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

RE: Docket Number 98P-0610/CP1

Dear Sir or Madam:

These comments are submitted to supplement the Citizen Petition dated July 22, 1998 submitted by Blue Cross of California, a subsidiary of WellPoint Health Networks Inc. ("WellPoint"). WellPoint's additional comments address the legal issues relating to the Food and Drug Administration's authority to switch drug products from prescription ("Rx") to over-the-counter status ("OTC").

Summary

On July 22, 1998, WellPoint (through its subsidiary Blue Cross of California) submitted a Citizen Petition requesting that the FDA remove the prescription exemption for three second-generation antihistamines: Allegra® and Allegra-D® (fexofenadine), Claritin® and Claritin-D® (loratidine), and Zyrtec® (cetirizine). On May 11, 2001, the FDA convened the Non-Prescription Drugs Advisory Committee and the Pulmonary - Allergy Drug Advisory Committee for a joint meeting and vote on whether the above three allergy drugs were safe and effective for OTC status. See 66 Fed. Reg. 17,431 (March 20, 2001). The two committees voted overwhelmingly that the data presented demonstrated that the 2nd generation antihistamine products were safe and that adequate directions for use by the lay public can be developed for OTC use.[1]

Despite the overwhelming votes by the scientific expert advisory committees that the safety data fully support an OTC switch for these products, there have been comments suggesting that either the FDA does not have the legal authority to initiate a switch of its own accord, or that for reasons not related to safety and effectiveness, the agency should choose not to initiate such a switch. However, an analysis of both the FDCA and FDA's implementing regulations demonstrate that not only does the FDA possess the statutory authority to initiate a switch, but under the FDA's regulations the Agency is **required** to initiate a switch when it finds that "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,

[1] The advisory committee's votes were 19-4 for Claritin and Zyrtec and 18-5 for Allegra.

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or the method of its use, or the collateral measures necessary to its use, and [the Commissioner] finds that the drug is safe and effective for use in self-medication as directed in proposed labeling." See 21 CFR § 310.200. The FDA acknowledged as much in its April 5, 2001, Memorandum on the Advisory Committee Meeting to Discuss OTC Antihistamines when it stated that it interprets the FDCA to mean, "any drug that can be used safely over the counter should be."

For the reasons explained below, because: (1) the safety and effectiveness of these 2nd generation antihistamine drug products have been examined by a committee of scientific experts and by overwhelming majority were found to be safe and effective for OTC drug use; (2) the FDA clearly possesses the statutory and regulatory authority; and (3) there has been ample opportunity for substantive public input and comment, the agency should, without due delay, initiate a switch from Rx to OTC status for these 2nd generation antihistamine drug products since the Rx exemption from adequate directions for use is no longer necessary for the protection of public health.

I. THE FEDERAL FOOD, DRUG, AND COSMETIC ACT ESTABLISHES A CLEAR MANDATE THAT ALL DRUG PRODUCTS MUST BE SOLD OTC UNLESS THEY MEET THE EXEMPTION CRITERIA FOR PRESCRIPTION CLASSIFICATION

Section 502(f) of the FDCA states that a drug is misbranded unless its labeling bears:

> (1) adequate directions for use; and
> (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users. . . .
>
> *Provided,* that where any requirement of clause (1) is not necessary . . . [FDA] shall promulgate regulations exempting [the product].

21 U.S.C. § 352(f). This section was passed in the original 1938 Act in order to protect the public from drugs that did not clearly explain their usage or potential dangers and required all such drugs to bear labeling that the lay public could understand. Although the Act has undergone significant changes since its passage in 1938, this provision has never been

removed. FDA regulations have documented this interpretation by defining "adequate directions for use" as "directions under which the layman can use a drug safely and for the purposes under which it is intended." See 21 CFR § 201.5. Thus, under this provision of the Act, all drug products, unless exempt, are to be labeled OTC with adequate directions for use for the average consumer.

Section 503(b) of the Act provides a definition of an Rx drug and then authorizes the exemption from the OTC labeling requirement for Rx drugs. This section reads:

> A drug intended for use by man which -
> (A) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug; or
> (B) is limited by an approved application under section 355 of this title to use under the professional supervision of a practitioner licensed by law to administer such drug;
>
> shall be dispensed only upon a written prescription of a practitioner licensed by law to administer such drug. . .
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> * * *
>
> 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 [adequate directions for use], if the drug bears a label containing the name and address of the dispenser, the serial number and date of the prescription or of its filling, the name of the prescriber, and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in such prescription.

