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Legislative Notes: The FDA's Over-the Counter Drug Review: Expeditious Enforcement by Rulemaking

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On May 11, 1972, the Commissioner of the Food and Drug Administration (FDA) issued a final order establishing procedures for review of all over-the-counter (OTC) drugs. The OTC drug review attempts to evaluate the safety, effectiveness and labeling of OTC drugs pursuant to the 1938 Federal Food, Drug and Cosmetic Act and the 1962 amendments to that act. It is an awesome undertaking. The FDA estimates that between 100,000 and 500,000 OTC drugs are currently on the market, the great majority of which have not undergone any premarket review by the FDA.

The OTC drug review represents a significant departure from traditional drug regulation in two respects. First, the review involves monographs—regulations for broad categories of OTC drugs—rather than case-by-case adjudication for individual drugs. Second, the FDA is relying heavily on non-FDA scientific experts to evaluate the drugs included in the review, rather than depending primarily on its own staff.

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2. The amended Act does not distinguish between prescription and OTC drugs. It does, however, define the conditions under which a drug can be marketed, 21 U.S.C. § 355(d) (1970); for example, whether it can be marketed OTC or only by prescription. In addition, it provides that a drug is misbranded when dispensed without a prescription if it is habit-forming, if it is toxic or otherwise potentially harmful, if its method of use is unsafe without supervision by a licensed practitioner, or if the approved NDA limits its dispensation to prescription sales. 21 U.S.C. § 353(b)(1) (1970). All other drugs are OTC drugs by implication and long-established understanding. Food Drug Cos. L. Rep. (CCH) ¶ 72,010.
This article attempts to show that the OTC drug review has distinct advantages over traditional drug regulation. Part I outlines briefly the traditional case-by-case approach to drug licensing and describes FDA enforcement efforts prior to the OTC drug review. Part II sets forth the new rulemaking approach and considers the use of advisory panels. Part III examines several procedural questions associated with the review and concludes that the use of monographs as regulatory standards will afford the FDA an expeditious enforcement mechanism by resolving complex scientific issues at the administrative rather than the judicial level. Judicial review should be available, however, to ensure the reasonableness of the monographs, especially where a final monograph does not incorporate panel recommendations.

I. NDA Approach

The 1938 Food, Drug and Cosmetic Act, as amended, requires that the FDA create an administrative review mechanism to ensure the safety and efficacy of any "new drug" before marketing. The 1938 Act defined a "new drug" as a drug which was "not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe." The 1962 amendments expanded the definition to encompass drugs not generally recognized as safe and effective (GRAS&E). Manufacturers of "new drugs" are required to submit new drug applications (NDAs) to the FDA prior to marketing. An application must contain a list of ingredients, samples of the drug, an example of the labeling, studies showing the drug to be safe and effective, and a descrip-

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9 Food, Drug and Cosmetic Act of 1938, § 505(a); 21 U.S.C. § 355(b) (1970). The need for premarket review was demonstrated by the deaths of 107 people from a sulfa preparation in which diethylene, a chemical related to antifreeze, was used as a solvent. The only tests conducted by the company were for appearance, flavor and fragrance. H. Teff & C. Munro, Thalidomide: The Legal Aftermath 108 (1976). The then existing Food and Drug Act of 1906, §§ 1, 2, 34 Stat. 768 (1906), was exclusively a policing statute prohibiting the sale of adulterated or misbranded food or drugs. The FDA instituted seizure actions after it learned of the deaths, but seizure was legally possible only because the drug was labeled an "elixir," which erroneously implied it contained alcohol. See M. Mintz, By Prescription Only 48-49 (1967).


11 21 U.S.C. § 321(p)(1) (1970), as amended by § 102(a)(1), 76 Stat. 780 (1962). The Thalidomide tragedy in Europe precipitated a general Congressional awareness that the 1938 Act might no longer be adequate. Thalidomide was absent from United States markets because of the stubbornness of a single FDA member rather than the provisions of the 1938 Act. See H. Teff & C. Munro, supra note 9, at 120-21. The amendments were primarily aimed at the testing of new drugs. See Mintz, supra note 9, Ch. 12.

12 21 U.S.C. § 355(b) (1970). Since general recognition is the crucial focus of inquiry, it is often not clear whether a drug is a "new drug." One relevant consideration is the marketing history of the drug. Section 201(p)(2) of the 1938 Act, 21 U.S.C. § 321(p)(2) (1970), specifically treats any drug as a "new drug" unless it has been marketed for a material length of time. One advantage of the OTC drug review is that a manufacturer will know whether a particular drug falls within the "new drug" definition, thus requiring an approved NDA before marketing. See notes 24-26 and accompanying text infra.
A "new drug" may not be marketed until the NDA is approved by the FDA. The vast majority are marketed on the assumption that they are GRAS&E, which puts the burden on the FDA to initiate regulatory action. More importantly, both the 1938 Act and the 1962 amendments contained grandfather clauses exempting most OTC drugs which had not gone through the NDA process from the statutory definition of a "new drug." Thus, a review of all OTC drugs was not possible under the premarket review mechanism provided by the amended 1938 Act.

The 1962 amendments required the FDA to evaluate all NDAs effective prior to 1962 to ascertain the effectiveness of the drugs covered by those applications, and to withdraw approval if "substantial evidence" of a drug's efficacy was lacking. To speed implementation of the 1962 amendments, the FDA was required to establish a process for reviewing NDAs submitted for drugs used prior to 1962. The process was a laborious one for both the FDA and the pharmaceutical manufacturers. Approximately 100 NDAs were being submitted to the FDA annually in 1974. By 1963, the typical NDA had grown in length from six to approximately 1,000 pages, and required nineteen to twenty-six months for processing. By 1969, each submitted NDA contained about thirty volumes constituting a stack ten to twelve feet high with some NDAs containing up to four hundred volumes of data.

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An anomaly exists between the grandfather clause of the 1962 amendments exempting certain drugs having no NDA from the definition of a "new drug" and § 107(c)(3)(B), which provides drugs with NDAs a two year exemption from the efficacy requirements. There is no perceptible reason for this difference.
amendments, the FDA contracted in 1966 with the National Academy of Sciences-National Research Council (NAS-NRC) to review the pre-1962 NDAs. A large number of drugs were found deficient, and after a review of the NAS-NRC findings submitted in 1969, the FDA implemented the results through its Drug Efficacy Study Implementation program. Only 25 percent of the OTC drugs evaluated by the NAS-NRC study were found to be "effective," and accordingly, the FDA decided to review all OTC drugs.

II. OTC Drug Review

A. Rulemaking Approach

The FDA adopted a rulemaking approach to circumvent the deficiencies of the NDA process. Monographs covering various therapeutic categories of OTC drugs establish "the conditions under which a category of OTC drugs is generally recognized as safe and effective and not misbranded." Drugs conforming to an applicable monograph are not "new drugs" and need not go through the NDA process. Drugs not within the

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20 MASHAW & MERRILL, supra note 14, at 470. Each NDA was evaluated separately on a continuum as follows: (1) effective; (2) probably effective; (3) possibly effective; (4) effective, but . . . better or safer drugs are available; (5) ineffective as a fixed combination; (6) ineffective. The evaluation of an NDA was typically a one-page summary giving the conclusion of the panel and perhaps a list of published articles used as references. The study was characterized as "cryptic and conclusory without any statement of supporting facts." U.S.V. Pharmaceutical Corp. v. Secretary of HEW, 466 F.2d 455, 461 (D.C. Cir. 1975).


