Wiley Rein & Fielding LLP
1776 K Street NW
Washington, D.C. 20006
202.719.7000

April 21, 2003

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

Re: Response To Citizen Petition Requesting That Certain Prescription Allergy Medication Be Switched To OTC Status
Docket No. 98P-0610/CP

I. INTRODUCTION

The undersigned submits these comments on behalf of the American Association of Physicians and Surgeons ("AAPS") and the Competitive Enterprise Institute ("CEI" – collectively "Commenters") in connection with the ongoing proceedings generated by the Citizen Petition filed by Blue Cross of California Pharmacy (now WellPoint Health Networks – "WellPoint") on July 22, 1998, Docket No. 98P-0610/CP. That petition requests that the Food and Drug Administration ("FDA") mandatorily switch Allegra/Allegra-D, Claritin/Claritin-D, and Zyrtec from prescription to over-the-counter ("OTC") drug status.

A. Descriptions and Interests of the Commenters.

AAPS is a non-profit, nationwide professional association of physicians in all practices and specialties. It was established in 1943 to preserve the practice of private medicine, and has remained dedicated to the Oath of Hippocrates and the sanctity of the patient-physician relationship, which APPS believes must be protected from all forms of third-party intervention. Since its founding over fifty years ago, AAPS has been the only national organization consistently supporting free market principles in medical practice. AAPS believes that FDA should confine its activities to issues of safety and effectiveness and that FDA should not attempt to stretch its mandate into interference with the purely economic decisions of manufacturers.

CEI is a non-profit public interest organization dedicated to the principles of free enterprise and limited government. CEI is nationally recognized for addressing a broad range of regulatory issues from a free market perspective. While acknowledging that regulatory agencies like FDA must fulfill their legislative mandates, CEI seeks to foreclose the unnecessary aggrandizement of agency functions and to prompt continuing recognition that government interference with market mechanisms is adverse to economic growth and consumer welfare.

Commenters believe that Congress has established FDA as a health and safety regulator whose essential functions with respect to new drug applications and labeling are to respond to and validate initiatives taken by the private sector and to take appropriate steps to assure the safety of drugs on the market. AAPS and CEI are concerned with assertions that FDA can assume the role of an unrestricted public health promoter exercising command and control authority over pharmaceutical manufacturers through broad, unsupported readings of its legislative authority. Thus, for example, Commenters have challenged successfully the legal basis for FDA's Pediatric Rule because that rule sought to extend FDA's new drug approval powers to direct intervention in the marketing strategy and target patient population selected by manufacturers.[1] AAPS and CEI are commenting in this proceeding because they believe that the "mandatory switching" authority being advocated by petitioner improperly, unlawfully and unwisely would extend FDA's authority under Section 503(b) of the Federal Food, Drug and Cosmetic Act ("FDCA").

B. Summary of Commenters' Position.

Commenters believe that the FDCA, read as an integrated whole, generally leaves the determination whether prescription drug or OTC drug labeling should be proposed for any new chemical entity up to its manufacturer(s). AAPS and CEI recognize that, as an exception to this general rule, FDA may restrict manufacturers to prescription labeling and distribution for certain drug products which cannot safely be dispensed OTC.[2] That judgment must be made on a scientific basis taking into account the specific characteristics of the drug under review and the indications prescribed, recommended or suggested in its label.[3] FDA should not, and lacks authority to, permit economic considerations to intrude into this scientific process.

Section 503(b)(3) of the FDCA, in Commenters' view, serves an equally important public purpose. This section permits FDA to consider additional scientific evidence with respect to drugs it has previously restricted to prescription sale and to withdraw the requirement of prescription dispensation. Once that requirement is withdrawn for a particular drug under 503(b)(3), manufacturers are free to propose OTC labeling which FDA must then approve so long as the labeling permits the drug to be safely and effectively dispensed directly to consumers.[4] Moreover, manufacturers wishing to continue prescription distribution of that drug cannot use the "Rx only" symbol, which signifies governmentally-required prescription status,

---

1 *Ass'n of American Physicians & Surgeons, Inc. v. FDA*, 226 F.Supp.2d 204 (D.D.C. 2002) (setting rule aside as in excess of FDA authority).

2 *See* 21 U.S.C. § 353(b)(1).

3 *Id.* at § 355(d).

4 *See* 21 C.F.R. § 310.200 (a drug shall be exempted from the prescription dispensing requirements "when the Commissioner finds that such requirements are not necessary for the protection of public health . . . and he finds that the drug is safe and effective for use in self-medication as directed in proposed labeling.").

and cannot rely on FDA's use of legal sanctions under the FDCA to foreclose OTC distribution by others.