21 U.S.C. § 353(b). This section provides a classification structure for Rx drugs, grants an exemption from OTC labeling requirements, and authorizes separate Rx labeling for products dispensed upon the prescription of a licensed practitioner.

Viewed in combination, these two sections unequivocally demonstrate that Congress intended that all drugs, unless exempted, bear directions for use that permit the lay consumer to use the drug safely OTC. An analysis of the legislative history of the Act further supports this analysis.[2]

Although today most new drugs that are approved under section 505 of the FDCA are exempted from the adequate directions for use provision because they are found unsafe for use except under the supervision of a medical practitioner and thus have the "Rx Only" designation, this longstanding statutory scheme and classification system has (1) served as the foundation for development of product labeling, (2) despite many changes to the FDCA, has never been removed or questioned by Congress; and (3) is only being questioned by certain factions of the pharmaceutical industry in the effort to prevent wide access to the 2nd generation antihistamines.

II. THE FDCA IS CLEAR IN ITS GRANTING OF THIS AUTHORITY TO THE FDA

A. The FDCA Clearly and Unambiguously Grants the FDA the Authority to Remove Drugs Subject to Section 505 From the Prescription Labeling Requirements

Section 503(b)(3) of the FDCA grants the agency the clear authority to remove drugs that have been approved by the new drug application ("NDA") process from the

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[2] Comments from the statement of Sen. Copeland shed light on what Congress was attempting to do, "There is no more common or mistaken criticism of this bill than that it denies the right to self-medication, or as the objector usually fit it, 'You can't take an aspirin tablet with a doctor's prescription.' Nothing could be further from the truth. The proposed law simply contributes to the safety of self-medication by preventing medicines from being sold as "cures" unless they are really cures . . . There must be plain and explicit directions for use, as well as warnings that in certain pathological conditions the use of drugs would not be safe. . . . When public health cannot be protected otherwise, the bill authorizes control through licensing. " 79 Cong. Rec. 4567 (1934) (reprinted in, CHARLES WESLEY DUNN, FEDERAL FOOD, DRUG, AND COSMETIC ACT: A STATEMENT OF ITS LEGISLATIVE RECORD 90 (FDLI 1987)). Sen. Copeland further stated, "It requires that all drugs bear explicit directions for use and appropriate warnings against their consumption by children or in certain disease conditions where the use is contra indicated and may be dangerous to health." Id. at 162.

Comments of Mr. Walter G. Campbell, Chief of the Food and Drug Administration of the Department of Agriculture, "But what is desired by this particular paragraph [requiring that the product bear the common name of the drug and the ingredients] and by others which impose restrictions on statements made about the remedial properties of the drugs is to make self-medication safe." Id.

prescription labeling requirement where it is no longer necessary to protect the public health. It states:

> [FDA] may by regulation remove drugs subject to section 505 [i.e., NDAs] from the requirements of paragraph (1) of this subsection [the prescription labeling exemption] when such requirements are not necessary for the protection of the public health.

21 U.S.C. § 503(b)(3).

This section of the Act was added in 195 1 by the Durham-Humphrey Amendment ("DH Amendment"). See ch. 578 § 1, 65 Stat. 648 (Oct. 26, 1951).[3] Congress passed the DH Amendment to give the FDA greater authority over the labeling of products which due to the circumstances of the time had created inconsistencies among similar or even identical products. Its stated dual purposes were to (1) protect the public from abuses in the sale of potent prescription drugs and (2) to relieve pharmacists and the public from unnecessary restrictions on the dispensing of drugs that are safe for use without the supervision of a physician. See Sen. R. No. 946 at 1, renrinted in 1951 U.S.C.C.A.N. 2454. The clear language of this statutory provision and its underlying purpose is applicable to the situation presented in the WellPoint petition, as it was to the situation that existed when the provision was promulgated in 195 1. In the instant situation, pharmacists and the public should be and would greatly benefit from being relieved from unnecessary restrictions on the dispensing of drugs, i.e., the 2nd generation antihistamines that are safe for use without the supervision of a physician.

