Syllabus

WEINBERGER, SECRETARY OF HEALTH, EDUCATION, AND WELFARE, ET AL. *v.* BENTEX PHARMACEUTICALS, INC., ET AL.

CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FOURTH CIRCUIT

No. 72-555. Argued April 17, 1973—Decided June 18, 1973

Respondent drug marketers filed suit for a declaratory judgment that their drugs containing pentylenetetrazol are generally recognized as safe and effective and thus are not "new drugs" within the meaning of § 201 (p) of the Federal Food, Drug, and Cosmetic Act of 1938, as amended. They also sought exemption under § 107 (c) (4), the grandfather clause, of the 1962 amendments to the Act. The Food and Drug Administration (FDA) Commissioner, based on NAS–NRC panel reports, concluded that there was a lack of substantial evidence that the drugs were effective for their intended uses and gave notice of his intention to initiate proceedings to withdraw approval of the new drug applications (NDA's). In light of FDA's position that withdrawal of approval of an NDA would operate to remove marketing approval for all drugs of similar composition, known as "me-too" drugs, whether or not expressly covered by an effective NDA, the Commissioner invited holders of NDA's for drugs containing pentylenetetrazol "and any interested person who might be adversely affected by their removal from the market" to submit "adequate and well-controlled studies" to establish the effectiveness of the drugs. Only one NDA holder submitted further evidence, which the Commissioner held did not satisfy the statutory standard. He gave notice of intent to issue an order withdrawing approval of the NDA's, and only one NDA holder requested a hearing but filed no supporting data. The Commissioner issued orders withdrawing approval of the NDA's and no appeal was taken. Respondents here all market "me-too" drugs, none of which was expressly covered by an effective NDA. The District Court held that FDA should resolve the "new drug" and "grandfather" issues in an administrative proceeding. The Court of Appeals reversed and remanded with directions to the District Court to determine whether the challenged drugs may lawfully be marketed without approved NDA's, holding that FDA has no juris-

diction, primary or concurrent, to decide what is a "new drug" for which an NDA is required. *Held:* The District Court's referral of the "new drug" and "grandfather" issues to FDA was proper. Pp. 649–654.

(a) While an FDA order denying an NDA and withdrawing one is reviewable by the Court of Appeals under § 505 (h), an order declaring a "new drug" status under § 201 (p) is reviewable under the Administrative Procedure Act by the District Court. Pp. 651–652.

(b) The reach of scientific inquiry under both § 505 (d) and § 201 (p) is the same, *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, *ante*, p. 609, and it is implicit in the regulatory scheme that FDA has jurisdiction to decide with administrative finality, subject to judicial review, the "new drug" status of individual drugs or classes of drugs. Pp. 652–653.

(c) The "new drug" and "grandfather" issues are peculiarly suited to initial determination by FDA with its specialized competence and expertise. Pp. 653–654.

463 F. 2d 363, reversed.

DOUGLAS, J., delivered the opinion of the Court, in which all Members joined, except BRENNAN, J., who took no part in the consideration or decision of the case, and STEWART, J., who took no part in the decision of the case.

Deputy Solicitor General Friedman argued the cause for petitioners. On the briefs were *Solicitor General Griswold, Assistant Attorney General Kauper, Deputy Solicitor General Wallace, Andrew L. Frey, Howard E. Shapiro, George Edelstein,* and *Peter Barton Hutt.*

George F. Townes argued the cause for respondents. With him on the brief were *Sol E. Abrams* and *C. Ben Bowen.**

**Bruce J. Terris, Joseph Onek,* and *Peter H. Schuck* filed a brief for American Public Health Assn. et al. as *amici curiae* urging reversal.

Briefs of *amici curiae* urging affirmance were filed by *Lloyd N. Cutler, Daniel Marcus,* and *William T. Lake* for Pharmaceutical Manufacturers Assn., and by *Thomas D. Finney, Jr., Thomas Richard Spradlin,* and *Daniel F. O'Keefe, Jr.,* for the Proprietary Assn.

MR. JUSTICE DOUGLAS delivered the opinion of the Court.

