

1800 M Street, N.W.
Washington, D.C. 20036-5869
202-467-7000
Fax: 202-467-7176

**Morgan, Lewis
& Bockius LLP**
C O U N S E L O R S A T L A W

Kathleen M. Sanzo
202-467-7209

February 28, 2000

VIA HAND DELIVERY & FACSIMILE

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 99N-2497
Comments to Proposed Rule Regarding the Submission of Citizen Petitions

Dear Madam or Sir:

On behalf of Pharmacia & Upjohn ("P&U"), we submit these comments concerning the proposed rule issued by the Food and Drug Administration ("FDA" or "the Agency") regarding the submission of Citizen Petitions to the Agency ("the proposed rule"). See Citizen Petitions: Actions That Can Be Requested by Petitions; Denials, Withdrawals, and Referrals for Other Administrative Action, 64 Fed. Reg. 66822 (Nov. 30, 1999). Pharmacia & Upjohn is a major innovator drug research and manufacturing company, and has a direct interest in the proposed rule.

P&U believes that the Agency should not finalize the proposed rule since it would preclude the public, including innovator drug manufacturers, from submitting, and the Agency from formally responding to, citizen petitions regarding FDA's approval of specific drug products. Further, the proposed rule will preclude effective judicial review of Agency action regarding the approval of specific drug products and, thus, improperly confer unreviewable discretion upon the FDA. Through these effects, the proposed rule improperly discriminates between and disadvantages one segment of drug manufacturers, innovator companies, to benefit another segment, generic drug manufacturers, without justification presented by the Agency and inconsistent with the Federal Food, Drug, and Cosmetic Act ("FFDCA" or the "Act").

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I. Introduction

The Administrative Procedure Act ("APA") specifically provides for judicial review of agency action to ensure that an agency has met its statutory mandate and not exceeded its authority. 5 U.S.C. § 706. The proposed rule, however, would effectively preclude the courts from conducting meaningful review of the FDA's actions concerning approval of specific drug products because the rule would allow the Agency to refrain from accepting and/or responding to citizen petitions that raise legitimate and critical scientific issues about the safety and efficacy of proposed drug products. Because FDA would not accept or respond to such citizen petitions, the Agency would not have the opportunity to compile an adequate and comprehensive administrative record that incorporates consideration of all of the relevant scientific issues that may be involved in approving a drug product. Together with the statutory confidentiality of the drug approval process, the proposed rule thus effectively would preclude a court from conducting any review of the Agency's decision-making process to ensure that the Agency has complied with its statutory mandate under section 505 of the FDCA, which requires the Agency to approve only safe and effective drug products. The proposed rule, therefore, improperly would provide the Agency with unreviewable discretion in carrying out its statutory mandate in violation of the APA.

II. Discussion

A. Proposed Rule On Citizen Petitions and Effect on Meaningful Consideration and Review of Drug Approval Process for Specific Drug Products.

Under FDA's current regulations, a citizen petition may be submitted to the Agency by any person to request the Agency to take some action concerning any issue for which FDA has jurisdiction.^{1/} The citizen petition process has been used by a wide range of persons and entities, including individuals, consumer groups, trade associations, and FDA-regulated companies, including both innovator and generic drug companies, to comment usefully on a wide range of issues within FDA's jurisdiction. These comments and FDA's responses have ensured that FDA has conducted a thorough review of the relevant safety and efficacy issues

^{1/} 21 C.F.R. § 10.30.

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concerning its regulation of drug and other products. Moreover, they serve as a critical basis for which the courts to review whether FDA has met its statutory obligations.

On November 30, 1999, however, FDA issued a proposed rule to amend its regulations pertaining to citizens petitions.^{2/} The proposed changes would severely limit the scope of actions that may be requested in a citizen petition, require petitioners to certify that they are not submitting the petition for any improper purpose^{3/} and that the petition includes information known to the petitioner that is unfavorable to the petition, allow FDA's denial of a citizen

^{2/} Citizen Petitions: Actions That Can be Requested by Petition; Denials, Withdrawals and Referrals for Other Administrative Action, 64 Fed. Reg. 66822 (Nov. 30, 1999).