B. When the Statute's Plain Meaning is Clear and Unambiguous the Analysis Stops

Under the well-established laws of statutory interpretation, when the statute is clear and unambiguous in its granting of authority, there is no need to conduct any further analysis. That is the case in the instant situation. The FDCA clearly grants the agency the

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[3] The 193 8 Act had set up a new drug application process whereby manufacturers would submit an NDA and unless FDA objected to the application, it would be deemed approved. Thus, the DH Amendment was passed during a period where many new drug applications had become effective by the NDA process. In addition to these drug "approvals," large numbers of products came onto the market as "me-too" versions of drugs already marketed, where manufacturers concluded on their own that their products were "generally recognized as safe." As a result of this system, at the time of the DH Amendment, it was not unusual to have numerous drug products, each with the same active ingredient, each bearing different labeling. In fact, it was not unusual for some products to be labeled as prescription while others with the same active ingredient were marketed as OTC.

authority to remove the exemption from adequate directions for use. When the plain meaning of the statute is clear and unambiguous, the inquiry must end.

Chevron Step I

Under Chevron U.S.A. Inc. v. Natural Resources Defense Council. Inc., 467 U.S. 837 (1984), courts employ a two-step test-in determining whether an agency has presented a permissible interpretation of a statute it administers. See id. at 842-43. First, courts consider the plain meaning of the statute. The plain meaning of a statute is derived from both the statutory language itself "as well as the language and design of the statute as a whole." See K Mart Corn. v. Carter. Inc., 486 U.S. 281,291 (1988); Bethesda Hosnital Ass'n. v. Bowen, 485 U.S. 399, 403-405 (1988). If the court determines that Congress has spoken to the precise question presented by the parties, the court must give effect to the unambiguously expressed intent of Congress. See Chevron, 467 U.S. at 842.

Congress clearly and unambiguously granted FDA the authority to remove the prescription exemption when it said "[FDA] may by regulation remove drugs subject to section 505. . ." It is difficult to imagine a more clear, concise, and unambiguous statement than section 503(b)(3) of the Act. The plain meaning of the statute makes it wholly unnecessary and inappropriate to look any further beyond the language of the statute.

C. Assuming Arguendo that the Statute is Ambiguous, the FDA's Interpretation is Followed as Long as It is Reasonable

Chevron Step II

Although the statute is clear on its face, assuming for the sake of argument that section 503(b)(3) is ambiguous in its granting of authority, the FDA's regulations at § 3 10.200 are a reasonable and permissible interpretation of the statute.

If a court determines that Congress has not spoken to the precise issue because "the statute is silent or ambiguous with respect to the specific issue," the court advances to the second step of Chevron. See Chevron, 467 U.S. at 843. Under Chevron step two, the court determines whether the agency's answer is based on a permissible construction of the statute. Id. Chevron step two is not invoked when the court first encounters a potential ambiguity:

> [G]iven that the judiciary remains the 'final authority on issues of statutory construction,' abdication of that authority and deference to an administrative construction is legitimate only where the court confronts a gap in the statute that cannot be bridged by traditional tools of statutory construction and which can properly be characterized as an express or implied delegation of authority by Congress to an agency.

See Abbott Lab. v. Young, 920 F.2d 984,995 (D.C. Cir. 1990) (Edwards, C. J., dissenting o.g.) (citing Chevron, 467 U.S. at 843 n. 9).

If, however, the court advances to Chevron step two, the court must defer to the agency's reasonable interpretation so long as it does not conflict with the statute's plain meaning. See K. Mart, 486 U.S. at 281. With respect to section 503(b)(3), although it is difficult to discern any ambiguity, to the extent there may be an ambiguity in the statute, the agency's regulatory interpretation in 21 CFR § 3 10.200 is clearly reasonable.

Given that statute is so clear and unambiguous on this issue it is not surprising that other comments have argued not that the statute does not grant FDA the authority, but rather that the statute does not really mean what it clearly says. Such arguments should be dismissed. Attempts have also been made to argue that the section is obsolete, or has been superseded. Such arguments are also without merit however, since Congress has several times made major alterations to the statute (including 1962, 1984, and 1997) which did not include or even contemplate removing this section. Further, whether an agency has used its power in the past has no bearing on whether it possesses that power in the first instance. See Jones Et Ex. v. Alfred H. Mayer Co., 392 U.S. 409,437 (1968); Sanders v. Dobbs Houses. Inc, 431 F.2d 1097 (5th Cir. 1970).

