United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued September 11, 1997 Decided October 28, 1997

No. 96-5371

SYNCOR INTERNATIONAL CORPORATION, ET AL.,
APPELLANTS

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
(95cv1627)

Alvin J. Lorman argued the cause for appellants, with whom *Gregory R. Firehock* was on the briefs.

Jay I. Bratt, Attorney, United States Department of Justice, argued the cause for appellees, with whom *Frank W. Hunger,* Assistant Attorney General, and *Eric H. Holder, Jr.,*

U.S. Attorney at the time the briefs were filed, were on the brief.

Before: SILBERMAN, ROGERS and TATEL, *Circuit Judges*.

Opinion for the Court filed by *Circuit Judge* SILBERMAN.

SILBERMAN, *Circuit Judge*: Appellants Syncor International Corporation, American College of Nuclear Physicians, Society of Nuclear Medicine, and American Pharmaceutical Association (collectively, Syncor) appeal the district court's decision that FDA's 1995 "Notice," entitled "Regulation of Positron Emission Tomography Radiopharmaceutical Drug Products; Guidance; Public Workshop," was a "non-substantive" rule not subject to notice and comment rulemaking. We reverse.

I.

Positron emission tomography (PET) is a diagnostic imaging method that uses a subset of radioactive pharmaceuticals, called PET drugs, to determine biochemistry, physiology, anatomy, and pathology within various body organs and tissues by measuring the concentration of radioactivity in a targeted area of the body. The active component of PET drugs is a positron-emitting isotope.[1] This component has a short half-life, so the drug remains effective for only brief periods of time. As a consequence, PET drugs are not manufactured by pharmaceutical companies; instead, they are prepared by physicians and pharmacists operating accelerators in facilities known as nuclear pharmacies, which most often are part of major teaching hospitals or their adjacent universities, and always are located very near to the place where the PET drug will be administered to patients. These nuclear pharmacists compound the isotope with a chemical

[1] Positrons are positively charged subatomic particles with the same mass and magnitude of charge as electrons, and are regarded as the antiparticle of negatively charged electrons because the two mutually annihilate each other when brought together. Isotopes are atoms of a certain element with an atypical number of neutrons in their nuclei. An isotope is positron-emitting when it is neutron deficient.

solution called a substrate. The substrate is used to carry the isotope to the targeted organ or tissue, and the precise solution used depends on the targeted area. For example, a nuclear pharmacist might combine an isotope with a glucose substrate if the brain was being targeted, since the brain is an area of high glucose uptake. In part for this reason, PET drugs are compounded pursuant to a prescription.

On February 25, 1995, FDA announced that PET radiopharmaceuticals "should be regulated" under the drug provisions of the Federal Food, Drug, and Cosmetic Act.[2] In this publication, labeled a "Notice," and referred to alternatively in its text as "guidance" and a "policy statement," FDA indicated that it would require PET "radiopharmaceutical manufacturers" to comply with the adulteration provision of § 501(a)(2)(B) of the Act (drugs are considered adulterated unless manufactured in conformance with current good manufacturing practices); the misbranding provision of § 502 of the Act (drugs are considered misbranded if the product labeling is false or misleading, if the drug is dangerous to health when used as suggested in the labeling, or if the labeling fails to include certain required information); the new drug provision of § 505 of the Act (new drugs must be the subject of approved new drug applications or abbreviated new drug applications before marketing); and the registration and listing provisions of § 510 of the Act (drug establishment must register with FDA, and file a list of all drugs that it makes or processes). *See* Regulation of Positron Emission Tomography Radiopharmaceutical Drug Products; Guidance; Public Workshop, 60 Fed. Reg. 10594, 10595 (1995).

