insufficient because Mylan's product may have dangerous lot-to-lot variation, the record contains graphs and other materials purporting to demonstrate that Mylan's product is at least as consistent as Dilantin, see J.A. 245-46 (depicting lot-to-lot dissolution profiles for both products), and Warner-Lambert makes no claim that the natural reading of these graphs--namely that the profiles are identical--is in error.

Given the consistency of the FDA's classification of the Mylan product with the language of the USP, with its stated criteria for making dosage form classifications, and with its specific dosage form classifications, there were no grounds for granting the requested injunction. The decision of the district court is

Affirmed.