III. FDA'S IMPLEMENTING REGULATIONS GIVE IT CLEAR AUTHORITY TO REMOVE THE LABELING EXEMPTION FOR PRODUCTS THAT ARE SAFE FOR USE WITHOUT MEDICAL SUPERVISION AND IN FACT REQUIRE IT TO DO SO WHEN THE EXEMPTION IS NO LONGER NECESSARY

A. The FDA's Regulations Require the Agency to Switch a Product to OTC Status When Prescription Labeling Is No Longer Necessary for the Protection of Public Health and Authorize the Agency to Do So On Its Own Initiative

With a classification system where drugs are presumptively OTC, it is not surprising that the statute and FDA regulations permit the agency to switch a product from Rx to OTC status where Rx labeling is no longer necessary to protect the public health. In spite of several comments challenging this authority, not only does the statute permit FDA to make such an Rx to OTC switch, but the FDA's implementing regulations **require** that the FDA remove the prescription drug dispensing requirements when it finds the requirements are no longer necessary for the protection of public health. 21 CFR § 3 10.200 reads:

> [a]ny drug limited to prescription use [under the FDCA] 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. A proposal to exempt a drug from the prescription-dispensing requirements of section 503(b)(l)(C) of the act may be initiated by the Commissioner or by any interested person. Any interested person may file a petition seeking such exemption, which petition may be pursuant to part 10 of this chapter, or in the form of a supplement to an approved new drug application

21 CFR § 310.200 (emphasis added).

This regulation is consistent with the FDCA's granting of this authority in section 503(b)(3) and the Act's presumption that drug products should be available to consumers OTC if medical supervision is not required.

Certain comments have stated that the Kefavuver-Harris Drug Amendments ("KH Amendments") in 1962 fundamentally altered the FDCA so that section 503(b)(3) and its implementing regulations were rendered ineffective. This argument is belied by an examination of the history and timing of 21 CFR § 3 10.200. In fact, the regulation stating FDA shall switch products OTC when the agency finds the restrictions are no longer necessary was proposed in 1963, shortly after the passage of the KH Amendments. See 28 Fed. Reg. 1449 (February 14, 1963). This disputes any argument that the KH Amendments so altered section 503(b)(3) as to render them inoperative. Based on the final and proposed rule it is clear that FDA considered the KH Amendments consistent with their authority to mandate an Rx to OTC switch. The final rule published on June 20, 1963 is substantially similar to that which remains today.

The provisions of the final rule published on June 20, 1963 are set forth below:

> Any drug limited to prescription use under section 503(b)(l)(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 measure necessary to its use, and he finds that the drug is safe and effective for use in self-medication as directed from proposed labeling. A proposal to exempt a drug from the prescription-dispensing requirements of section 503(b)(l)(c) of the Act may be initiated by the Commissioner or by any interested person. Any interested person may file a petition seeking such exemption, stating reasonable grounds therefor, which petition may be in the form of a supplement to an approved new-drug application. Upon receipt of such a petition, or on his own initiative at anv time, the Commissioner will publish a notice of proposed rule making and invite written comments. After consideration of all available data, including any comments submitted, the Commissioner may issue a regulation granting or refusing the exemption, effective on a date specified therein.. . .

21 CFR § 130.101 (published at 28 Fed. Reg. at 6385 (June 20, 1963), (emphasis added).[4]

Thirteen years later, the FDA again opined on this regulation. In 1976, the agency published a final rule on the OTC review procedure found at Part 330. See 41 Fed. Reg. 32,580 (August 4, 1976). In the proposed rule the FDA outlined the two procedures "by which a prescription drug ingredient may lawfully be marketed for OTC use." See 40 Fed, Reg. 56,675 (December 4, 1975). In the preamble the agency explains:

> Prior to the OTC drug review, the procedures for obtaining approval to market a prescription ingredient as an OTC ingredient were by petition to the [FDA] following procedures set forth under § 3 10.200 . . . This procedure may be initiated by the Commissioner or by a petition from any interested person. . . .

Id. Section 3 10.200 clearly grants the FDA the authority for the type of switch requested by WellPoint and arguments that it is an obsolete provision are not supported by the FDA's actions and preambles to its regulations. Moreover, the FDA's regulations were promulgated through notice and comment rulemaking. The fmal regulations were adopted without any substantive comments from the industry or public. The only comments have come forth recently, after the expert advisory panel voted that the 2nd generation antihistamines are safe and can be adequately labeled for OTC use.