Thus, a 503(b)(3) rulemaking determination removes a significant regulatory constraint on manufacturer discretion and creates substantial economic incentives for OTC distribution. Neither the wording nor statutory context of 503(b)(3), however, suggests that the section goes further and permits FDA to prohibit prescription distribution or require OTC distribution.

The petition, however, seeks to extend the 503(b)(3) process directly into economic issues. While it asserts conclusorily that the drugs at issue can be used safely OTC,[5] its principal arguments center on the insurance consequences of a forced switch to OTC distribution. Petitioner points out that its insurance policies do not cover OTC drugs so that a mandatory switch will directly reduce its costs.[6] However, it fails to point out that this will be largely at the expense of its policyholders – health care consumers.[7] Petitioner also claims that OTC distribution will force manufacturers to reduce existing prices. Whether or not these arguments are valid, they have no place in the 503(b)(3) process. It is well beyond the mandate of an agency charged with "protect[ing] public health by ensuring that . . . [drug products] are safe and effective"[8] to determine whether particular drug purchases should be covered by insurance. It is equally beyond FDA's purview to seek to regulate or affect manufacturer pricing. Moreover, marketplace analysis and the effects of distribution restrictions on pricing, which are complicated economic subjects, are well beyond FDA's traditional expertise.

In seeking to limit 503(b)(3) proceedings to their proper scientific scope and consequences, Commenters wish to make clear that they are not seeking to limit the removal of unnecessary government restrictions on OTC distribution. AAPS and CEI have great confidence in the ability of American consumers to use drug products wisely and to determine for themselves whether medical consultation is appropriate. By focusing Section 503(b)(3) on removing government restrictions no longer dictated by safety concerns, rather than imposing new mandates on manufacturers, FDA can avoid the political quagmire arising from injecting itself into economic collisions between different industries inherent in mandatory switch contests

---

5 WellPoint argues that the drugs should be switched to OTC sale because, *inter alia*, they are safer than the antihistamine and antihistamine/decongestant alternatives currently available for OTC sale. The petitioner does not cite to any data that support this contention in its petition. However, WellPoint did later submit supplements to its petition containing reported adverse drug events for over-the-counter, non-sedating antihistamines available in Canada (April 30, 1999; Supplement 1) as well as an Evidence Report comparing safety and effectiveness of first-generation and second-generation antihistamines for the treatment of allergic rhinitis (Oct. 4, 2000, Supplement 2).

6 *See* WellPoint Health Networks, *FDA Petition Questions & Answers,* Question 6, *at* http://www.wellpoint.com/fda/questions.htm. WellPoint anticipates a savings of approximately $90 million from a switch.

7 For effects on consumer costs, *see* Francesca Lunzer Kritz, *Blowing Money: Your Allergy Medications May Cost More This Year -- or Be Changed Entirely*, WASH. POST, March 25, 2003, at HE01.

8 21 U.S.C. § 393(b)(2)(B).

and can properly permit market forces to regulate distribution choices. Moreover, by giving manufacturers additional distribution options consistent with patient safety, FDA can enable them to explore distribution and differential pricing options which expand drug availability to low-income consumer populations while permitting a reasonable recovery of development costs.

For these reasons, Commenters request that FDA make a threshold jurisdictional determination that the issue of mandatory switch is outside the proper bounds of the ongoing proceedings in Docket No. 98P-0610/CP and proceed promptly to a scientific determination whether the drugs at issue[9] should be removed from the prescription-only requirements of Section 503(b)(1) of the FDCA.

II. THE PETITION PROVIDES NO BASIS UNDER FDCA FOR FORCING A SWITCH.

A. Statutory Overview

FDA's authority to exempt a drug from prescription-only use requirements is established by Section 503(b)(3) of the FDCA. That section is one part of the prescription-dispensing provisions of the FDCA – Section 503(b) – that were added to the statute in 1951 by the Humphrey-Durham Amendments.[10] Prior to these amendments, FDA had no authority to determine whether drugs were required to be dispensed by prescription; such determinations were left solely to the discretion of drug manufacturers.

1. Concerns Giving Rise To The Humphrey-Durham Amendments.

The lack of a standard prior to the passage of the Humphrey-Durham Amendments for which drugs should be dispensed only by prescription led to a number of health and safety concerns.[11]

- Congress found a troubling number of allegedly unsafe drugs being sold over-the-counter. The lack of a clear standard for the drugs that should be limited to prescription distribution resulted in "many cases of indiscriminate and unauthorized over-the-counter sales of dangerous drugs and other drugs which should be used only under medical supervision."[12]

---

[9] Claritin, which was the top selling prescription drug at the time the petition was filed, has since been switched voluntarily by its manufacturer to OTC distribution. Zyrtec and Allegra, however, remain prescription drugs.