^{3/} In Pharmacia & Upjohn's view, this certification requirement is unwarranted. First, what constitutes an "improper" purpose is indistinct and insufficiently defined. Second, to the extent the Agency intends to prevent petitions motivated by competitive purposes, such action raises serious questions of denial of First Amendment rights to petition. Challenges to FDA approvals of generic drug applications by petitions to the Agency, even if motivated solely by anticompetitive purposes, are not violations of the antitrust laws by reason of the Noerr - Pennington immunity doctrine, which is based on the First Amendment right to petition. Indeed, the courts have rejected such antitrust challenges specifically in the precise context of challenges to filings of citizen petitions to the Agency concerning generic drug approvals. See e.g., In re Warfarin Sodium Antitrust Litigation, 1999-1 Trade Cas. (CCH) ¶ 72,457 (S.D.N.Y. 1998) (holding that a pioneer company's use of citizen petitions to challenge approval of a generic version of Coumadin (warfarin), and a petition to USP, cannot be used to prove allegations of violation of the antitrust laws; see also Professional Real Estate Investors, Inc. v. Columbia Pictures Industries, 508 U.S. 49 (1993), City of Columbia v. Omni Outdoor Advertising, Inc., 499 U.S. 365 (1991); Cheminor Drugs, Ltd. v. Ethyl Corp., 993 F. Supp 271 (D. N.J. 1998). We note that we are unaware of any judicial concurrence in or administrative agency adoption of restrictions on the Constitutional right to petition of the type advocated by the single law review article published five years ago upon which the Agency apparently relies as its sole support for this far-reaching proposed new certification requirement. Further, unlike the antitrust laws, whose purpose and focus is competition and the competitive process, the Federal Food, Drug, and Cosmetic Act contains no proper basis upon which such a competition-focused certification requirement lawfully could be based. The Agency states no such basis in its preamble to the proposed rule.

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petition to be “brief” (i.e., non-substantive), and authorize FDA to consolidate multiple petitions on the same subject or product.^{4/}

FDA’s proposed rule would limit the actions that may be requested in a citizen petition to the following: (1) issue, amend, or revoke a regulation; (2) amend or revoke an order that the Agency has issued or published; or (3) take an action that is specifically authorized by another FDA regulation.^{5/} A petition that seeks, for example, a regulation directly or indirectly prohibiting the approval of a particular drug product, declaring a particular drug product to be unsafe, ineffective, or not bioequivalent, or prohibiting approval of a class of drug products including generic drug products, thus would be precluded by the proposed rule because FDA does not generally issue regulations to approve individual drug products.^{6/} Similarly, a petition from generic manufacturers requesting clarification from FDA that it will approve a specific class of drug products under the Abbreviated New Drug Application (“ANDA”) mechanism, or requesting that FDA declare certain drug products therapeutically equivalent, would be precluded. In addition, under the proposed rule, a citizen petition could not be used to request that FDA amend pending orders or issue future FDA orders related to the approval of a particular drug or class of drug products.^{7/} The proposed rule therefore would significantly inhibit the Agency from generating a comprehensive administrative record in its approvals or disapprovals of particular proposed drug products.

The Agency asserts that its proposal does not prevent a person from contacting FDA or curtail access to FDA and suggests that persons who desire to present information to FDA would still be able to do so through letters, electronic mail, meetings, discussions, and other avenues of communication.^{8/} FDA, however, is under no legal obligation ever to respond formally to informal communications such as letters or electronic mail, or to agree to meetings. Consequently, any informal response FDA officials might provide will not be on the public record and, thus, would not be open to view and public comment, and may not be written and thus would not be available for judicial review.

4/ Id.

5/ Id. at 66823.

6/ Id.

7/ Id.

8/ Id. at 66824.

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In the absence of a formal response and public comment on the issues, therefore, the administrative record will consist primarily of an applicant's submission and the Agency's views of that submission. An applicant seeking approval hardly can be expected to criticize the methodology or evidence it submits to demonstrate that a drug product is safe and/or effective. Thus, to the extent that the Agency is unaware of substantive controversies and/or unfavorable information about the proposed drug product, the administrative record may reflect only select information submitted by the applicant and/or known to the Agency. This record likely will not include other information that may be known by others but not available to the Agency; decision making by the Agency thus will not reflect a complete and balanced view of issues, including the safety and effectiveness of the proposed drug product.

As a result of finalizing this rule, a reviewing court effectively will be precluded from conducting review of the Agency's decisions because the court will be limited to a review of an Agency administrative record that is not developed through a notice-and-comment process and does not contain comprehensive consideration of the relevant issues. The rule thus will confer unreviewable discretion on FDA in violation of principles of Section 706(2)(A) of the APA, which provides that an agency not engage in arbitrary and capricious action which is not supported by reasoned decision-making.

B. Presumption of Reviewability of Agency Action.

The APA specifically provides for judicial review of agency action except to the extent that: (1) the statute precludes review; or (2) agency action is committed to discretion by law. See 5 U.S.C. § 706 (2)(A) (providing that a "reviewing court shall . . . hold . . . unlawful and set aside agency action . . . found to be arbitrary, capricious, an abuse of discretion or otherwise not in accordance with law"); see also 5 U.S.C. § 701(a).