As already noted, the 1962 amendments require the FDA to prohibit the marketing of any "new drugs" whose efficacy has not been demonstrated by "substantial evidence." 21 U.S.C. §§ 355(d) (disapproval of a submitted NDA) and 355(e) (withdrawal of an outstanding NDA). However, the FDA is required to give the manufacturer notice and opportunity for hearing before disapproval or withdrawal of the NDA. Id. In order to expedite the withdrawal of drugs found not to be effective in the NAS-NRC study, the FDA promulgated regulations elaborating the types of "substantial evidence," as defined in the Act, necessary to show drug efficacy. The regulations impose strict conditions on the conduct of clinical studies. If the manufacturer cannot or does not submit adequate and well-controlled studies after receiving notice from the FDA, the NDA is disapproved or withdrawn without an opportunity for hearing. This summary judgment procedure was upheld in Weinberger v. Hynson, Westcott & Dunning, Inc., 412 U.S. 609 (1973).

22 37 Fed. Reg. 85 (1972). The 25 percent figure may be somewhat misleading because the panel members in the Drug Efficacy Study used a very exacting substantial evidence requirement for an "effective" ranking, which led to liberal use of the "probably effective" and "possibly effective" ratings. J. MASHAW & R. MERRILL, supra note 14, at 471.


25 A manufacturer is provided with a safe harbor from regulatory enforcement if it complies with the terms of the monograph. One issue is whether the manufacturer will be allowed to prove that the drug is GRAS&E and not misbranded under the statute if it does not conform to the monograph. See notes 95-120 and accompanying text infra.
parameters of an applicable monograph are subject to regulatory action by the FDA unless already covered by an approved NDA.\textsuperscript{26}

The misbranding\textsuperscript{27} requirement is intended to circumvent the grandfather clauses exempting most OTC drugs from the "new drug" definition.\textsuperscript{28} A drug whose label contains false representations is misbranded.\textsuperscript{29} The final monograph specifies the labeling that must appear on drugs in that therapeutic category. If its labeling is changed to avoid liability for misbranding, the drug loses its grandfather clause protection and falls within the definition of a "new drug."\textsuperscript{30} Thus, the FDA has been able to use the threat of misbranding sanctions to regulate the effectiveness of grandfathered drugs through the OTC drug review.\textsuperscript{31}

To implement the new program the FDA formed scientific advisory panels composed of eminent non-FDA medical experts to study OTC

\textsuperscript{26} C.F.R. § 330.10(b)(1977). The OTC drug review does not supplant the NDA process entirely, but rather provides an alternative procedure to follow. An expedited or abbreviated version of an NDA can be utilized by making use of the final monograph. See 21 C.F.R. § 330.11 (1977). Abbreviated NDAs were originally used to implement the results of the Drug Efficacy Study. See notes 18-22 and accompanying text supra. Drugs found "effective" by an NAS-NRC panel could be marketed. The abbreviated procedure was intended to eliminate the need for redundant studies. McEniry, Drug Monographs, 29 FOOD DRUG COSM. L.J. 166 (1974).

\textsuperscript{27} The Act provides that a drug shall be deemed misbranded if its labeling is in any way false or misleading, if its labeling bears inadequate directions for use, or if it is dangerous to health when used with the dosage, frequency, or duration prescribed, recommended, or suggested in the labeling. 21 U.S.C. § 352(a), (f), (j) (1970). The FDA's misbranding authority is a carryover of its power under the 1906 Act, see note 9 supra, and is in addition to its licensing power for "new drugs." Misbranding is a prohibited act, 21 U.S.C. § 331(b) (1970), and involves the same sanctions as marketing a "new drug" without an NDA. See note 14 supra.

\textsuperscript{28} See note 17 supra.

\textsuperscript{29} See note 27 supra.

\textsuperscript{30} See note 17 supra.

\textsuperscript{31} The Supreme Court in Weinberger v. Bentex Pharmaceuticals, Inc., 412 U.S. 645 (1973), recognized the primary jurisdiction of the FDA over all issues pertaining to "new drugs" rather than limiting the FDA to its express statutory jurisdiction, §§ 505(d) (disapproval of a submitted NDA) and 505(e) (withdrawal of an outstanding NDA). 412 U.S. at 652. The primary jurisdiction doctrine involves situations where both a court and an administrative agency have concurrent original jurisdiction, yet it is presumed that the agency is a better forum for reaching an initial decision. "The principal criterion in deciding whether the doctrine is applicable usually is not legislative intent but is judicial appraisal of need or lack of need for resort to administrative judgment." DAVIS, ADMINISTRATIVE LAW TEXT § 19.06 (3d ed. 1972). The specialized expertise of an agency and the desirability for uniformity are the usual justifications for according an agency primary jurisdiction. The claim of the FDA's specialized expertise is buttressed when it relies on the expert advisory panels.

While the Supreme Court has recognized the FDA's primary jurisdiction over the "new drug" issue, it is unclear whether the FDA has primary jurisdiction to determine misbranding of drugs. Misbranding has traditionally been resolved by the courts in individual enforcement proceedings. MASHAW & MERRILL, supra note 14, at 541. 21 U.S.C. § 334(a) (1970) states that a misbranded drug "shall be liable to be proceeded against . . . in any district court . . ." and does not mention administrative enforcement. See generally Ames & McCracken, supra note 21, at 55-72, supporting primary jurisdiction over misbranding as it pertains to the OTC drug review.
drugs.\textsuperscript{32} Twenty-six therapeutic drug categories were established,\textsuperscript{33} and seventeen panels were created to review these categories.\textsuperscript{34} Each panel was responsible for certain therapeutic categories.\textsuperscript{35}

The panels are expected to lay the groundwork for the monographs that will govern the therapeutic drug categories. They are "to evaluate the safety and effectiveness of OTC drugs, to review OTC drug labeling, and to advise[the Commissioner] on the promulgation of monographs."\textsuperscript{36} The panels may solicit opinions and information from any individual or group,\textsuperscript{37} and interested parties may submit data and opinions to the panels for consideration.\textsuperscript{38} After evaluation of the data, each panel submits a report to the Commissioner containing its conclusions and recommendations, including a recommended monograph or monographs.\textsuperscript{39}