[10] Humphrey Durham Drug Prescription Act, Pub. L. No. 82-215, 65 Stat. 648-649 (1951) (amending 21 U.S.C. § 353(b)).

[11] H.R. REP. NO. 82-700, at 6 (1951).

[12] *Id.*

- Under the then-existing law, if a manufacturer chose to sell over-the-counter a product that FDA thought should be limited to distribution by prescription due to its potential for harm, FDA could prevent OTC sale only by obtaining an injunction. However, an injunction was only binding as to the particular product and manufacturer against whom the injunction was sought.[13] If fifty manufacturers were on the market with the same drug, FDA would conceivably have had to go to court fifty times to enforce prescription marketing of the product.

- Pharmacists were often confused about how particular products should be sold. Before these amendments, as now, drugs not labeled for "prescription-only" use by their manufacturers were required to be labeled with adequate directions for consumer use. However, it was known that many manufacturers were failing to do so. Thus, pharmacists who did not "know whether the labeling [for a drug met] the requirements of the FDC Act and regulations," were concerned about liability for improperly dispensing a drug that the manufacturer had not labeled properly for OTC use or that was meant to be limited to prescription sale.[14] They understandably wanted the law to require a manufacturer of a drug to ". . . label it in a manner wherein its sale by the druggist would not constitute an unlawful act of selling a misbranded drug."[15] Pharmacists wanted a reformed scheme that would "take the guesswork out of labeling" by making it clear which drugs could be dispensed only on prescription and mandating that manufacturers of a drug not labeled with the prescription legend "must label the drug to meet all of the labeling requirements of the [FDCA] and that the product can lawfully be sold over the counter."[16]

- A related lack of uniformity in how the same drug was labeled and sold by different manufacturers led to dozens of drugs containing the same active ingredient and dosage form on the market bearing different labeling; some brands were labeled for prescription sale, some for OTC distribution.[17] Under the FDCA's provisions at the time, manufacturers of products similar to those already holding FDA authorization could enter the market without notice to FDA if they

---

13 *Hearings Before the S. Subcomm. on Health of the Comm. on Labor & Public Welfare on S. 1186 and H.R. 3298*, 82d Cong. 9 (1951) (Statement of George P. Larrick, Deputy Comm'r of Food and Drugs, FDA).

14 *Id.* at 52 (Statement of Roy S. Warnack, Retail Druggist).

15 *Id.* at 49.

16 *Id.* at 50.

17 *Id.* at 6-7, 53 (examples of drugs being sold both prescription and OTC, including quinidine sulfate, theobromine with sodium salicylate, dehydrochloric acid, iron tablets, and tincture of hyoscyamus); H.R. REP. NO. 82-700, at 5-6 (1951).

concluded their products were "generally recognized as safe." These manufacturers were not bound to use the same labeling as the original manufacturer, but could market with either prescription or over-the-counter labeling.

- Lack of uniformity in labeling was deemed to be to the "detriment of the public, because in some instances they [we]re able to purchase drugs for self-medication, which they c[ould not] safely and properly so use, and harm . . . resulted. On the other hand, in some cases it unnecessarily prevent[ed] lay persons from buying drugs which they should [have] be[en] able to buy for self-medication."[18] It also contributed to the confusion among pharmacists. Drugs with identical active ingredients and dosages had different conditions imposed on their sale by their various manufacturers, making it difficult for pharmacists to determine how to properly dispense these drugs.

The Humphrey-Durham Amendments responded to these problems, "strengthen[ed] the protection of the public health against dangerous abuses in the sale of prescription drugs" and "relieve[d] retail druggists and the public from burdensome and unnecessary restrictions on the dispensing of drugs which may be safely used without supervision by a physician."[19]

2. FDA's Enhanced Authority Under Humphrey-Durham.

The specific authority Congress granted to FDA in the Humphrey-Durham Amendments in response to the concerns identified above is of critical importance to the disposition of the petition at issue. To determine whether and how to respond to a mandatory switch petition, the agency must look to the precise authority Congress provided in the statute itself.

- New Section 503(b)(1) directly addressed the protection of consumers from the dangers arising from OTC dispensation of drugs which could not safely be used without physician supervision. That section forbade the OTC sale of any drug which FDA determined "because of its toxicity or other potential for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except for under the supervision of a practitioner licensed by law to administer such drugs."[20]

---

[18] *Hearings Before the S. Subcomm. on Health of the Comm. on Labor & Public Welfare on S. 1186 and H.R. 3298*, 82d Cong. 7 (1951).

[19] *Id.* at 5.