Pursuant to the APA, the courts traditionally have held that there is a strong presumption of reviewability of final agency action. See, e.g., Dunlop v. Bachowski, 421 U.S. 560, 566 (1975) (stating that the agency has the heavy burden of overcoming the strong presumption that Congress did not mean to prohibit all judicial review); see also id. at 567 (noting that judicial review should not be precluded unless there is clear and convincing evidence that Congress intended to do so); Dickson v. Secretary of Defense, 69 F.3d 1396 (D.C. Cir. 1995) (noting that the standard of deference afforded to agencies does not mean that the action should receive no review at all); Cardozo v. Commodity Futures Trading Commission, 768 F.2d 1541 (7th Cir. 1985) (holding that courts should only restrict access to judicial review upon a showing of clear and convincing evidence of a contrary legislative intent.). Accordingly, the

courts have held reviewable several agency actions, including an agency's decision not to act and decisions that have contravened the plain language or legislative intent of the statute. See Berger v. Heckler, 771 F.2d 1556 (2d Cir. 1985) (holding that the court had the authority to review the Secretary of Health and Human Services' refusal to promulgate regulations implementing a consent decree and requiring promulgation of such regulations); Bresgal v. Brock, 637 F. Supp. 280 (D. Or. 1986) (finding that Secretary of Labor was required to enforce a safety statute and, therefore, granting injunction requested by forestry workers to amend regulations to implement the statute). Absent a clear exception in the agency's enabling statute to this general rule, therefore, the courts have an obligation to review agency action to ensure that an Agency has followed its statutory mandate.

Under the FFDCA, the FDA is required to refuse to approve an application for a drug product that has not been shown to be safe and effective. 21 U.S.C. §355(d). Moreover, the statute mandates that the Agency ensure that it has considered fully the evidence that supports, or is adverse, to such approvals. Nothing in the Act or the legislative history suggests that Congress intended to preclude judicial review of Agency decisions regarding the approval of specific drug products or commit such decisions solely to the Agency's discretion. Accordingly, the Agency is not entitled to unreviewable discretion in approving drug products. The unavoidable result of promulgation of the proposed rule, however, will be to confer unreviewable discretion on the Agency because the public and the courts will have no opportunity effectively to evaluate whether the FDA has followed its statutory mandate or to determine whether the Agency's action is arbitrary, capricious, an abuse of discretion or not otherwise in accordance with the law.

C. Judicial Review Effectively Will Be Precluded by the Absence of a Comprehensive Administrative Record That Includes Provision and Evaluation of Public Comment Regarding the Safety and Efficacy of Proposed Drug Products.

1. The Standard of Judicial Review of Agency Action

Pursuant to the APA and judicial precedent, in evaluating whether an agency's action is arbitrary, capricious, an abuse of discretion or otherwise not in accordance with law, a court "must ascertain whether the agency's decision 'was based on consideration of the relevant factors and whether there has been a clear error of judgment' based on the administrative record. Duke Power Co. v. Nuclear Regulatory Commission, 770 F.2d 386, 390 (4th Cir.1985)

(quoting Citizens to Preserve Overton Park, Inc. v. Volpe, 401 U.S. 402, 415-16 (1971). However, the record must be one that “the agency presents to the reviewing court.” Florida Power & Light Co. v. Lorion, 470 U.S. 729, 744 (1985); Camp v. Pitts, 411 U.S. 138, 142 (1973) (stating that a reviewing court must review the administrative record as assembled by the agency; the court cannot pursue its own fact finding.); Bristol-Myers Squibb Co. v. Shalala, 923 F. Supp. 212, 216 (also noting that “the court must review the administrative record assembled by FDA; it does not pursue its own fact finding.”); see also Upjohn v. Kessler, 938 F. Supp 439 (W.D. Mich. 1996) (stating that the starting point for reviewing an agency’s actions in consideration of the administrative record compiled by the agency.) The courts are precluded from conducting a *de novo* review of agency action and generally assume that an agency has conducted an adequate and relevant review of the issues concerning its decisions. Bar MK Ranches v. Yuetter, 994 F.2d 735, 740 (10th Cir. 1993) (assumption that agency properly designated the administrative record absent clear evidence to the contrary); Somerset Pharmaceuticals, Inc. v. Shalala, 973 F. Supp 443 (D. Del. 1997).