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[4] 21 CFR § 130.101 was re-codified by the agency in 1974 and is now § 310.200. See 39 Fed. Reg. 11,680 (March 29, 1974).

B. The Regulations Do Not Require that A Manufacturer Consent to a Switch in a Product's Status from Rx to OTC

The regulations require a medical, scientific and factual based inquiry to determine whether Rx labeling is required for the protection of public health. Once these protections are no longer medically/scientifically justified, the regulations specify they should be removed. For this reason, the regulations do not require that a switch be initiated by the drug manufacturer or that the manufacturer agrees to the proposal. Although for obvious reasons in such a situation it is preferable that the manufacturer concurs with the switch, there is no basis in either the regulations or the statute for a manufacturer to be permitted to ignore a determination that Rx labeling is no longer necessary for the product. Clearly, the manufacturers of Allegra, Claritin and Zyrtec have a right to be heard and submit data on the issue, but it is the FDA and not the drug manufacturers who have the final say on whether a product is safe and effective or in this case whether is a product is safe and effective for self-medication. Both Schering and Aventis were unable to specifically identify any safety concern or study, whether contemplated or underway, to address a safety concern with respect to the OTC marketing of the products. Two expert scientific advisory committees have reviewed the data, evaluated the issues presented by Pfizer, Schering, Aventis and the FDA, and voted overwhelmingly that Allegra, Claritin and Zyrtec are safe for OTC use.

IV. THE COMMENTS ARE INCORRECT WHEN THEY CLAIM THAT REMOVAL OF THE EXEMPTION IS A DEPRIVATION OF PROPERTY

A. Companies May Possess a "Property Right" in Their Approval and Proprietary Data

Several comments have argued that drug companies possess a "property right" in the ownership of a drug's approval and the data contained in the NDA. This fact is not disputed. The issue is whether the switch in labeling from Rx to OTC would be considered a regulatory "taking." It is clear that no court has ever found a government "taking" in a regulatory switch of a product's marketing status from Rx to OTC. This seems logical since in most cases such a switch is desired by the drug manufacturer because such a switch may lead to further exclusivity[5] and/or increased sales.

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[5] At the May 11,200 1 Advisory Committee meeting, Agency staff clearly stated that no additional information would be essential for approval of the switch. Thus, the companies would not be eligible for three years of market exclusivity under Section 505(j)(5)(D)(iv).

The Supreme Court has treated the issue of whether a taking has occurred as "essentially an 'ad hoc, factual,' inquiry. . . [but] has identified several factors that should be taken into account when determining whether a governmental action has gone beyond 'regulation' and effects a 'taking'." Ruckelshaus v. Monsanto Co., 467 U.S. 986, 1005 (1984). This examination entails inquiry into such factors as the "character of the governmental action, its economic impact, and its interference with reasonable investment-backed expectations." Id. A taking has been held to not only include an actually physical invasion of property but also an action the effect of which is to deprive the owner of all or most of his or her interest in the subject matter. See United States v. General Motors Corp., 323 U.S. 373 (1945). A switch in regulatory status of a drug from Rx to OTC is a "taking" is a novel legal argument, but ultimately meritless.

B. The Comments are Mistaken in Their Belief that the Removal of the Prescription Drug Exemption Would Constitute a "Deprivation of Property"

As noted above, a "takings" claim here would be predicated on the belief that a change in marketing status from Rx to OTC would constitute a "deprivation of property." It may be helpful here to note initially what changes the agency could require in order to effectuate a change, and conversely what types of changes the agency cannot compel under a switch.

Changes that would be required:

- removal of Rx designation;
- proposed labeling for OTC use

The status quo (i.e., things that would not be changed):

- FDA's decision would have no effect on the validity of the patents or any other exclusivity on the product (i.e., generic competition would not be introduced);
- FDA's decision would have no effect on the price at which the product may be sold;
- FDA's decision would not require FDA to disclose trade secret or privileged information;

Although no court has ruled on this specific issue, an examination of other takings clause cases that are similar demonstrates that a takings claim in this case has no merit. In the Ruckelshaus case cited above, the Monsanto Company objected to the Environmental Protection Agency ("EPA") using its safety data to evaluate another application for

registration. Ruckelshaus is easily distinguished from an Rx-to-OTC switch because in such a switch, the agency action does not involve using a company's "property right" for the benefit of another party. It is simply a change in the marketing status of the drug to be available without a prescription. Further still, in Ruckelshaus the Supreme Court determined that Monsanto, while possessing a property right in its data, did not have a takings claim where Monsanto was "aware of the conditions under which the data are submitted, and the conditions are rationally related to a legitimate Government interest, a voluntary submission of data by an applicant in exchange for the economic advantages of a registration can hardly be called a taking" Ruckelshaus, 467 U.S. at 1007. These "conditions" included the fact that the data could be used with out Monsanto's permission.