[20] 21 U.S.C. § 353(b)(1); *see also* S. REP. NO. 82-946, *reprinted in* 1952 U.S.C.C.A.N. 2454, 2456. Section 503(b)(1) also initially barred OTC sale of habit-forming drugs subject to Section 502(d) and drugs determined to require prescription dispensing in a Section 505 application process. However, this provision was eliminated when Section 502(d) was amended in 1997.

Thus, where consumer safety was potentially jeopardized, FDA was given the power to restrict the method of dispensation for all manufacturers. In these circumstances, while Commenters recognize that Congress intended to limit manufacturer distribution discretion and consumer OTC access, they believe that this power should be used only when necessary and can be used only when scientific evidence supports the FDA's safety conclusion.

- New Section 503(b)(2), supplemented by Section 503(b)(4), addressed the problem of pharmacists needing guidance on how a drug could be lawfully marketed. Under Section 503(b)(2) and (4), a drug required by FDA to be marketed under prescription was required to have "Rx only" on its label, thus: (a) exempting it from any statutory duty to have adequate directions for consumer use and (b) making it unlawful for a pharmacist to dispense it without a prescription.[21] A drug not required by FDA to be dispensed under prescription could not bear the "Rx only" mark and could be sold OTC if the manufacturer supplied adequate instructions for consumer use. The instruction requirement was expressly made inapplicable to all prescription drug sales, including both those with "Rx only" on the label and those requiring prescription by manufacturer direction.[22]

Accordingly, the presence of the "Rx only" symbol advised pharmacists that FDA required a drug to be dispensed with a prescription so that the pharmacist could avoid the legal risks of selling it OTC. Although manufacturers choosing voluntarily to dispense by prescription could not use the "Rx only" symbol, they would have to label their drugs with FDA-approved prescription labeling,[23] and could not put pharmacists *in terrorem* with respect to selling identical drugs sold OTC because the absence of the "Rx only" symbol made it clear that OTC dispensation was FDA sanctioned.

- New Section 503(b)(3) addressed Congress' concern that consumer access to OTC medication not be unduly impaired. The section required FDA to reverse a Section 503(b)(1) determination that a drug be dispensed by prescription only through a rulemaking process "when such requirements are not necessary for the protection of the public health."[24] Thus, when new scientific evidence

---

21 21 U.S.C. §§ 353(b)(2); (b)(4).

22 *Id.* at § 353(b)(2), stating: "Any drug dispensed by filling or refilling a written or oral prescription of a practitioner licensed by law to administer such drug shall be exempt from the requirements of Section 502 [adequate directions for consumer use] . . . ." This definition applies to all drugs dispensed by a prescription, rather than only those required to be labeled "Rx only" under 21 U.S.C. § 353(b)(4)(A).

23 Pursuant to 21 C.F.R. § 201.100, prescription drug labeling – in lieu of adequate directions for consumer use – is required to contain adequate information for use of the drug at the dosage and for the indications recommended, prescribed or suggested in such labeling under which practitioners licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended.

24 21 U.S.C. § 353(b)(3).

> establishing that OTC dispensation would be safe came to FDA's attention, FDA, on request or at its own initiative, could remove mandatory prescription requirements. A removal of the requirement foreclosed manufacturers from applying the "Rx only" mark, so that pharmacists and other concerned individuals could be made aware that FDA no longer required prescription sale. Manufacturers were also free to propose OTC labeling since OTC distribution was no longer barred.[25] However, nothing in the section prohibited a manufacturer from continuing to limit distribution to prescription-only at its own discretion, as long as the drug continued to have approved prescription labeling.

Section 503(b), taken as a whole, created powerful pressures for uniform dispensation in response to the concerns raised about potential confusion. Where consumer safety was at issue, uniform prescription status could be mandated. Where safety issues did not preclude OTC sale, the prohibition against using "Rx only" in the labeling not only facilitated that sale but also permitted competitors, distributors and consumers to exert market leverage to force OTC labeling. As a consequence, Congress could reasonably conclude that multisource drugs not requiring prescription limitations by FDA almost certainly would be available OTC. Moreover, the exercise of manufacturer discretion to continue prescription distribution in single source situations would be without the government imprimatur conveyed by the "Rx only" symbol, and would neither cause safety concerns nor confusion at the pharmacy.

B. Mandatory Switching Is Not Authorized By Section 503(b)(3).

The "mandatory switching" relief sought by petitioner to force the drugs at issue to be dispensed OTC would require FDA to take three independent legal actions. However, the petitioner has not even suggested how FDA would accomplish two of the three, thus providing no legal basis for the mandatory switches it seeks. Moreover, were FDA to attempt the third, the agency would be acting unlawfully.