FDA indicated that its 1995 publication was to supersede its prior 1984 publication—which had been directed at all nuclear pharmacies, not just those compounding PET radiopharmaceuticals—entitled "Nuclear Pharmacy Guideline; Criteria for Determining When to Register as a Drug Establishment." The 1984 Guideline had unequivocally stated that nuclear pharmacists who operated an accelerator to produce

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[2] The drug provisions of the Federal Food, Drug, and Cosmetic Act are codified at 21 U.S.C. § 351 *et seq.* (1994).

radioactive drugs to be dispensed under a prescription—which precisely describes the process by which nuclear pharmacies compound PET radiopharmaceuticals—were not required to register under § 510 of the Act. The Guideline also indicated that if a nuclear pharmacist was not required to register, that other of the Act's requirements, including the new drug provision and compliance with current good manufacturing practices, would not apply.

Syncor filed suit in the district court challenging FDA's 1995 publication. Syncor brought three claims, alleging that: (1) FDA lacked jurisdiction over PET drugs under the new drug provision of § 505 of the Act, which requires premarket approval for drugs introduced or delivered for introduction into interstate commerce, because PET drugs do not move in interstate commerce; [3] (2) FDA violated the Tenth Amendment to the United States Constitution by regulating pharma-

[3] Elaborating its statutory argument, Syncor claims that FDA's theory for why it can subject nuclear pharmacies compounding PET radiopharmaceuticals to the new drug provision of § 505 of the Act—that if any ingredient of a compounded pharmaceutical has moved in interstate commerce, the finished compound is itself introduced or delivered for introduction into interstate commerce—renders all compounding activities by pharmacists subject to § 505's requirements. That result, according to Syncor, is also contrary to § 510(g)(1) of the Act, which specifically exempts pharmacies in compliance with "applicable local laws regulating the practice of pharmacy" and "regularly engaged in dispensing prescription drugs, upon prescriptions of [licenced] practitioners," from the registration and drug listing requirements of § 510 and the inspection provisions of § 704(a). *See* 21 U.S.C. § 360(g)(1) (1994). And, although pharmacists are not specifically exempt from other provisions of the Act, FDA has largely pursued a "hands-off" approach towards pharmacists that meet the requirements of the § 510(g)(1) exemption from registration, listing, and inspection. Syncor suggests that if FDA may define "the scope of the regular course of the practice of the profession of pharmacy" so as not to include PET compounding activities, that it may do so for all pharmacists' compounding activities, whether nuclear or not, effectively circumventing the statutory exemption. FDA's not entirely satisfactory response is that it will exercise its broad jurisdiction wisely.

cies in the absence of clear congressional authorization to do so, since pharmacy is an area traditionally reserved for state regulation; and (3) FDA violated the Administrative Procedure Act's requirement that an agency engaged in rulemaking give notice of its proposed rulemaking to the public, 5 U.S.C. § 553(b) (1994), and "give interested persons an opportunity to participate in the rule making through submission of written data, views, or arguments." 5 U.S.C. § 553(c) (1994). The district judge granted summary judgment in FDA's favor on all three claims. We consider the APA claim first since if notice and comment are required we think it prudent to defer deciding the other two issues which presumably would be explored in a future rulemaking.

II.

The APA exempts from notice and comment interpretative rules or general statements of policy. 5 U.S.C. § 553(b)(3)(A) (1994). Before the district court the FDA characterized its 1995 publication as merely "guidance" (a general statement of policy). The district judge disagreed, concluding that it was a rule, but an interpretative one. Here, FDA concedes that the publication is a "rule," and adopts the district court's conclusion. Syncor still contends that the publication is a substantive regulation.