In this case Bentex and some 20 other firms that market drugs containing pentylenetetrazol filed this suit for a declaratory judgment that their drugs containing pentylenetetrazol are generally recognized as safe and effective, and thus not "new drugs" within the meaning of § 201 (p)(1) of the Federal Food, Drug, and Cosmetic Act of 1938, as amended, 76 Stat. 781, 21 U. S. C. § 321 (p)(1). They also sought exemption from the new effectiveness requirements by reason of § 107 (c)(4) of the 1962 amendments to the Act, known as the "grandfather" clause.

As part of the Food and Drug Administration's (FDA's) Drug Efficacy Study Implementation program, three separate National Academy of Sciences-National Research Council (NAS–NRC) panels reviewed the evidence concerning these drugs, and each concluded that the drug was "ineffective" for the indicated use. The Commissioner concluded there was a lack of substantial evidence that these drugs were effective for their intended uses and gave notice of his intention to initiate proceedings to withdraw approval of the new drug applications (NDA's). FDA had taken the position that withdrawal of approval of an NDA would operate to remove marketing approval for all drugs of similar composition, known as "me-too" drugs, whether or not they were expressly covered by an effective NDA.[1] Accord-

[1] Volume 37 Fed. Reg. 23187, adding § 130.40 to 21 CFR, defines "identical, related, or similar drug" as used in this Act to include "other brands, potencies, dosage forms, salts, and esters of the same drug moiety as well as of any drug moiety related in chemical structure or known pharmacological properties." It also provides all persons with an interest in such drugs an opportunity for hearing on any proposed withdrawal of NDA approval for the basic drug. A district court order directing FDA to apply the NAS–NRC evaluation to all "me-too" drugs is reproduced in 37 Fed. Reg. 26623–26624.

ingly, the notice invited the holders of the NDA's for drugs containing pentylenetetrazol, "and any interested person who might be adversely affected by their removal from the market," to submit "adequate and well-controlled studies" to establish the effectiveness of the drugs. See § 505 (d), 21 U. S. C. § 355 (d). Only one NDA holder submitted further evidence, which the Commissioner held did not satisfy the statutory standard. He thereupon gave notice of intent to issue an order withdrawing approval of the NDA's under § 505 (e), 21 U. S. C. § 355 (e). Again, all those who might be adversely affected by withdrawal of the NDA's were given the opportunity to participate. Only one NDA holder requested a hearing but filed no data to support it. The Commissioner issued orders withdrawing approval of the three NDA's (35 Fed. Reg. 14412); no appeal was taken. This suit in the District Court followed. It appears that all of the parties to this suit market "me-too" drugs, none of which was expressly covered by an effective NDA.

The District Court held that although it could determine whether the drugs were "new" or "grandfathered" drugs, its jurisdiction was concurrent with that of FDA and that FDA should resolve the "new drug" issue in an administrative proceeding. It entered an injunction to preserve the status quo and ruled that if FDA should decline to hold a hearing it would determine the issue. The Court of Appeals reversed and remanded with directions that the District Court determine whether the challenged drugs may lawfully be marketed without approved NDA's. 463 F. 2d 363. It held that FDA has no jurisdiction, either primary or concurrent, to decide in an administrative proceeding what is a "new drug" for which an NDA is required. In its view the 1962 Act established two forums for the regulation of drugs: an administrative one for premarketing clear-

ances for "new drugs" or withdrawal of previously approved NDA's, with the right of appeal; and, second, a judicial one for enforcement of the requirement that "new drugs" be cleared as safe and effective before marketing by providing the Government with judicial remedies of seizure, injunction, and criminal prosecution available solely in the District Court. *Id.*, at 371–372.

We reverse the Court of Appeals.

FDA, as a result of an NAS–NRC study and after due notice, faced up to the problem of proposing withdrawal of drugs found to be lacking in substantial evidence of effectiveness. One method would be to have 1,000 withdrawal hearings—perhaps as many as 3,500, each one lasting probably for weeks. The cost in time and budget would be enormous. Accordingly, FDA issued regulations,[2] already discussed in *Weinberger* v. *Hynson, Westcott & Dunning, Inc., ante,* p. 609, defining the "scientific principles which characterize an adequate and well-controlled clinical investigation,"[3] which elaborates on the statutory "substantial evidence" test. And, as we held in *Hynson,* no basis for a hearing under these regulations would be laid unless a party seeking a hearing proffered at least some evidence of that nature and quality.