First, since the drugs at issue are currently under prescription and covered by Section 503(b)(1), FDA must determine that an "Rx only" requirement is "not necessary for the protection of the public health."[26] Since Section 503(b)(3) authorizes FDA to make this determination based on proper scientific evidence, petitioner's request that the agency take this particular step is properly before FDA.

---

[25] As with any rulemaking conducted pursuant to the Administrative Procedure Act, Commenters believe that FDA must give all interested persons access to the information on which FDA intends to rely. *See* 5 U.S.C. § 553; 21 C.F.R. § 10.40(b). To the extent FDA wishes to rely on manufacturers' proprietary files, FDA must resolve the concerns raised by Pfizer Inc and PhRMA under, *inter alia*, 18 U.S.C. § 1905. *See* Comments Submitted on Behalf of Pfizer Inc, Docket No. 98P-0610/CP1, May 11, 2001; Comments Submitted on Behalf of PhRMA, Docket No. 00N-1256, August 25, 2000.

[26] 21 U.S.C. § 353(b)(3).

Second, FDA would have to develop OTC labeling which would permit the drugs to be dispensed safely and effectively OTC in accordance with 21 C.F.R. § 314.70(b)(3). The plain language of Section 503(b)(3) addresses only the removal of drugs "from the requirements of [Section 503(b)(1)]." Neither that language nor FDA practice in past "switch" actions suggests that such removal by itself suffices to permit OTC distribution or to foreclose continued prescription distribution at the manufacturer's discretion. In fact, a 503(b)(3) determination is a necessary but not sufficient condition for an OTC distribution switch.[27] FDA's own regulations make clear that the Agency will not grant 503(b)(3) relief unless FDA is prepared to approve proposed OTC labeling.

> "Any drug limited to prescription use under section 503(b)(1)(C) of the act shall be exempted from prescription-dispensing requirements when the Commissioner finds such requirements are not necessary for the protection of the public health by reason of the drug's toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, and he finds that the drug is safe and effective for use in self-medication as directed in proposed labeling."[28] (Emphasis added).

The responsibility for proposing OTC labeling for a drug sold pursuant to an NDA under the FDCA and FDA's implementing regulations lies with its manufacturer.[29] In any event, the petitioner has made no labeling proposal and FDA (even assuming it had the requisite authority) has also not proposed a safe and effective OTC label. Thus, the Docket provides no legal foundation for permitting, let alone mandating, OTC sale.

Third, FDA would have to withdraw approval of the prescription labeling in the approved NDA, and somehow overcome the manufacturer's willingness to delete the "Rx only" legend but continue to sell only for prescription use in conformity with 503(b)(4). The mandated withdrawal of FDA approval for prescription labeling would require a determination that such labeling would not permit the drugs at issue to be dispensed safely and effectively.[30] That determination would seem impossible to make in circumstances where the petitioner claims that current methods of distribution are, if anything, too safe. Moreover, while a 503(b)(3)

---

[27] By contrast, a 503(b)(1) determination is both a necessary and sufficient condition for a mandatory switch from OTC to prescription status.

[28] 21 C.F.R. § 310.200(b).

[29] *See Id.* (requiring submission of proposed labeling for a switch in status); *Id.* at 314.70(b)(3) (requiring submission of a supplement by the NDA applicant before this labeling change can be made); *Id.* at 314.71(a) (specifying that only the NDA applicant can submit a supplement to its application). Thus, it is clear that only the NDA applicant can submit proposed labeling for approval.

[30] 21 U.S.C. § 355(e) (limiting FDA's ability to revoke approval for a drug to situations where new evidence indicates the drug is not safe or effective or the labeling is false or misleading).

determination would require the deletion of the "Rx only" legend to conform to Section 503(b)(4), there is no basis for finding that this deletion forecloses a manufacturer from establishing a legend stating that "manufacturer requires that this drug be dispensed only in accordance with a prescription from a licensed practitioner" or that doing so would impair the drug's safe and effective use. As described below, blocking such a legend would also conflict with other sections of the FDCA.

In short, petitioner's premise that Section 503(b)(3) provides a legal basis for mandatory switching is without merit. FDA has never ordered a switch over the objection of a manufacturer nor has it proceeded directly under 503(b)(3) when there was only one source for a drug.[31] Rather, FDA has awaited the voluntary filing of supplemental NDA's seeking OTC approval and the abandonment of prescription status, thus permitting the 503(b)(3) issue to be considered together with the question of whether OTC distribution can be authorized "as directed in proposed labeling."[32] FDA's mission to "protect the public health by ensuring that ... [such products] are safe and effective" for use as labeled[33] permits no more and demands no less.