After receiving an advisory panel report, the Commissioner is to publish a proposed monograph, allowing ninety days for written comments and an additional thirty days for reply comments.\textsuperscript{40} After reviewing all

\begin{itemize}
\item 21 C.F.R. § 330.10(a)(1) (1977). The FDA has made extensive use of advisory panels since the inception of the OTC drug review, 21 C.F.R. § 14.100 (1977); see generally Schmidt, Communication as the Basis of Regulation, 29 FOOD DRUG COSM. L.J. 9 (1974).
\item 21 C.F.R. § 330.5 (1977). A catch-all category for miscellaneous products was divided into the categories of internal and external products. Saccharin was initially included for review in the Miscellaneous Internal Products Panel. 42 Fed. Reg. 19,996, 20,004 (1977).
\item The regulations provide that "a single advisory review panel shall be established for each designated category of OTC drugs and every OTC drug category will be considered by a panel." 21 C.F.R. § 330.10(a)(1). Overlap between several categories led to their consolidation for consideration by only one panel, however. Yingling, The Over-The-Counter-Drug-Review, 28 FOOD DRUG COSM. L.J. 273 (1973). More comprehensive consideration of combination drugs was given as a justification for the consolidation. Id. A combination drug is one that contains two or more active ingredients to treat multiple symptoms. See 21 C.F.R. § 330.10(a)(4)(iv) (1977) for the FDA's policy concerning combination OTC drugs.
\item Id.
\item Id. § 330.10(a)(2) (1977).
\item Id. § 330.10(a)(3).
\item Id. § 330.10(a)(5)(i). The report is a review of product ingredients and dosages, not a review of individual brand-name products. The panels are asked to place ingredients in one of three categories: Category I (GRAS&E); Category II (not GRAS&E); or Category III (more studies necessary). 21 C.F.R. § 330.10 (1977). Category III drugs can be marketed pending completion of the necessary studies under conditions prescribed by the FDA. 42 Fed. Reg. 19,137 (1977). There is no provision in the law for a Category III listing, and such status may be incompatible with continued lawful marketing absent an approved NDA. The issue is being litigated in Health Research Group v. Kennedy, Civ. No. 77-0734 (D.D.C.).
\item With submission of the final report, the FDA terminates the panel pursuant to 21 C.F.R. § 14.55 (1977), and deletes it from the list of standing advisory panels in § 14.100. For example, the Laxative, Antidiarrheal, Emetic and Antiemetic Drug Panel was terminated on July 17, 1977. 42 Fed. Reg. 41,851 (1977). Interestingly, its conclusions were published more than two years earlier. 40 Fed. Reg. 12,902 (1975). This panel was one of those recommended for elimination in President Carter's reorganization plan. See The President's Advisory Committee Reduction Program, Prepared by the Subcommittee on Reports, Accounting and Management of the Senate Committee on Governmental Affairs, 95th Cong., 1st Sess., 78 (1977).
\item 21 C.F.R. § 330.10(a)(6). The reply comments are to respond to initial comments rather than to reiterate previously indicated positions. Id. Originally, sixty days were allowed for written comments but this period was extended to ninety days. 42 Fed. Reg. 54,800 (1977). 21 C.F.R. §330.10(a)(6) (1977) has not yet been revised to reflect this change.
comments, a tentative final monograph is to be published, allowing thirty
days for specific written objections and requests for an oral hearing. After reviewing written objections and considering arguments made at
any hearing, the Commissioner publishes the final monograph.

There are several advantages to the FDA's rulemaking approach. First, given the large number of OTC drugs on the market, case-by-case review would put a tremendous burden on the limited resources of the FDA as well as on the courts, the pharmaceutical industry, and the scientific community. Moreover, the FDA, in its own estimation, has been quite unsuccessful in proceeding on a case-by-case basis. Second, the length of time required for case-by-case review leads to inequitable results; some products remain on the market indefinitely while similar drugs are subject to legal action. Third, rulemaking for specific OTC drug categories is practical and more efficient because OTC drugs are composed of relatively few active ingredients.


Although formal rulemaking appears unnecessary, the informal "notice and comment" procedures provided by the APA may be deficient under the due process clause of the fifth amendment because of the importance of the monographs. The District of Columbia Court of Appeals has expressed approval of "notice and comment-plus" procedure. Mobil Oil Corp. v. FPC, 483 F.2d 1238 (D.C. Cir. 1973); International Harvester Corp. v. Ruckelhaus, 478 F.2d 615 (D.C. Cir. 1973) (providing a limited right of cross-examination); Walter Holm & Co. v. Hardin, 449 F.2d 1009 (D.C. Cir. 1971). See generally Williams, Hybrid Rulemaking Under the Administrative Procedure Act: A Legal and Empirical Analysis, 42 U. CHI. L. REV. 401 (1975). The FDA has not provided the opportunity for cross-examination at any stage during the OTC drug review, but it is evidently hoped that the inclusion of reply comments and tentative final monographs will comport with expanded notions of due process in supplementing the APA's "notice and comment" procedures. Cross-examination is not a requisite element whenever "notice and comment-plus" rulemaking is necessary; courts have been more concerned with ensuring a thorough ventilation of the issues rather than the means used by the agency to discuss these issues. National Research Defense Council v. U.S. Nuclear Regulatory Commission, 547 F.2d 633, 644 (D.C. Cir. 1976). Cross-examination would permit more meaningful court review, but the potential for delay makes it an unattractive alternative for the FDA. The classic paradigm of delay associated with cross-examination is the ten year proceeding conducted under the formal rulemaking procedures of 21 U.S.C. § 701(e) (1970), concerning the quantity of peanuts in a product required before the product could be labeled "peanut butter." Hamilton, Rulemaking on a Record by the Food and Drug Administration, 50 TEX. L. REV. 1132, 1142-45 (1972).


44 See generally Use of Advisory Committees by the Food and Drug Administration Part II: Hearings before the Subcommittee on Intergovernmental Relations and Human Resources of the House Committee on Government Operations, 94th Cong., 1st Sess. 65-72 (1975) (testimony of Peter Baron Hutt, former FDA Chief Counsel) [hereinafter cited as Advisory Committee Hearings].

45 This inequity was recognized in Weinberger v. Bentex Pharmaceuticals, Inc., 412 U.S. 645, 653 (1973), which upheld the FDA's primary jurisdiction over the "new drug" issue.

Except for cases of patent fraud or serious health hazard, a moratorium on drug enforcement is in effect until publication of a final monograph for a particular therapeutic category.\(^{47}\) The moratorium has been defended on the grounds that the long term benefits outweigh the short term dislocations.\(^{48}\) It has created several problems, however. First, enforcement is delayed during the lengthy time period between panel recommendations and the promulgation of the final monograph.\(^{49}\) The delays have been criticized by members of the House Committee on Governmental Operations as being detrimental to the public by permitting the continued marketing of ineffective drugs.\(^{50}\) On balance, however, it would appear appropriate to stay enforcement unless continued marketing poses a health threat.\(^{51}\)

Second, the moratorium has encouraged some manufacturers to convert their prescription drugs to OTC status. A manufacturer may decide on its own to market a drug OTC,\(^{52}\) gambling that it is GRAS&E as an OTC drug and thus not subject to regulatory action for not having an approved NDA.\(^{53}\) The FDA has expressly approved use of the OTC drug review as a means for converting from prescription to OTC status.\(^{54}\) The OTC drug panels may review any prescription drugs which they believe can be safely and effectively used as OTC drugs,\(^{55}\) and a drug manufacturer may specifically request an advisory panel to review a particular prescription drug.\(^{56}\)

As a result of the drug moratorium, a few manufacturers marketed drugs OTC on the basis of preliminary panel findings instead of waiting


A number of exceptions to the moratorium have been established. Perhaps the most prominent example is the FDA’s 1972 restrictions on the use of hexachlorophene, an antibacterial agent, because of the health threat it posed to infants. 37 Fed. Reg. 20,160 (1972). The FDA’s position is now contained at 21 C.F.R. § 250.250 (1977).