We have long recognized that it is quite difficult to distinguish between substantive and interpretative rules. *See Paralyzed Veterans of Am. v. D.C. Arena L.P.,* 117 F.3d 579, 587 (D.C. Cir. 1997); *American Mining Congress v. Mine Safety & Health Admin.,* 995 F.2d 1106, 1108-09 (D.C. Cir. 1993); *see also American Hosp. Ass'n v. Bowen,* 834 F.2d 1037, 1045 (D.C. Cir. 1987) ("spectrum between a clearly interpretive rule and a clearly substantive one is a hazy continuum"); *General Motors Corp. v. Ruckelshaus,* 742 F.2d 1561, 1565 (D.C. Cir. 1984) (en banc) ("the distinction between legislative and interpretative rules is enshrouded in considerable smog") (citation omitted). Further confusing the matter is the tendency of courts and litigants to lump interpretative rules and policy statements together in contrast to substantive rules, a

tendency to which we have ourselves succumbed on occasion. *See Community Nutrition Inst. v. Young,* 818 F.2d 943, 946 (D.C. Cir. 1987).[4] That causes added confusion because interpretative rules and policy statements are quite different agency instruments. An agency policy statement does not seek to impose or elaborate or interpret a legal norm. It merely represents an agency position with respect to how it will treat—typically enforce—the governing legal norm. By issuing a policy statement, an agency simply lets the public know its current enforcement or adjudicatory approach. The agency retains the discretion and the authority to change its position—even abruptly—in any specific case because a change in its policy does not effect the legal norm. We thus have said that policy statements are binding on neither the public, *see, e.g., Bechtel v. FCC,* 10 F.3d 875, 878 (D.C. Cir. 1993); *Pacific Gas & Elec. Co. v. FPC,* 506 F.2d 33, 38-39 (D.C. Cir. 1974), nor the agency. *See Vietnam Veterans of Am. v. Secretary of the Navy,* 843 F.2d 528, 537-39 (D.C. Cir. 1988). The primary distinction between a substantive rule—really any rule—and a general statement of policy, then, turns on whether an agency intends to bind itself to a particular legal position. *See United States Tel. Ass'n v. FCC,* 28 F.3d 1232, 1234 (D.C. Cir. 1994).

An interpretative rule, on the other hand, typically reflects an agency's construction of a statute that has been entrusted to the agency to administer. The legal norm is one that Congress has devised; the agency does not purport to modify

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[4] The majority in that case stated that it was considering the question of whether an FDA pronouncement setting forth "action levels" informing food producers of the permissible levels of aflatoxins in corn was a legislative rule or "nothing more than nonbinding statements of agency enforcement policy." *Community Nutrition Inst.,* 818 F.2d at 946. But it also noted that FDA did not dispute that its publication was a rule. *Id.* at 945 n.2. And, the third judge, who concurred in part and dissented in part, characterized the question as whether FDA's action levels constituted a legislative or interpretative rule in a later case. *See Alaska v. DOT,* 868 F.2d 441, 445 (D.C. Cir. 1989).

that norm, in other words, to engage in lawmaking. To be sure, since an agency's interpretation of an ambiguous statute is entitled to judicial deference under *Chevron,*[5] it might be thought that the interpretative rule—particularly if it changes a prior statutory interpretation as an agency may do without notice and comment—is, in reality, a change in the legal norm. Still, in such a situation the agency does not claim to be exercising authority to itself make positive law. Instead, it is construing the product of congressional lawmaking "based on specific statutory provisions." *See United Technologies Corp. v. EPA,* 821 F.2d 714, 719 (D.C. Cir. 1987); *see also Connecticut Dep't of Children and Youth Servs. v. HHS,* 9 F.3d 981, 984 (D.C. Cir. 1993) (interpretative rule "purport[s] to define statutory terms"); *National Latino Media Coalition v. FCC,* 816 F.2d 785 (D.C. Cir. 1987). That is why we have said that "[t]he distinction between an interpretative rule and substantive rule ... likely turns on how tightly the agency's interpretation is drawn linguistically from the actual language of the statute." *Paralyzed Veterans,* 117 F.3d at 588.[6]

We should note, in order to be complete (although this variation is not implicated in the case before us), that an interpretative rule can construe an agency's substantive regulation as well as a statute. *See Paralyzed Veterans,* 117 F.3d at 586; *American Mining Congress,* 995 F.2d at 1107-08. In that event, the interpretative rule is, in a sense, even more binding on the agency because its modification, unlike a modification of an interpretative rule construing a statute, will likely require a notice and comment procedure. Otherwise, the agency could evade its notice and comment obli-

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[5] *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.,* 467 U.S. 837 (1984).