Because evidence or data not presented to an agency in the course of developing its administrative record thus ordinarily will not be accepted or reviewed by a court, developing a complete administrative record is critical to ensuring that the courts can properly review agency action in accordance with the APA. Recognizing the importance of an adequate administrative record to ensure appropriate judicial review, the courts have held that an agency has an obligation to consider all the evidence and provide adequate explanation for its decision in the administrative record. See City of Charlottesville v. Federal Energy Regulatory Commission, 661 F.2d 945, 950 (D.C. Cir. 1981); Asarco Inc. v. Environmental Protection Agency, 615 F.2d 1153, 1159 (9th Cir. 1980) (holding that an agency has a duty to consider all the evidence and to explain its decision fully.). These principles have been applied to inadequate FDA decision-making in the past, where courts have reversed Agency action that did not properly develop or address significant substantive and procedural concerns. See United States v. Nova Scotia Food Products Corp., 568 F.2d 240, 251 (2d. Cir. 1977) (stating that the “inadequacy of comment leads to arbitrary decision-making.”).

2. Judicial Deference to Agency Decisions Concerning Scientific and Technical Issue Increases the Necessity of a Complete and Adequate Administrative Record.

The importance of a complete and adequate record that reflects thorough consideration of the substantive and procedural issues regarding drug approvals is increased due to the high degree of deference the courts afford agency decisions regarding scientific or technical issues. The

courts have held that, in reviewing scientific and technical matters, “a reviewing court must generally be at its most deferential.” Baltimore Gas & Electric v. Natural Resources Defense Council, Inc., 462 U.S. 87, 103 (1983); Tri-Bio Laboratories Inc. v. United States, 836 F.2d 135, 142 (3d Cir. 1987) (“In evaluating scientific evidence in the drug field, the FDA possesses an expertise entitled to respectful consideration by this court.”); see also A.L. Pharma, Inc. v. Shalala, 62 F.3d 1484, 1490 (D.C. Cir. 1995); Schering Corp. v. FDA, 51 F.3d 390, 399 - 400 (3d. Cir. 1995); Serono Laboratories, Inc. v. Shalala, 158 F.3d 1313 (D.C. Cir. 1998). Where an agency action such as the FDA’s decision to approve a specific drug product involves scientific and technical issues, therefore, it is essential that the public have the opportunity to comment and provide data and evidence regarding such decisions to ensure that the record includes adequate development and consideration of the relevant evidence and, thus provides a basis for proper judicial review in the event of challenge. The proposed rule, however, will effectively exempt FDA’s reasons from public criticism, comment, or judicial review.

D. The Confidentiality of the Drug Approval Process, Coupled with the Prohibition of Agency Receipt and Response to Citizen Petitions Regarding Specific Drug Approvals, Will Preclude the Development of a Comprehensive Administrative Record and, Thus, of Judicial Review of Actions by the Agency.

Pursuant to the Act and FDA’s regulations, the drug approval process is confidential. See 21 C.F.R. § 314.430 (stating that FDA will not publicly disclose the existence of an application or abbreviated application before an approvable letter is sent to the applicant.). No direct public comment or participation is possible. Consequently, the Agency’s proposed further limitation on acceptance of public comment by its proposed Citizen Petition rule, coupled with application of the general rule that judicial review will be limited to an agency’s administrative record, effectively confers unreviewable discretion on FDA decisions on drug applications.

The application of the prevailing rule that judicial review should only be on the administrative record results in there being no opportunity or no possibility of presenting data, analyses, or other scientific evidence at any stage in the review process, thus allowing FDA to completely structure the record and effectively secure unreviewable discretion for its decision-making in this area. Such a result is both unwarranted from the standpoint of proper, informed decision making by FDA and unlawful as effectively committing the Agency’s decisions to its unreviewable discretion, in violation of both the FFDCA and the APA. See Adams v. Richardson, 480 F.2d 1159, 1162 (D.C. Cir. 1973) (*en banc*), (rejecting agency’s argument that

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its inaction was committed to its unreviewable discretion, holding that the agency had “consciously and expressly adopted a general policy which is in effect an abdication of its statutory duty.”).

III. Conclusion

It is inconsistent with congressional intent in the FDCA and a violation of the APA, for FDA to implement the proposed citizen petition rule. FDA would in effect confer on itself unreviewable discretion over the approval of drug products. Accordingly, the FDA should refrain from adopting and implementing the proposed rule.

Sincerely,



Kathleen M. Sanzo
Counsel for Pharmacia & Upjohn, Inc.

cc: Larry Moore
Vice President and Associate General Counsel of Global Business
Pharmacia and Upjohn

Phillip L. Chao
Office of Policy (HF-23)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857