\(^{48}\) Advisory Committee Hearings, supra note 44 at 70 (testimony of Peter Baron Hutt, former FDA Chief Counsel). The primary benefit of the OTC drug review will be the expeditious enforcement mechanism available to the FDA. The short term detriment is the suspension, as a practical matter, of drug enforcement against OTC drugs.

\(^{49}\) For example, on September 13, 1974, the Commissioner issued a proposal to establish a monograph for OTC topical antimicrobial products for daily human use along with the report of the OTC Antimicrobial I Panel which was responsible for that category. 39 Fed. Reg. 33,103 (1974). Publication of the tentative final monograph did not occur until January 6, 1978. 43 Fed. Reg. 1,210 (1978).

\(^{50}\) HOUSE COMM. ON GOVT. OPERATIONS, USE OF ADVISORY COMMITTEES BY THE FOOD AND DRUG ADMINISTRATION, H.R. REP. No. 94-787, 94th Cong., 2d Sess. 64 (1976) (hereinafter cited as ADVISORY COMMITTEE REPORT).

\(^{51}\) Advisory Committee Hearings, supra note 44 at 75.

\(^{52}\) A drug manufacturer may also petition the FDA for approval of supplemental NDAs permitting OTC sale under the FDA switch regulations. 21 C.F.R. § 310.200 (1977).

\(^{53}\) The drug will have an NDA for prescription but not OTC distribution. The marketing history of the prescription drug may indicate to the manufacturer that OTC status may be legitimately claimed.


\(^{56}\) Id. § 310.10(a)(3).
for publication of the final monograph.\footnote{Pinco, supra note 47, at 144.} In response, the FDA published so-called "anti jump-the-gun" regulations which limit the permissible circumstances for conversions under the OTC drug review.\footnote{41 Fed. Reg. 32,580 (1976).} Basically, any prescription drug marketed OTC prior to the publication of the proposed monograph will be subject to regulatory action.\footnote{21 C.F.R. § 330.13(a) (1977).} After publication of the proposed monograph and before the effective date of the final monograph, a prescription drug found by the panel to be GRAS&E and not misbranded can be marketed but is subject to the risk that the Commissioner will not accept the panel findings and will take regulatory action.\footnote{Id. § 330.13(b)(2). The drug must also be marketed in compliance with the terms of a proposed or tentative final monograph to avoid regulatory action. Id. § 330.13(b)(2). A drug found by the panel to be Category II (not GRAS&E or misbranded) requires an approved NDA before being marketed as an OTC drug. Id. § 330.13(c)(2). A drug found by the panel to be Category III (more studies necessary) requires either a determination by the Commissioner that the drug is GRAS&E or an approved NDA before marketing is permitted. Id. § 330.13(d)(2).} 

B. OTC Advisory Panels

The regulations establishing the OTC drug review provide that panel members shall be qualified experts appointed by the Commissioner and "may include persons from lists submitted by organizations representing professional, consumer, and industry interests."\footnote{Id. § 330.10(a)(1). Allowing the regulated industry a voice in the selection of panelists may raise the spectre of "cronyism" between the FDA and the industry. However, a former FDA chief counsel has said that "in the OTC Drug Review we have, if anything, gone overboard in making certain that everybody has an opportunity to participate." Hutt, \textit{Views on Supreme Court/FDA Decisions}, 28 \textit{FOOD DRUG CosM. L.J.} 662, 666 (1973). The Commissioner is not required to include panelists from the submitted lists, but the opportunity to submit names is another facet of the FDA's desire to go beyond mere "notice and comment" rulemaking. See note \textit{41 supra}.} The actual selection of panel members has shown a heavy dependence upon the academic community.\footnote{By way of illustration, the voting members of the Internal Analgesic and Antirheumatic Review Panel, which submitted its final report April 5, 1977, are as follows: Weldon Bellville, M.D., Chairman from August 1976, University of California, school of medicine, replacing Henry W. Elliott, M.D., Ph.D., who died in August 1976; William Barr, Ph.D., Virginia Medical College, pharmacy dept.; Ninfa Redmond, Ph.D., Concordia University, Montreal, Quebec, Canada; Naomi Rothfield, M.D., University of Connecticut, school of medicine; George Sharpe, M.D., National Bureau of Standards, health unit. 42 Fed. Reg. 35,347 (1977).} Pharmaceutical manufacturers have criticized this practice on the theory that academics may be biased against OTC drugs.\footnote{O'Keefe, \textit{The Over-the-Counter Drug Review—Helping the Client Make Decisions}, 29 \textit{FOOD DRUG CosM. L.J.} 262, 271 (1974); DiPrima, \textit{The OTC Review - Viewpoint of the Industry House Counsel}, 27 \textit{FOOD DRUG CosM. L.J.} 532, 540 (1972).} The industry argues that they are exposed to patients whose attempts at self-medication have failed rather than to the majority of cases where OTC drugs have given relief.\footnote{O'Keefe, supra note 63 at 271. As a factual matter, however, many conditions are self-alleviating.} However, caution in reviewing the drugs is
desirable, and the selection of qualified experts not associated with the academic community should not be *sine qua non* of an effective advisory panel. The relevant pool of expertise outside academia is limited to physicians and pharmacists in private practice or associated with the pharmaceutical industry. Private practitioners are subject to the same concerns about bias as members of the academic community, and choosing panel members associated with the pharmaceutical industry poses obvious conflict of interest problems. In any event, the preeminent concern should be obtaining a diversity of qualified expertise capable of evaluating drugs in the given therapeutic category.

In addition to voting panel members, two liaison members are included on each panel, one representing industry interests and the other representing consumer interests. The primary purpose of the liaison members is to instill confidence in the OTC drug review by keeping the lines of communication open; they are to act as conduits between the panel and the interests they represent.

Special problems arise because of the representative status of the liaison members. Although the industry liaison is to represent the industry as a whole, it is possible that a member will act in the interests of a particular manufacturer rather than another manufacturer or the rest of the industry. For example, studies submitted for panel consideration containing trade secrets could be conveyed to the manufacturer’s competitor. To minimize this danger, certain safeguards have been developed to prevent the industry liaison from being exposed to confidential material.

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65 An individual is likely to first resort to self-medication, contacting a physician only if the symptoms persist. Note that many medical professors also maintain private practices.

66 Voting members must be cleared as special government employees who have no personal financial stake in the outcome and no significant ties to pharmaceutical manufacturers or sellers. 21 C.F.R. § 14.80(a)(2) (1977).

67 *Id.* § 14.80(b)(1)(i). Panels are to consist of individuals with expertise in the particular subject matter under consideration. The members are also to “have diverse professional education, training, and experience so that the committee will reflect a balanced composition of sufficient scientific expertise to handle the problems that come before it.” *Id.*

A scientific challenge to panel expertise might arise with the miscellaneous panels. Relatively unrelated categories are combined in the miscellaneous grouping, and it has been charged that the miscellaneous panels have evaluated drugs more properly within the expertise of specialized panels. DiPrima, *supra* note 7, at 408.

68 21 C.F.R § 14.84(a) (1977). The FDA was cognizant of criticism leveled at the NAS-NRC panels, see text accompanying notes 20-22 *supra*, due to the closed nature of the deliberations and the preponderance of panelists from academia. *Advisory Committee Hearings, supra* note 44, at 339 (testimony of Peter Baron Hutt, former FDA Chief Counsel).