III. FORCED SWITCHES CONFLICT WITH OTHER PROVISIONS OF THE FDCA.

In addition to the absence of legislative authority under Section 503(b)(3), the petitioner fails to consider the conflict between forced switches and other critical provisions of the FDCA. The Supreme Court has held that FDA must interpret the FDCA "'as a symmetrical and coherent regulatory scheme' and 'fit, if possible, all parts into an harmonious whole.'" *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000) (citations omitted). Thus, any reading of 503(b)(3) must harmonize with broader FDCA principles.

---

[31] Dennis Cauchon, *Why Allergy Drugs Cost So Much*, USA TODAY, Apr. 12, 2000, at 1A ("The FDA has never moved a drug to over-the-counter status unless a manufacturer made the request."); FDA, *Transcript of the Joint Meeting of Nonprescription Drugs Advisory Committee and Pulmonary-Allergy Drugs Advisory Committee,* at 69 (No. 98P-0610), *available at* http://www.fda.gov/ohrms/dockets/ac/01/transcripts/3737t1.rtf ("Blue Cross, a party with no legal or regulatory oversight responsibility has requested extraordinary action with respect to three distinct drug products .... Only once in the last 18 years has the FDA approved over-the-counter sales of a prescription drug without the support of the drug's maker. The FDA had, however, to switch the drug Alupent back to a prescription status shortly after it went OTC."). It should be further noted that Alupent's manufacturers, while not initiating the switch (FDA did so by publishing a notice of proposed rulemaking in the form of a tentative final monograph), did not oppose it, and in fact told FDA that they intended to market the product OTC. *See* 48 Fed. Reg. 24925 (1983).

[32] "FDA's Prescription to Over-the-Counter Drug Switch," *Hearing Before the Subcomm. on Oversight and Investigations of the Comm. on Energy and Commerce, House of Representatives*, 98th Cong., 1st Sess. (June 6, 1983), at 11 (testimony of Arthur Hull Hayes, Jr., Comm'r, FDA).

[33] 21 U.S.C. § 393(b)(2)(B).

A. Conflict With Section 505

Section 505 is the central vehicle through which new drugs come to market and the provision under which the drugs at issue were approved for prescription sale. Under Section 505(d), the FDA determines whether the manufacturer's proposed "use under the conditions prescribed, recommended or suggested in [its] proposed labeling" would be safe and effective. If those findings are made, the statute requires FDA to approve the application whether or not FDA would prefer different proposed conditions or methods of distribution.[34] FDA has the power to deny applications under 505(d) on safety and effectiveness grounds. It has no power to rewrite such applications or to refuse approval for other reasons.

Here, FDA has found that each of the drugs at issue under conditions of prescription labeling and use meet the criteria of Section 505 and has approved their sale in interstate commerce. The fact that FDA determines that sale under alternative conditions – *i.e.*, OTC labeling – also would be acceptable provides no lawful basis for modifying FDA's prior determination of safety and effectiveness.

In fact, Congress has specified the exclusive grounds for withdrawal of approval in Section 505(e) of the FDCA, which provides that FDA, "after due notice and opportunity for hearing to the applicant," may withdraw approval of an application if:

> (1) [a] drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) new evidence . . . shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) . . . there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; . . . or (5) . . . the application contains any untrue statement of material fact . . . . The Secretary may also . . . withdraw the approval of an application . . . if [he] finds . . . that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.[35]

The plain language of this provision does not give FDA the authority to withdraw approval for any of the drugs in this proceeding. A prescription drug approved as safe and

---

[34] *See Ass'n of American Physicians & Surgeons, Inc., supra* note 1 (finding it would take an Act of Congress to permit FDA to initiate and then mandate an indication for a drug product).

[35] 21 U.S.C. § 355(e).

effective based on the labeling submitted with its NDA can hardly be said to be unsafe for use based on its labeling or to lack effectiveness if the FDA finds it safe enough to switch to OTC status. Such labeling is also not "false or misleading;" a determination that a drug is safe for OTC use hardly makes approved prescription labeling false or misleading so long as the "Rx only" symbol is deleted. FDA thus lacks the legal authority to revoke approval for an NDA of a drug in an attempt to force an OTC switch.[36]

If Congress had intended the Humphrey-Durham Amendments to give FDA the power to override Section 505(e) and to force manufacturers to stop distributing a product by prescription once it was determined the drug was safe for OTC sale, Congress would have amended Section 505 of the Act as well as Section 503(b) and allowed revocation of an NDA's approval when a manufacturer – after FDA made an administrative determination that its drug was safe enough for OTC sale – refused to submit OTC labeling and sell that drug OTC upon approval of such labeling. As enacted, however, the Humphrey-Durham Amendments amended only Section 503(b); nowhere in the FDCA is FDA given authority to order how a manufacturer chooses to market a drug when there is no safety or efficacy problem. To allow it to do so here would be a major deviation from agency practice inconsistent with the FDCA's overall statutory scheme.