By May 1972, 102 final orders effecting withdrawal of approval for 452 NDA's had been issued; and they resulted in the removal from the market of an additional 1,473 "me-too" drugs.[4] FDA was still troubled because under the 1962 Act no census of the marketplace was authorized. That is why Congress enacted the Drug

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[2] 35 Fed. Reg. 3073 and 7250.

[3] See the Appendix in *Hynson, ante,* p. 634.

[4] Hearings on the Present Status of Competition in the Pharmaceutical Industry before the Subcommittee on Monopoly of the Senate Select Committee on Small Business, 92d Cong., 2d Sess., pt. 22, p. 8525.

Listing Act of 1972, 86 Stat. 559, 21 U. S. C. §§ 331 (p), 335 (e), 360 (e), (f), (c), (d) (1970 ed., Supp. II). That Act requires manufacturers to submit to FDA a list of all drugs they market, including data showing their composition, labeling, and advertising.[5] The Senate Report stated: [6]

> "The effective enforcement of the drug provisions of the Act requires the ready availability of a current inventory of all marketed drugs. The Secretary is just completing a thorough review of the effectiveness of drugs marketed pursuant to new drug applications during the period 1938–1962, as required by the Drug Amendments of 1962. Application of the results of this important review to related drugs would be frustrated if a list of all marketed drugs were not easily obtained."

FDA also realized that it is impossible to apply the 1962 amendments to over-the-counter (OTC) drugs on a case-by-case basis. There are between 100,000 and 500,000 of these products, few of which were previously approved by FDA. In May 1972 FDA adopted a procedure for determining whether particular OTC products, not covered by NDA's are safe products, not ineffective, and not misbranded. 37 Fed. Reg. 9464. The procedure involves the establishment of independent expert panels for different categories of OTC drugs (*e. g.*, antacids, laxatives, analgesics) which would review all available data and prepare monographs prescribing drug composition, labeling, and manufacturing controls. OTC's conforming to the monograph will not be considered either misbranded or a "new drug" requiring an NDA. The regulation provides for a hearing before the expert panel, comments and rebuttal comments on the monograph, and

[5] Filings are due in June 1973. 37 Fed. Reg. 26432.

[6] S. Rep. No. 92–924, p. 2.

finally a hearing before the Commissioner and judicial review. *Id.*, at 9475.

This case, like the cross-petition in the *Hynson* case (No. 72–414) raises the question whether FDA has authority to decide in an administrative hearing whether a drug satisfies the new effectiveness requirements of the Act. As noted, the Commissioner ordered that three NDA's for the drugs in question be withdrawn. Review of the order was not sought in the Court of Appeals as provided in § 505 (h), 21 U. S. C. § 355 (h). Rather, the aggrieved manufacturers of "me-too" drugs filed suit in the District Court, with the results we have already detailed. The narrow question is whether the FDA may decide whether a drug is a "new drug" on referral from a district court.

As already noted, an order denying an NDA or withdrawing one is reviewable by the Court of Appeals, § 505 (h); and we see no reason why Congress could not make one method of review the exclusive one. Certainly an order that does not deny or withdraw an NDA is reviewable under the Administrative Procedure Act, if it declares a "new drug" status. See *Hynson*, *supra*, at 627. In bolstering that conclusion we should note in passing that *Abbott Laboratories* v. *Gardner*, 387 U. S. 136, 144, said that the provisions stated in this Act for judicial review do not manifest "a congressional purpose to eliminate judicial review of other kinds of agency action." While § 505 (h) would appear to be the exclusive method of obtaining judicial review of FDA's order withdrawing an NDA covering the instant drugs, the Government apparently did not oppose the District Court's taking jurisdiction, or appeal from its action, and presents no objection to the exercise by the courts of jurisdiction in this case. It does, however, strenuously oppose the conclusions reached by the Court of Appeals.