69 The liaison members function in much the same manner, including the approval of panel minutes and planning future meetings, but they do not have the right to vote on substantive matters such as establishing the recommended monographs. 21 C.F.R. § 14.86(a)(1) (1977). Additionally, their advocacy is limited in that they are not to exercise undue influence over other members of the advisory panel. *Id.* § 14.86(c)(6). Although the regulations do not clearly delineate when a liaison member abuses his or her position, the Commissioner has the power to remove any member who exceeds permissible bounds. *Id.* § 14.86(d).

70 *Id.* § 14.86(c)(4).

71 First, the industry liaison is not allowed to attend meetings whenever the topic covers
The major problem with the consumer liaison member involves the initial selection process. The FDA initially turned to an ad hoc consortium of consumer organizations and asked them to choose a representative, not questioning their selection. However, to formalize the selection of consumer liaison members and to make the selection more democratic, the FDA made several changes in procedure. Generally, nominations are received by the FDA, and consumer groups registered with the FDA vote for one of the nominees. These changes will be of limited use in the OTC drug review because it is nearing completion, but the future selection of liaison members in other programs will be benefited by the procedures developed.

The FDA has also promulgated regulations concerning the right of the public to attend panel meetings, as well as the corollary right of access to panel meeting records. The regulations generally provide that the meetings will be open unless trade secrets or information that invades an individual's privacy will be discussed.

"trade secrets or confidential commercial or financial information." Id. § 14.27(c)(1). Second, the industry liaison is barred access to such information even after it has been discussed by other members in a closed meeting. Id. § 14.86(a)(2).

The FDA leaves the ultimate selection of liaison members to the respective groups. However, unlike the drug industry with its well-established trade associations, consumers are not uniformly represented. The Proprietary Association represents the OTC drug industry while the Pharmaceutical Manufacturers Association represents 90 percent of the manufacturers of prescription drugs and those OTC drugs used in health professions. Abbott Laboratories v. Gardner, 387 U.S. 136, 138 (1967). On the other hand, consumers are an amorphous category without substantial internal cohesiveness, and consumer groups are often self-appointed representatives representing different segments of the consuming public. Nonetheless, the consumer liaison member will help allay suspicion of "cronyism" between the FDA and the regulated industry by serving as a counter-weight to the industry liaison.

The organizations included the Consumer Federation of America, the Consumers Union, and the Federation of Homemakers of America. See generally Advisory Committee Hearings, supra note 44, at 136.

Notice will now be published in the Federal Register requesting nominations for the particular advisory panel. 21 C.F.R. § 14.84(c) (1977). Although nominations can come from any interested person, individuals are encouraged to submit the nominations through FDA recognized groups. Id. § 14.84(c)(1). Although these groups are entitled to vote on the nominees, id. § 14.84(c)(3), the FDA limits the number of nominees, id. § 14.84(c)(4). The ballots and the curriculum vitae of the eligible nominees are sent to recognized organizations on file with the FDA, and the individual receiving the plurality of votes will be the consumer liaison member. Id. § 14.84(c)(4).

The determination to close a meeting must now be made in accordance with 5 U.S.C. § 552(b)(3) (1976) (also a part of the Sunshine Act). The applicable agency has to properly determine the disclosure of information would fall into certain enumerated categories. The FDA regulations concerning advisory panels
The minutes of panel meetings are also available for public inspection. While minutes should not disclose confidential information, it is important to ensure that they contain enough specificity so that the public right of access is not eviscerated. The Federal Advisory Committee Act requires that "detailed minutes of each meeting of each advisory committee shall be kept and shall contain a record of the persons present, a complete and accurate description of matters discussed and conclusions reached." Detailed minutes not only protect the public right of access to information, but also check against undue pressure by FDA personnel over panel members.

III. SELECTED PROCEDURAL ISSUES IN THE OTC DRUG REVIEW

A. Panel Recommendations and "New Drug" Status

Panel members are eminent experts in their fields, and the statute closely conform to the Sunshine Act by permitting only those closings allowable under 5 U.S.C. § 552(b)(3). 21 C.F.R. § 14.27(b)(2) (1977). Generally, a meeting now may be closed only upon the Commissioner's determination and justification in the Federal Register. 21 C.F.R. § 14.27(b) (1977).

The regulations also require every panel meeting to have an open hearing component in which an interested party may participate through written and oral presentations. Id. § 14.27(a). It is now possible that a meeting can have four separate segments: an open public hearing, open panel deliberations where the public can only observe, closed presentation of exempted data, and closed committee deliberations subject to the written authorization of the Commissioner. Id. § 14.25.

78 The transcripts and minutes of the open portions of the meetings are publicly available, 21 C.F.R. § 14.74(a)(2), (3) (1977), as are the written data submitted for the panel's consideration during an open meeting. Id. § 14.75(a)(1), (5). A brief summary of a closed portion is available upon demand. Id. § 14.75(a)(4). Even if material is found confidential, the minutes of the executive portion of the meeting can be released if the panel report or advice has received action, or the Commissioner determines that the minutes or portions thereof can be open to public disclosure without undue interference to panel or agency operations. Id. § 14.75(a)(6).

79 Section 10(c), 86 Stat. 770.

80 An example is the OTC Antacid Panel deliberations regarding the proposed removal of Alka-Seltzer from the market. Some panel members almost resigned because of "what they regarded as 'insuperable' restrictions placed upon their independent consideration of scientific evidence." ADVISORY COMMITTEE REPORT, supra note 50, at 61-62. Detailed records would have allowed an independent determination as to whether the FDA did exert undue pressure upon panel members. In this instance, the independent determination would have been made by the Congressional Subcommittee studying FDA use of advisory committees. Id.

Unlike the Drug Efficacy Study, discussed in the text accompanying notes 20-22 supra, the FDA has taken an active role in the OTC drug review. FDA facilities and personnel are available to the panels, and the FDA Chief Counsel made introductory remarks to each of the panels outlining the purposes and procedures to be followed. ADVISORY COMMITTEE REPORT, supra note 50, at 8. Members of the Chief Counsel's staff regularly attend panel meetings, and preliminary panel reports are reviewed by the staff for ambiguities and inconsistencies. The purpose of increased FDA participation is to avoid problems of the Drug Efficacy Study; the NAS-NRC panels were totally disassociated from the FDA and operated without communication between each other. Consequently, the standards used in evaluating the effective NDAs varied greatly from one panel to another. MASHAW & MERRILL, supra note 14, at 471.
defines a "new drug" as a drug not generally recognized by experts as safe and effective.\textsuperscript{81} It has thus been suggested that a panel determination that a drug is safe and effective for OTC distribution might automatically remove the drug from the "new drug" category.\textsuperscript{82} This question of administrative delegation arose in conjunction with \textit{Parke, Davis \& Company v. Mathews},\textsuperscript{83} which involved OTC marketing of Benylin Cough Syrup. Parke, Davis submitted data on Benylin to the Cough, Cold, Allergy, Bronchodilator and Antiasthmatic Drug Panel (CCABA Panel) for OTC review.\textsuperscript{84} The CCABA Panel recommended approval of the active ingredient in Benylin,\textsuperscript{85} but the Commissioner issued a proposed monograph disagreeing with the panel's conclusions.\textsuperscript{86} Parke, Davis then brought suit in federal district court seeking a declaratory judgment that Benylin is not a "new drug," and in the alternative, that the FDA be enjoined from initiating enforcement action pending final determination of Benylin's status. The court did not grant the declaratory judgment\textsuperscript{87} but did enjoin enforcement until thirty days after the FDA's final determination.\textsuperscript{88}