[6] "If the statute ... to be interpreted is itself very general, using terms like 'equitable' or 'fair,' and the 'interpretation' really provides all the guidance, then the latter will more likely be a substantive regulation," *Paralyzed Veterans,* 117 F.3d at 588, because then the agency's rule gives content to the legal norm in question.

gation by "modifying" a substantive rule that was promulgated by notice and comment rulemaking. *See Paralyzed Veterans,* 117 F.3d at 586.

A substantive rule has characteristics of both the policy statement and the interpretative rule; it is certainly in part an exercise of policy, and it is a rule. But the crucial distinction between it and the other two techniques is that a substantive rule *modifies* or *adds* to a legal norm based on the agency's *own authority*. That authority flows from a congressional delegation to promulgate substantive rules, to engage in supplementary lawmaking. And, it is because the agency is engaged in lawmaking that the APA requires it to comply with notice and comment.

It is apparent to us, in light of the foregoing discussion, that FDA's 1995 publication is not an interpretative rule. It does not purport to construe any language in a relevant statute or regulation; it does not interpret anything. Instead, FDA's rule uses wording consistent only with the invocation of its general rulemaking authority to extend its regulatory reach. *See American Mining Congress,* 995 F.2d at 1112. The publication is entitled "*Regulation* of Positron Emission Tomography Radiopharmaceutical Drug Products." In the text, FDA explained that "as [PET] technology has advanced, questions have been raised about the most appropriate approach to *regulation* of PET radiopharmaceuticals." And then FDA stated, "[h]aving considered the available information, including that presented to the agency at the hearing and in written materials, FDA has *concluded* that radiopharmaceuticals *should be regulated* under the drug provisions of the Federal Food, Drug, and Cosmetic Act." [7]

FDA made a careful, considered decision not to exercise the full extent of its regulatory authority—whatever that may be—over nuclear pharmacies in 1984. In its "Nuclear Phar-

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[7] FDA did say that "facilities that manufacture PET radiopharmaceuticals are not exempt from registration under § 1A207.10 [21 C.F.R. § 207.10 (1997)] because their activities do not fall within the scope of the regular course of the profession of pharmacy," but it does not claim that this statement made the rule interpretative.

macy Guideline; Criteria for Determining When to Register as a Drug Establishment," it said that "the criteria for registration as a drug establishment for nuclear pharmacies *should* be the same as those for traditional pharmacies" under the pharmacy exemption of § 510(g)(1) of the Act. And, therefore, "in a situation where the nuclear pharmacy is operating within applicable local laws regulating the practice of pharmacy and only prepares and dispenses a radioactive drug upon receipt of a 'valid prescription,' the pharmacy exemption clearly applies." Persons who simply operated an accelerator in the course of compounding radioactive drugs to be dispensed under a prescription specifically were found not to be required to register.

Syncor tells us, and FDA does not dispute, that PET manufacturers today operate within applicable local laws governing pharmacy, and only prepare and dispense PET radiopharmaceuticals under a prescription, as they did in 1984. FDA does claim that PET technology has advanced and that PET has many more applications today than it did in 1984. And, after "[h]aving considered the available information," FDA has concluded, by way of its challenged rule, that PET manufacturers "*should* be regulated." Their activities—which clearly fell within the scope of the regular course of the practice of the profession of pharmacy in 1984—are thought no longer to fall within that scope. This is not a change in interpretation or in enforcement policy, but rather, is fundamentally new regulation. The reasons FDA has advanced for its rule—advancement in PET technology, the expansion of procedures in which PET is used, and the unique nature of PET radiopharmaceuticals—are exactly the sorts of changes in fact and circumstance which notice and comment rulemaking is meant to inform. *Cf. Bechtel v. FCC,* 957 F.2d 873, 881 (D.C. Cir. 1992) (changes in factual and legal circumstances may impose upon an agency the obligation to reconsider settled policy or explain its failure to do so); *American Horse Protection Ass'n v. Lyng,* 812 F.2d 1, 5 (D.C. Cir. 1987) (rulemaking may be required on the basis of a radical change in the factual premises underlying a previous position).