That court, in holding that FDA has no jurisdiction to determine the "new drug" status of a drug, stated that the question of "new drug" status is never presented when an application of a manufacturer for approval is filed. Parties, of course, cannot confer jurisdiction; only Congress can do so. The line sought to be drawn by the Court of Appeals is FDA action on NDA's pursuant to § 505 (d) and § 505 (e), on the one hand, and the question of "new drug" determination on the other. We can discern no such jurisdictional line under the Act. The FDA, as already stated, may deny an NDA where there is a lack of "substantial evidence" of the drug's effectiveness, based, as we have outlined, on clinical investigation by experts. But the "new drug" definition under § 201 (p) encompasses a drug "not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use." Whether a particular drug is a "new drug," depends in part on the expert knowledge and experience of scientists based on controlled clinical experimentation and backed by substantial support in scientific literature. One function is not peculiar to judicial expertise, the other to administrative expertise. The two types of cases overlap and strongly suggest that Congress desired that the administrative agency make both kinds of determination. Even where no such administrative determination has been made and the issue arises in a district court in enforcement proceedings, it would be commonplace for the court to await an appropriate administrative declaration before it acted. See *Myers* v. *Bethlehem Shipbuilding Corp.*, 303 U. S. 41, 50–51; *FPC* v. *Louisiana Power & Light Co.*, 406 U. S. 621, 647. It may, of course, be true that in some cases general recognition that a drug is efficacious might be made without the kind of scientific support necessary to

obtain approval of an NDA. But, as we indicate in *Hynson, supra,* at 631, the reach of scientific inquiry under both § 505 (d) and § 201 (p) is precisely the same.

We think that it is implicit in the regulatory scheme, not spelled out *in haec verba,* that FDA has jurisdiction to decide with administrative finality, subject to the types of judicial review provided, the "new drug" status of individual drugs or classes of drugs. The deluge of litigation that would follow if "me-too" drugs and OTC drugs had to receive *de novo* hearings in the courts would inure to the interests of manufacturers and merchants in drugs, but not to the interests of the public that Congress was anxious to protect by the 1962 amendments, as well as OTC drugs and drugs covered by the 1972 Act. We are told that FDA is incapable of handling a caseload of more than perhaps 10 or 15 *de novo* judicial proceedings in a year. Clearly, if FDA were required to litigate, on a case-by-case basis, the "new drug" status of each drug now marketed, the regulatory scheme of the Act would be severely undermined, if not totally destroyed. Moreover, a case-by-case approach is inherently unfair because it requires compliance by one manufacturer while his competitors marketing similar drugs remain free to violate the Act. In a case much more clouded with doubts than this one, we held that we would not "in the absence of compelling evidence that such was Congress' intention . . . prohibit administrative action imperative for the achievement of an agency's ultimate purposes." *Permian Basin Area Rate Cases,* 390 U. S. 747, 780. And see *Ricci* v. *Chicago Mercantile Exchange,* 409 U. S. 289, 304–306.

We conclude that the District Court's referral of the "new drug" and the "grandfather" issues to FDA was appropriate, as these are the kinds of issues peculiarly suited to initial determination by the FDA. As the District Court said: "Evaluation of conflicting reports as to

the reputation of drugs among experts in the field is not a matter well left to a court without chemical or medical background." The determination whether a drug is generally recognized as safe and effective within the meaning of § 201 (p)(1) necessarily implicates complex chemical and pharmacological considerations. Threshold questions within the peculiar expertise of an administrative agency are appropriately routed to the agency, while the court stays its hand. As we stated in *Far Eastern Conference* v. *United States*, 342 U. S. 570, 574–575: "[I]n cases raising issues of fact not within the conventional experience of judges or cases requiring the exercise of administrative discretion, agencies created by Congress for regulating the subject matter should not be passed over. This is so even though the facts after they have been appraised by specialized competence serve as a premise for legal consequences to be judicially defined. Uniformity and consistency in the regulation of business entrusted to a particular agency are secured, and the limited functions of review by the judiciary are more rationally exercised, by preliminary resort for ascertaining and interpreting the circumstances underlying legal issues to agencies that are better equipped than courts by specialization, by insight gained through experience, and by more flexible procedure." And see *Port of Boston Marine Terminal Assn.* v. *Rederiaktiebolaget Transatlantic*, 400 U. S. 62, 68; *Ricci* v. *Chicago Mercantile Exchange*, *supra*, at 304–306.

Reversed.

MR. JUSTICE BRENNAN took no part in the consideration or decision of this case. MR. JUSTICE STEWART took no part in the decision of this case.