In making its holding, the court did not treat the panel recommendations as binding on the FDA.\textsuperscript{89} The court was clearly correct in this regard. The purpose of the panels is "to advise [the Commissioner] on the promulgation of monographs."\textsuperscript{90} The FDA is empowered to administratively determine the sufficiency of evidence concerning general recognition.\textsuperscript{91} Any delegation of this power\textsuperscript{92} would be an abdication of the

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\item \textsuperscript{82} The Pink Sheet, FDC REPORTS, December 6, 1976, at 16. As a practical matter, the Commissioner will usually abide by panel findings. However, it is unlikely that any interested parties would be willing to forego the procedural safeguards provided before publication of the final monograph. See notes 40-41 and accompanying text \textit{supra}.
\item \textsuperscript{84} Id. at 3. Prescription sale previously had been the only authorized method of distribution. See notes 52-60 and accompanying text \textit{supra} concerning the conversion of prescription drugs to OTC status.
\item \textsuperscript{85} 41 Fed. Reg. 38,311, 38,340 (1976). During this time, Parke, Davis also filed for two supplemental NDAs but the FDA deferred action on these applications until completion of the OTC drug review. \textit{Parke, Davis, supra} note 83, at 3.
\item \textsuperscript{86} \textit{Parke, Davis, supra} note 83, at 4. At the same time, a denial of the supplemental NDAs was published. \textit{Id.} at 5.
\item \textsuperscript{87} The court concluded that "these issues are currently under consideration by the FDA which has primary jurisdiction over such actions." \textit{Parke, Davis, supra} note 83, at 7.
\item \textsuperscript{88} The court found that Parke, Davis has relied on prior FDA assurances that OTC marketing was permissible so that the present action withdrawing Benylin was arbitrary and capricious. \textit{Parke, Davis, supra} note 83, at 9.
\item \textsuperscript{89} However, the court was influenced in its decision by the fact that "the advisory panel made a thorough study of the drug, its recommendation is supported by the affidavits of several other eminent experts in the field, and, in contrast, the Commissioner's tentative decision not to permit OTC sale is rather incompletely supported." \textit{Parke, Davis, supra} note 83, at 9. Such a situation will be a relevant consideration when the manufacturer seeks pre-enforcement judicial review of the final monograph. See notes 121-40 and accompanying text \textit{infra}.
\item \textsuperscript{90} 21 C.F.R. § 330.10(a)(1) (1977) (emphasis added).
\item \textsuperscript{91} The FDA's primary jurisdiction over the "new drug" definition was recognized in \textit{Weinberger v. Bentex Pharmaceuticals, Inc.}, 412 U.S. 645, 653 (1973).
\item \textsuperscript{92} The FDA has not delegated this power to the panels and has very clearly reserved the
FDA's statutory responsibilities would raise the spectre of private government.

B. Legislative-Interpretive Issue

The final monographs issued by the FDA should be characterized by the courts in enforcement proceedings as legislative rather than interpretive. A legislative rule is as valid and binding upon a court as a statute if it is within the granted power, issued pursuant to proper procedure, and reasonable. On the other hand, agency interpretations of substantive legislation have been viewed as "not controlling upon the courts by reason of their authority [but merely] a body of experience and informed judgment to which courts and litigants may properly resort for guidance."

It has been suggested that this distinction is of no practical significance because of the judicial deference routinely accorded all technical administrative regulations. Judicial deference, however, will be much less pronounced if the panel report is at odds with the final monograph as promulgated by the FDA. A court probably will be more willing to support the Commissioner if the final monograph is supported by a comprehensive panel report.

More importantly, if the monographs are interpretive, the court en-
forcement proceedings must determine whether the drug is GRAS&E and not misbranded. If the monographs are legislative, the issue before the court is limited to whether the drug complies with the monograph. The FDA clearly is seeking to avoid the potential for protracted litigation inherent in interpretive rules. By defining the critical statutory terms by legislative regulation, the FDA can avoid the potential for protracted litigation inherent in interpretive rules. Given the FDA’s need for expeditious enforcement procedures and its capacity to resolve complex scientific issues, monographs should be accorded legislative status.

The significance of the potential for delay can best be understood by examining the FDA’s pre-OTC drug review procedures. The FDA has sought to expedite enforcement by using summary judgment motions supported by affidavits of medical experts, contending that affidavits denying a drug’s general recognition would be conclusive in establishing it as a “new drug.”101 The FDA’s position has not been well received by the courts. Although one court allowed summary judgment where both the manufacturer and the FDA submitted affidavits as to “general recognition,”102 subsequent decisions have permitted summary judgment only when affidavits submitted by defendants did not even make a prima facie case of “general recognition.”103 As a result, the FDA cannot be assured of summary judgment whenever the manufacturer produces affidavits tending to show that the particular product is GRAS&E.

A final monograph eliminates reliance on affidavits and the inherent delay in obtaining them,104 but the same judicial uncertainty as to the appropriateness of summary disposition is likely if the monographs are given interpretive effect. A court ultimately may abide by the monograph regardless of its characterization, but permitting the case to come to trial on the issues of GRAS&E and misbranding introduces time delay. Giving the monograph legislative effect would lead to administrative resolution, and remove the manufacturers’ incentive to engage in protracted litigation.105

101 Mashaw & Merrill, supra note 14, at 464. See generally Advisory Committee Hearings, supra note 44, at 45-50.

The FDA has also tried to show lack of general recognition by demonstrating an absence of any medical or scientific literature. The theory is that general recognition cannot exist in the absence of such literature because of exchanging information about a drug’s safety or effectiveness. See United States v. An Article of Drug Labeled “Entrol-C Medicated,” 362 F. Supp. 424 (S.D. Cal. 1973), aff’d, 513 F.2d 1127 (9th Cir. 1975).


103 United States v. 7 Cartons ** Ferro-Lac, 293 F. Supp. 660, 662 (S.D. Ill. 1968), aff’d 424 F.2d 1364 (7th Cir. 1970) (criticizing Merritt as equating “general recognition” with unanimity); AMP v. Gardner, 389 F.2d 825, 831 (2d Cir. 1968), cert. denied, 393 U.S. 825 (1968) (allowing summary judgment because the FDA affidavit was addressed to the lack of “general recognition” while the AMP affidavit was one doctor’s opinion as to safety unsupported by other affidavits). The AMP court expressed reservations about summary judgments whenever there are affidavits presenting not only a difference of opinion as to safety but also as to “general recognition.” Id. at 831.

104 Obtaining the affidavits of eminent experts is itself time consuming. See Advisory Committee Hearings, supra note 44, at 44, concerning the FDA’s efforts in removing Vice Spice, a fraudulent aphrodisiac containing paprika, from the market.