The FDA nevertheless focuses on *American Mining Congress,* in which, recognizing that an agency often has an

option to proceed through *adjudication,* we warned against construing the interpretative rule exception to the APA's notice and comment provisions "so narrowly as to drive agencies into pure [adjudicatory] ad hocery—an ad hocery, moreover, that affords less notice, or less convenient notice, to affected parties." *American Mining Congress,* 995 F.2d at 1112. Accordingly, we identified four factors, any one of which, if present, would identify a supposed interpretative rule as really legislative.[8] The first of those factors, on which FDA concentrates, is whether in the absence of the rule there would not have been "an adequate legislative basis for enforcement action or other agency action to confer benefits or ensure the performance of duties," which is another way of asking whether the disputed rule really adds content to the governing legal norms.

The government contends that the rule in question qualifies as an interpretative rule, under that factor, because in the absence of its issuance the government could have proceeded to enforce regulatory requirements against manufacturers of PET drugs. In the past, pursuant to FDA's 1984 Guideline, those requirements were merely "deferred." The government does not clearly explain what it means by "deferred," but seems to suggest that it exercised enforcement discretion in not asserting regulatory authority over appellants until 1995, and therefore simply is reversing that discretionary

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[8] The four factors are: "(1) whether in the absence of the rule there would not be an adequate legislative basis for enforcement action or other agency action to confer benefits or ensure the performance of duties, (2) whether the agency has published the rule in the Code of Federal Regulations, (3) whether the agency has explicitly invoked its general legislative authority, or (4) whether the rule effectively amends a prior legislative rule." *American Mining Congress,* 995 F.2d at 1112.

Within the three rules at issue in that case, the Mine Safety & Health Administration purported to be interpreting the term "diagnosis" as used in its own substantive regulation that had been adopted by notice and comment rulemaking. We note, however, that one or more of these rules might have been, at least in part, policy statements. *See id.* at 1108.

decision. The obvious difficulty with the government's argument is that it is supportive of a claim that the rule was really a policy statement—a claim which the government abandoned on appeal. As we have said, enforcement discretion is relevant in determining whether an agency intended to bind itself, and therefore, in determining whether a pronouncement is a legislative rule or a general statement of policy, but "tells one little about whether a rule is interpretive." *American Mining Congress,* 995 F.2d at 1111.

In any event, we think the government misreads *American Mining Congress*. We never suggested in that case that a rule that does not purport to interpret *any* language in a statute or regulation could be thought an interpretative rule.[9] We do not have to decide, therefore, whether FDA could have succeeded in an enforcement proceeding against a nuclear pharmacy that was operating pursuant to the 1984 Guideline, under the secure impression that their activities were totally unregulated (although we find it hard to imagine the government facing a hospitable reception in any federal district court). We think it a kindness also to say that we doubt that the government would have done any better in this case to have relied on the policy statement exception on appeal. The 1995 publication is as far removed from the typical policy statement as it is from an interpretative rule; it drew a boundary to the agency's regulatory reach.

Accordingly, we reverse and remand to the district court with instructions to enter summary judgment in Syncor's favor, and to vacate FDA's rule as not in accordance with law. The district court should also dismiss Syncor's substantive claims without prejudice.

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[9] It should also be noted that this is not a situation in which the agency has the option to proceed to adopt its new regulatory extension through internal adjudication; it must seek enforcement in federal district court.