B. Conflict With Misbranding Authority

Congress gave FDA numerous bases upon which it could deem a drug misbranded and thereby foreclose its sale. The power given the agency to prohibit the sale of misbranded drugs provides strong incentives for drug manufacturers to modify their products' labeling in order to cure any problem perceived by FDA. Thus, were a 503(b)(3) determination sufficient to make a prescription drug misbranded, it could be argued that Congress had at least implicitly authorized mandatory switches. The misbranding provisions, however, cannot support this construction.

First, while Section 503(b)(4) denies continuing use of the "Rx only" legend to drugs not subject to 503(b)(1), manufacturers are not barred from alternative labeling under which they take responsibility for the prescription requirement – *e.g.*, "[Manufacturer] requires that this drug be dispensed only in accordance with a prescription from a licensed practitioner." Indeed, to the contrary, during its consideration of the Humphrey-Durham Amendments, Congress rejected a version of Section 503(b)(4) which would have barred non-503(b)(4) use of the "Rx only" legend "or [of] any other statement which represents or implies that the dispensing of the drug without the prescription of a licensed practitioner is prohibited."[37] In part, this action responded to the common sense point that if a drug can be "safely used without medical supervision, it may

---

[36] Moreover, even if FDA did use this provision to withdraw approval and attempt to force a switch, and prevailed in the hearing it is required to provide for the applicant, the remedy is to uphold FDA's withdrawal of approval – not to require the manufacturer to submit an application to market the drug by a distribution channel it does not want to use.

[37] *See* H.R. REP. NO. 82-700, at 2 (1951).

perhaps be better used with that supervision."[38] Thus, manufacturer-elected prescription dispensing requirements are clearly consistent with Section 503(b)(4).

Second, while Section 502(f) renders a drug misbranded if it does not have adequate labeling warnings "for the protection of users", prescription drugs are exempted from this requirement under 21 C.F.R. § 201.100 so long as adequate safety information is conveyed to licensed practitioners.[39] Thus, if a manufacturer maintains all labeling information presented to physicians prior to a Section 503(b)(3) determination and imposes its own clear prescription dispensation requirement, the drug continues to be eligible for exemption under Section 503(b)(2) and 21 C.F.R. § 201.100 and the drug is not misbranded.

In short, Congress's grant of misbranding authority was not designed, directly or indirectly, to permit FDA to mandate switches from prescription to OTC status.

IV. A VOLUNTARY SWITCH REGIME IS CONSISTENT WITH SOUND PUBLIC HEALTH POLICY.

The petition at issue makes it clear that FDA is being asked to act as a cat's paw for health insurers who seek to exclude allergy medications from their drug coverage. AAPS and CEI have no objection to insurers fashioning whatever drug coverage they believe will be efficient and sustainable in marketing their insurance product. Indeed, Commenters note that without FDA action, "many insurers, following the lead of WellPoint Health Networks, shrank or withdrew coverage for the entire class of non-sedating antihistamines" at issue in the petition.[40] To the extent, if any, that Section 503(b)(1) status inhibits insurers from making market decisions about drug coverage to be offered, FDA should allocate resources to determining whether the continuation of that status is scientifically justified under Section 503(b)(3). However, FDA should remain neutral with respect to coverage issues and permit the interplay of market forces between manufacturers, consumers and insurers to sort them out. Commenters are concerned that FDA, by presenting itself as a potential economic regulator, will retard the development of such market mechanisms.

Moreover, FDA has neither the legal authority nor the need to override manufacturer decisions on the desirability of physician practitioner supervision of a particular drug's use.

---

[38] *Hearings Before the S. Subcomm. on Health of the Comm. on Labor & Public Welfare on S. 1186 and H.R. 3298*, 82d Cong. 107 (1951) (statement of Charles Wesley Dunn, General Counsel, American Pharma. Manuf.'s Ass'n).

[39] While prescription drugs are not required to have adequate directions for use by a layman, they are required to be labeled with adequate information under which practitioners licensed by law can use the drugs safely and for the purposes they were intended. *See* 21 U.S.C. § 352(f)(1) (statutory requirement); 21 C.F.R. § 201.5 (general regulation); 21 U.S.C. § 353(b) (prescription drug exemption); 21 C.F.R. § 201.100 (prescription drug labeling requirement).

[40] Kritz, *supra* note 7, at HE01.