105 Harlow, supra note 99, at 258-59. Manufacturers will concentrate their energies on the advisory panels. The comments to the proposed OTC drug review indicated that “the
The monographs are promulgated under Section 70l(a) of the 1938 Act. Section 70l(a) generally vests authority to promulgate regulations for the efficient enforcement of the Act in the Secretary of Health, Education and Welfare (HEW), who has delegated this power to the Commissioner of the FDA. The FDA contends that Section 70l(a) allows it "to proceed by substantive rule making rather than on a case-by-case basis, to particularize general statutory standards." 

The pharmaceutical industry claims that Congress never intended Section 70l(a) to give the FDA authority to promulgate legislative regulations. One commentator notes that Section 70l(e) specifically permits legislative rulemaking in certain situations and that the lack of similar language in Section 70l(a) means that legislative authority was not intended for regulations under Section 70l(a). The legislative history reveals that Section 70l(e) regulations were intended to "have the force of law and must be observed" while no such statement was made for Section 70l(a). In addition, Section 70l(e) contains a number of procedural protections which are not present in Section 70l(a).

Judicial treatment of similar regulatory schemes nonetheless indicates that the final monographs should be given a legislative characterization. The Second Circuit's decision in National Nutritional Foods regulations will be substantially followed by the industry." 37 Fed. Reg. 85 (1972). Compliance may be forthcoming regardless of the characterization of the monographs as legislative or interpretive, but the likelihood of compliance is greater if manufacturers are exposed to summary court procedures. See notes 121-40 and accompanying text infra concerning those situations where a manufacturer is supported by a comprehensive panel report, but the Commissioner fails to abide by panel recommendations.

The court in National Petroleum Refiners Association v. FTC, 482 F.2d 672 (D.C. Cir. 1973), cert. denied, 415 U.S. 951 (1974), upheld the FTC's legal authority to promulgate legislative trade regulation rules (TRRs) for the purpose of carrying out the agency's duties in preventing "unfair methods of competition in commerce and unfair or deceptive acts or practices in commerce." 15 U.S.C. § 45(a) (1970). The FTC derives its authority to issue regulations from section 6(g) of the FTC Act, 15 U.S.C. § 46(g) (1970), which provides that the Commission has the power "... to make rules and regulations for the purpose of carrying out the provisions of sections 41 to 46 and 47 to 58 of this title." This case is analogous because the FDA has similarly broad powers under section 70l(a) of the Food Drug and Cosmetic Act. See also Mourning v. Family Publication Services, Inc., 411 U.S. 356 (1973).
Ass'n v. Weinberger,\textsuperscript{114} upholding regulations classifying vitamins A and D in excess of specified dosages as prescription drugs,\textsuperscript{115} provides particularly strong support for the legislative effect of the monographs. The court construed Section 701(a) as giving the FDA authority "to promulgate substantive regulations having the binding force of law rather than mere 'interpretive' statements enforceable only on a case-by-case basis."\textsuperscript{116} The court found the general delegation of authority in Section 701(a) sufficient to sustain legislative rulemaking.\textsuperscript{117} The specific procedures set forth in Section 701(e) were found to be in addition to and not in derogation of the general rulemaking power under Section 701(a).\textsuperscript{118} The court emphasized the lack of any legislative rulemaking prohibition under Section 701(a) rather than express recognition of such power in Section 701(e).\textsuperscript{119} The Second Circuit's analysis of Section 701(a) is equally applicable to the OTC drug review, and has been so interpreted by commentators.\textsuperscript{120}

C. Pre-Enforcement Judicial Review

Although the amended 1938 Act contains no provision for judicial review of regulations promulgated under the authority of Section 701(a),\textsuperscript{121} a manufacturer has at least two ways of challenging monographs in court. It can resist, as a defendant in an enforcement proceeding, by contesting the validity of the final order.\textsuperscript{122} Alternatively, a manufacturer may seek declaratory judgment and injunctive relief\textsuperscript{123} in an action for pre-enforcement review.\textsuperscript{124}

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  \item \textsuperscript{114} 512 F.2d 688 (2d Cir. 1975), cert. denied, 423 U.S. 827 (1975). The trial court had referred to the OTC drug regulations as "of clearly substantive proportion" during the course of its opinion. 376 F. Supp. 142, 147 n.7 (S.D.N.Y. 1974).
  \item \textsuperscript{115} All preparations of vitamin A containing more than 10,000 IU (international units) per dosage form and of vitamin D containing more that 400 IU per dosage form were prescription drugs. 38 Fed. Reg. 20,723 (1973).
  \item \textsuperscript{116} 512 F.2d at 697.
  \item \textsuperscript{117} Id. at 696.
  \item \textsuperscript{118} "Where once we may have demanded proof of specific delegation of legislative authority to an agency purporting to promulgate substantive rules we have learned from experience to accept a general delegation as sufficient in certain areas of expertise." Id. at 696.
  \item \textsuperscript{119} Id. at 698.
  \item \textsuperscript{120} Ames & McCracken, supra note 21, at 57.
  \item \textsuperscript{121} Review by the court of appeals is explicitly provided for by regulations promulgated under section 701(e). The Food, Drug and Cosmetic Act, § 701(f), 21 U.S.C. § 371(f) (1970).
  \item \textsuperscript{122} Administrative Procedure Act (APA), § 10(b), 5 U.S.C. § 703 (1977). See also Davis, supra note 97, § 23.07.
  \item \textsuperscript{123} Administrative Procedure Act (APA) § 10(b), 5 U.S.C. § 703 (1977). See also Davis, supra, note 97, § 23.04.
  \item A preliminary issue is whether the federal district court has jurisdiction over the controversy. 28 U.S.C. § 1331(a) (1970) formerly required an amount in controversy exceeding $10,000, but the 1976 amendments to the APA eliminated this requirement, 28 U.S.C.A. § 1331(a) (West Supp. 1978). The Supreme Court has recently ruled that section 10 of the APA does not provide an independent grant of subject matter jurisdiction permitting federal judicial review of agency action. Califano v. Sanders, 430 U.S. 99 (1977).
  \item Pre-enforcement review of interpretive regulations promulgated under the authority of section 701(a) of the 1938 Act, 21 U.S.C. § 371(a) (1970), was at one time thought to be
\end{itemize}
The Administrative Procedure Act (APA) determines the scope of judicial review in these actions. The FDA promulgates the monographs under the “notice and comment” procedures of Section 4(b) of the APA\textsuperscript{125} rather than the formal “on the record” rulemaking of Sections 6 and 7.\textsuperscript{126} Although the APA is not clear, it is generally assumed that review under informal “notice and comment” rulemaking is governed by an “arbitrary or capricious” standard\textsuperscript{127} rather than the “substantial evidence” test\textsuperscript{128} followed for formal rulemaking.\textsuperscript{129}

Courts under the “arbitrary or capricious” standard have generally been more tolerant of administrative action than under the “substantial evidence” test.\textsuperscript{130} This standard may still require close judicial examination. The Second Circuit in *Nutritional Foods Association v. Weinberger* concluded “even under the ‘arbitrary, capricious’ standard agency action will not be upheld where the inadequacy of explanation frustrates review.”\textsuperscript{131} There is a trend towards increased judicial scrutiny of administrative actions under the “arbitrary or capricious” test.\textsuperscript{132} Judge Lumbard’s concurring opinion in *National Nutritional Foods Ass’n v. Weinberger* merges the two standards: “when an agency engages in substantive rulemaking, it abuses its discretion (or acts arbitrarily or capriciously) if its actions are not supported by substantial evidence.”\textsuperscript{133}

The FDA’s use of outside experts in the formulation of monographs has led some commentators to suggest that courts are unlikely to find FDA

\footnotesize{unavailable; challenge had to come during an enforcement proceeding. Bass, *supra* note 109, at 450. This position is not tenable after Abbott Laboratories v. Gardner, 387 U.S. 136 (1967). Abbott Laboratories had the option of complying with regulations of debatable validity requiring the generic name of a prescription drug to follow each appearance of the proprietary name on the drug label or facing regulatory enforcement. The Court held this dilemma presented a sufficient controversy to warrant judicial review prior to FDA enforcement. 387 U.S. at 152-154. The same dilemma faces OTC drug manufacturers concerning compliance with the final monograph. Compliance with the monograph may entail relabeling or recomposition of the product, while non-compliance assures regulatory action which can be costly in terms of public image and litigation expenses.