Similarly, a drug is marketed as an Rx drug only under certain conditions. If a drug no longer meets the conditions upon which an exemption from adequate directions for use was granted, it must be regulated as an OTC drug. As with Monsanto, this regulatory condition is well known by drug companies and often utilized to their benefit. Therefore, as in Ruckelshaus, it is no "taking" to change the regulatory status of a drug product, even if the drug company objects to the switch. To further support this position, it is also clear that the regulatory action has no effect on the companies' ability to market or sell the product. For these reasons it is clear that neither the character of the act, nor the economic impact, tit into the category of actions that would constitute a regulatory taking.

V. WHEN PROMULGATING REGULATIONS SPECIFICALLY RELATED TO THE REQUESTED REMOVAL OF THE PRESCRIPTION STATUS EXEMPTION, FDA IS NOT REQUIRED TO DISCLOSE INFORMATION THAT IS SUBJECT TO TRADE SECRET PROTECTION.

Comments have argued that under the APA, FDA must publicly disclose the data upon which any proposed rule is based. However, no trade secret data must be disclosed by FDA in order to promulgate a regulation removing the exemption from adequate directions for use. Of course, the general disclosure rules exempts the disclose of trade secret information.[6] It is well known that certain data and information in an NDA is trade secret protected.[7] However, these comments fail to note that much of the information contained in an NDA is not protected as trade secret information and in fact is disclosable

[6] See United States v. Nova Scotia Food Products Corn. 568 F.2d 240, 25 1 (2d Cir. 1977) (the general rule is that an agency disclose scientific material that is the basis of a rule making, but there is "an exception for trade secrets or national security").

[7] See 2 1 CFR § 20.6 1 for FDA's definition of "trade secret" and "commercial or financial information which is privileged or confidential."

under the Freedom of Information Act. See 5 U.S.C. § 552 et seq. Under 21 CFR § 3 14.430, the following information contained in an NDA is already made available to the public:

- the summary basis of approval;
- study protocols;
- adverse event reports;
- lists of inactive ingredients;
- assay methods; and
- correspondence and summaries of verbal communications with FDA.

Only information that qualifies as trade secret or commercial and financial information that is confidential is not able to be disclosed. This information would not be relevant in an Rx to OTC switch. What is most relevant here is primarily the adverse events reports concerning the three products. These reports demonstrate a low incidence of significant adverse reactions associated with the three drug products. FDA has reviewed the data and presented a summary of the data at the public advisory committee meeting held on May 11, 2001. This information is not trade secret protected.

Furthermore, what is relevant in this instance has already been narrowed by the agency. The agency has not raised any questions as to the effectiveness of the 2nd generation antihistamines for the relief of symptoms of allergic rhinitis. The only item at issue is whether the products are safe for OTC use. This is a much more limited inquiry than a full NDA approval. The issue of whether trade secret information needs to be disclosed in order to evaluate this matter has already been answered. The advisory committee members have fully examined the safety information provided by the agency and voted on May 11, 2001, by a overwhelming majority, that these products are safe for OTC use. This determination did not require the disclosure of trade secret information. There is no reason that FDA cannot promulgate its rulemaking without the disclosure of protected information.

VI. THE COMMENTS' CLAIM OF A LACK OF DUE PROCESS ARE INCORRECT IN THAT THE DUE PROCESS REQUIREMENT IS MET BY THE CITIZEN PETITION AND NOTICE AND COMMENT PROCEDURE

A. Section 505(e) of the FDCA Requires the FDA to Provide a Formal Hearing Only When the FDA is Seeking to Withdraw an NDA

Several of the comments to the docket claim that any "modification" of an NDA requires the agency to provide a formal hearing. However, the FDCA and the FDA's implementing regulations do not provide for a hearing for a "modification" of an NDA. In fact, both the statute and regulations provide for a hearing only when the FDA proposes to withdraw an NDA. The statute at section 505(e) states in pertinent part:

> [FDA] shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds . . .

21 U.S.C. § 355 (emphasis added). The statute then enumerates five different situations under which approval can be withdrawn. They are:

1. data shows that the drug is unsafe;
2. new evidence shows that the drug is not safe;
3. new information shows that the drug is not effective;
4. patent information was not timely filed; and,
5. the application contains an untrue statement of material fact.

Id.[8] If the FDA proposes to withdraw an NDA based on one of the above reasons, a formal evidentiary hearing is required. However, the statute does not require a hearing for a proposal to modify an application, i.e., a change from Rx to OTC status or for any other change to an application other than withdrawal. As the FDA is not proposing to withdraw approval of any of these products, section 505(e) is inapplicable.

B. Arguments that the Administrative Procedure Act ("APA") Requires a Formal Hearing are Incorrect and Further, Any Due Process Concerns Are Adequately Addressed In The Notice And Comment Procedure Utilized In This Process

Several comments have argued that the APA, 5 U.S.C. § 551 et seq., itself provides an independent source of authority for a hearing were the FDA to initiate a switch of a product from Rx to OTC. However, a close examination of the provisions of the APA and relevant case law demonstrate that this is not correct.

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[8] FDA's regulations at 21 CFR § 3 14.150 provide a hearing only for situations where the agency has proposed to withdraw an application.

Assuming first that an NDA meets the requirements for a "license," [9] section 558 of the APA provides that, "except in cases of willfulness or those in which public health, interest, or safety requires otherwise, the withdrawal, suspension, revocation, or annulment of a license is lawful only if, before the institution of agency proceedings therefor, the licensee has been given notice . . . and opportunity to demonstrate or achieve compliance with all lawful requirements." 5 U.S.C. § 558. Again it is clear that the switch of a product from Rx to OTC does not constitute the "withdrawal, suspension, revocation, or annulment" of a license. Therefore this provision of the APA is not applicable.

Under the APA an agency may act through either rulemaking or adjudicatory procedures. In adjudication, a formal hearing on the record is required. The adjudication procedures are defined in section 554 of the APA. The adjudication provisions apply, "in every case of adjudication reauired bv statute." See 5 U.S.C. § 554(a) (emphasis added). However, the APA in itself "imposes no requirement of an adversary hearing before an agency, but only specifies the procedure to be followed when a hearing is required by some other statute." See Conley Electronics Corp. v. FCC, 394 F.2d 620 (10th Cir. 1968); see also Democratic Nat'1 Committee v. FCC, 460 F.2d, 891,912 (D.C. Cir. 1972) ("Since there is no requirement of a hearing under the Communications Act this section of the APA is clearly inapplicable"); Joseph E. Seagram & Sons. Inc. v. Dillion, 344 F.2d 497, 501 (D.C. Cir. 1965). Since the FDCA does not provide for a hearing in this instance, and in fact specifies that the agency may "by regulation," remove the prescription exemption, no hearing is required in this case.

In any event, issues of due process, and notice and comment are dubious since the Citizen Petition requesting this action has been pending for three years and no party can claim to not have had an opportunity for its voice to be heard. Moreover, there has been ample opportunity to provide input and comment through the public Advisory Committee meetings that have been held to hear discussion of the issues. One can only surmise what type of information the drug companies would provide at a hearing that has not already been provided to the agency. One wonders whether it is due process at issue or due delay. To the extent that due process is at issue, the notice and comment procedure that FDA is required to perform is sufficient to meet those demands.

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In conclusion, under the Food, Drug, and Cosmetic Act and FDA's implementing regulations the FDA clearly possesses the statutory authority to initiate a switch and under

[9] A "license" is defined as "a whole or a part of an agency permit, certificate, approval, registration, charter, membership, statutory exemption or other form of permission." 5 U.S.C. § 551(8).

FDA's regulations, the agency is **required** to initiate a switch when the Rx only requirement is not necessary for the protection of the public health. The statutory and regulatory scheme has been in effect for a very long time and has served to protect the health and safety of the public. The Advisory Committees fully evaluated the scientific evidence and overwhelmingly voted that Allegra, Claritin, and Zyrtec are safe and can be adequately labeled for use by the lay public.

The undersigned hereby again requests that the agency immediately initiate a switch from Rx to OTC status for the 2nd generation antihistamine drug products since the Rx exemption from adequate directions for use is no longer necessary for the protection of public health.

Respectfully submitted,

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