Manufacturers have powerful incentives to broaden consumer promotion and increase sales by switching from prescription to OTC dispensing. Indeed, if insurers use self help to avoid the artificial incentives arising from the difference between perceived consumer cost (*e.g.* "co-pay") and actual cost (*i.e.*, cost paid through insurance premium), FDA determinations under Section 503(b)(3) may have a powerful market impact. On the other hand, manufacturers may be more risk averse than FDA in evaluating safety issues,[41] particularly in a liability system where OTC labeling approvals are not necessarily preemptive,[42] unforeseeable risks may arise after OTC use commences[43] and damage awards can be monumental. Commenters believe that it is far more appropriate for at-risk manufacturers, rather than FDA, to make decisions on distribution alternatives which at least equally protect the interests in drug safety and effectiveness which FDA is charged with protecting.

Finally, even with regard to the availability and cost of drugs, a voluntary switch policy has much to offer in terms of flexibility in pricing and distribution systems. This flexibility is extremely important, given the incredibly high development cost of new drugs coupled with the drastically lower marginal cost of their production. That situation is aptly expressed by the cliché that, for a new medicine, the very first pill costs $500 million, while every pill after that costs ten cents a piece. If pharmaceutical companies are forced to sell their products at marginal cost, then their huge development costs will never be recouped and future drug development will be crippled.

Pharmaceutical manufacturers are just beginning to explore through Medicare discount cards differential pricing regimes which permit drugs to be sold at reduced prices to those whose limited means make their demand for such drugs highly elastic. In order to engage in such differential pricing, manufacturers need to be free to choose their distribution systems so that different segments of the market can be differentially addressed and government-managed arbitrage reduced. Prescription dispensing requirements are a useful tool for such purposes even in cases where the same active ingredient is made available OTC. By correctly interpreting Section 503(b)(3), FDA can permit this tool to be used where market forces make it appropriate. Continuing analysis of this type of pricing in the deregulated airline industry established its enormous potential for expanding use at advantageous prices for consumers.

---

41 *See, e.g.*, Press Release, Aventis Pharmaceuticals Inc., Aventis Pharmaceuticals Opposes Petition to Switch Rx Antihistamines to OTC, May 11, 2001, *at* http://www.aventispharma-us.com/main/0,1003,EN-US-28791-45481--,FF.html.

42 *See Motus v. Pfizer, Inc.*, No. 00-00298 (C.D. Cal. 2000) Sept. 3, 2002 Statement of Interest of the United States; *In re Paxil Litigation*, No. 01-07937 (C.D. Cal. 2002) Statement of Interest of the United States; *Dowhal v. SmithKline Beecham Consumer HealthCare, LP* (Cal.App.4th 2002) Statement of Interest of United States Food and Drug Administration; *Bernhardt v. Pfizer Inc.* (S.D.N.Y. 2000) Statement of Interest of United States Food and Drug Administration.

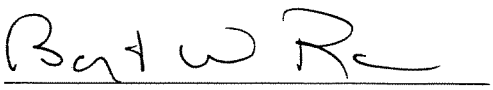
43 *See* Transcript of the Joint Meeting of Nonprescription Drugs Advisory Committee and Pulmonary-Allergy Drugs Advisory Committee, *supra* note 31, at 66-67 (statement of Dr. Francoise Nader, M.D., Senior VP, Medical and Regulatory Affairs, Aventis Pharmaceuticals, North America).

V. CONCLUSION

Through its petition, WellPoint is requesting that FDA take action that is beyond the agency's authority; FDA's mandate in this area is limited to protecting public health by ensuring that drug products are safe and effective for use as labeled. Section 503(b)(3), properly read, allows the agency to remove the prescription requirement for drugs; it does not give the agency control over manufacturers' distribution choices involving such drugs.

While AAPS and CEI believe FDA should not unnecessarily restrict manufacturers' ability to sell their products OTC, it is also their position that the agency should not go beyond its statutory mandate and engage in economic regulation. Accordingly, Commenters request that FDA make a threshold jurisdictional determination that the issue of mandatory switch is outside the proper bounds of these proceedings and continue on to a properly focused and prompt determination based on the scientific evidence presented in Docket No. 98P-0610/CP of whether the drugs at issue should be removed from the prescription dispensation requirements of Section 503(b)(3).

Respectfully submitted,



Bert W. Rein
Andrew S. Krulwich
Kristin I. Davis
WILEY, REIN & FIELDING LLP
1776 K Street, N.W.
Washington, D.C. 20006
Telephone: (202) 719-7000

Counsel for:

Association of American Physicians and Surgeons, Inc.
Competitive Enterprise Institute

Association of American
Physicians and Surgeons, Inc.
Andrew Schlafly, General Counsel
1601 N. Tucson Blvd. Suite 9
Tucson, AZ 85716-3450
Phone: (800) 635-1196

Competitive Enterprise Institute
Sam Kazman, General Counsel
1001 Connecticut Avenue, N.W.
Suite 1250
Washington, D.C. 20036
Phone: (202) 331-2265