\textsuperscript{125} 5 U.S.C. § 553 (1970). The FDA has added several procedural steps such as reply comments and a tentative final monograph so as to meet the possible judicial requirements of “notice and comment-plus” rulemaking. See note 41 *supra*.


\textsuperscript{129} National Ass’n of Food Chains v. I.C.C., 535 F.2d 1308, 1313 (D.C. Cir. 1976).

It has been asserted that the monographs, if given interpretive effect, should be reviewed under the “substantial evidence” test. Harlow, *supra* note 99, at 254. Interpretive rules are exempt from the “notice and comment” procedures of section 553. A “substantial evidence” test, however, seems untenable because the monographs are not promulgated under the formal rulemaking procedures of sections 556 and 557. However, courts will give less deference to interpretive rules than to legislative regulations. Shell Oil Co. v. FPC, 491 F.2d 82, 88 (5th Cir. 1974), and the scope of review may lie somewhere between that for legislative rules and that for agency adjudications. Opelika Nursing Home, Inc. v. Richardson, 356 F. Supp. 1338, 1341-42 (M.D. Ala. 1973).

\textsuperscript{130} MASHAW & MERRILL, *supra* note 14, at 262-63.

\textsuperscript{131} 512 F.2d 688, 701 (2d Cir. 1975).


\textsuperscript{133} 512 F.2d at 705.
action in promulgating monographs arbitrary or capricious.\textsuperscript{134} Where the Commissioner does not follow panel recommendations, however, a court may find that the FDA acted in an arbitrary or capricious manner. The FDA's final monograph must be supported by the administrative record,\textsuperscript{135} and the court must consider panel recommendations because judicial review is of the record as a whole.\textsuperscript{136} The court must therefore examine not only the justifications for the administrative action but also evidence that undercuts the decision.\textsuperscript{137}

The 1938 Act makes the \textit{general recognition} of a drug the crucial inquiry in determining "new drug" status. It may be argued that a drug cannot be GRAS&E when there is disagreement between the Commissioner and the panel.\textsuperscript{138} General recognition does not have to be unanimous, however, because even properly conducted studies may produce disagreement,\textsuperscript{139} but the FDA will be obliged to support its position with well-documented facts.\textsuperscript{140} Pre-enforcement judicial review will be a feasible course for plaintiffs whose position is supported by a comprehensive panel report.\textsuperscript{141}

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\item[134] Bass, \textit{supra} note 109, at 452; Harlow, \textit{supra} note 99, at 257.
\item[135] The grounds for agency action must clearly appear in the record, and the agency's analysis and reasoning must be plainly apparent. Petroleum Institute \textit{v.} EPA, 540 F.2d 1023, 1029 (10th Cir. 1976).
\item[136] Administrative Procedure Act (APA), § 10(e), 5 U.S.C. § 706 (1970). Judicial review under the "arbitrary or capricious" test is not restricted to the record before the administrative body. Beckham \textit{v.} United States, 375 F.2d 782, 785 (Ct. Cl. 1967). An agency in preenforcement review cannot designate which items it considers to be in the administrative record. Smith \textit{v.} FTC, 403 F. Supp. 1000, 1008 (D. Del. 1975).
\item[137] Davis, \textit{supra} note 97, § 29.01. See also Universal Camera Corp. \textit{v.} NLRB, 340 U.S. 474, 487 (1951).
\item[138] The House Committee on Government Operations found the FDA staff to be competent for resolving many of the issues put before the advisory panels. Advisory Committee \textit{Report, supra} note 50, at 5, in making its charge that the FDA is making nonessential use of the panels. However, this charge ignores the enormousness of the regulatory task confronting the FDA. The staff is also not likely to be as knowledgeable as the panel members on the particulars of any therapeutic category.
\item[139] United States \textit{v.} Articles of Food and Drug, Etc., 518 F.2d 743, 746 (5th Cir. 1975); United States \textit{v.} 7 Cartons, * * * Ferro-Lac, 293 F. Supp. 660, 662 (S.D. Ill. 1968), aff'd 424 F.2d 1364 (7th Cir. 1970).
\item[140] See \textit{note 21 supra} concerning the types of evidence that must be shown under §§ 505(d), (e) of the amended 1938 Act. The Court in Weinberger \textit{v.} Bentex Pharmaceuticals, Inc., 412 U.S. 645 (1973), held the same sort of inquiry applicable to the "new drug" issue; simple assertions will not be sufficient to establish GRAS&E.
\item[141] After the publication of the final monograph, several administrative alternatives are available. A manufacturer or consumer can petition the Commissioner to amend the final monograph, 21 C.F.R. § 330.10(a) (12) (1977). See 42 Fed. Reg. 19,137 (1977). A manufacturer can also file an NDA with the FDA. In an attempt to reduce the time and resources necessary for the approval of an NDA, an abbreviated procedure has been created whereby an application must include a statement "that the product meets all the conditions of the applicable monograph except for the deviation for which approval is requested and may omit all information except that pertinent to the deviation." 21 C.F.R. § 330.11 (1977). Neither procedure may be feasible if the FDA is adamant about the position taken in the final monograph unless the manufacturer can present new information.
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IV. Conclusion

The OTC drug review is an industrious effort by the FDA to improve its marketing controls over OTC drugs.\textsuperscript{142} The deficiencies of the traditional NDA licensing approach, including the enormous amount of time and resources necessary to process individual drug applications and the grandfather clauses exempting most OTC drugs from the "new drug" definition, required innovation by the FDA. By defining GRAS&E and misbranding, the FDA provides all parties with more certainty concerning the status of individual drugs under the Act. In addition, it also eliminates the inequities caused when some drugs remain on the market indefinitely while competitive drugs are subjected to FDA enforcement.

The advisory panels are essential to the review because of the prestige that the panel members contribute to the review and because of their effectiveness in evaluating data and formulating comprehensive reports. The panel framework also allows maximum visibility and accessibility to panel operations through the liaison members and by allowing interested persons to attend and participate in panel meetings.

The OTC drug review provides for expeditious enforcement because the question whether particular drugs are GRAS&E and not misbranded is determined administratively. The courts, to which the FDA must ultimately resort for enforcement, will likely accord the monographs legislative effect, which will limit judicial inquiry to whether a drug complies with the applicable monograph. The role of the courts will be to determine whether there is an adequate evidentiary basis to support the FDA, especially when the final monograph does not incorporate panel recommendations.

—David Selmer