

May 11, 2001

Comments

**Submitted to the Advisory Committee Meeting
Convened to Consider the Prescription/Nonprescription
Status of Three Second Generation Antihistamines**

On Behalf of Pfizer, Inc.

**In Response to the Citizen Petition Filed by
Blue Cross of California
Docket No. 98P-0610/CP1**

62 Fed. Reg. 17431 (March 30, 2001)

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May 11, 2001

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Re: Citizen Petition 98P-0610/CP1
Blue Cross of California
Prescription/Nonprescription Status of Three Second Generation Antihistamines
62 Fed. Reg. 17431 (March 30, 2001)

These comments are submitted on behalf of Pfizer, Inc. on Citizen Petition 98P-0610/CP1, filed by Blue Cross of California, which requests that the Food and Drug Administration (FDA) convert from prescription to nonprescription status three different drugs – fexofenadine hydrochloride, loratadine, and cetirizine hydrochloride – each marketed by a single manufacturer under an approved new drug application (NDA).

SUMMARY

Zyrtec is a second generation prescription antihistamine manufactured and marketed by Pfizer. FDA approved Pfizer's new drug application for Zyrtec Tablets in December 1995 and for Zyrtec Syrup in September 1996. One of the conditions set out in the approved NDAs is the inclusion of the following prescription legend in the labeling

of the products: "Caution: Federal law prohibits dispensing without a prescription."¹ On March 30, 2001, FDA requested comment on a citizen petition filed by Blue Cross of California requesting that FDA modify the NDAs for Zyrtec and two other so-called second generation antihistamines to delete the prescription legend from the approved labeling of these products.²

Blue Cross of California did not identify the procedure by which the three proposed switches from prescription to nonprescription status could be accomplished. As explained below, however, section 505(e) of the FD&C Act explicitly requires FDA to provide notice and an opportunity for a formal evidentiary public hearing under 21 C.F.R. part 12, whenever it modifies or withdraws an approved NDA. Moreover, even if there were no section 505(e) in the FD&C Act, general principles of administrative law and constitutional due process would require FDA to provide an opportunity for an evidentiary hearing before it may modify an NDA without the owner's consent. Finally, the switch of a prescription drug to nonprescription status would require the use, consideration, and under the Agency's regulations governing rulemaking, the disclosure of proprietary information in the owner's NDA. Such disclosure would violate section

¹ Section 503(b)(1) of the FD&C Act limits certain drugs to prescription use, including any drug that is not safe for use except under the physician's (or other licensed professional's) supervision and any drug that is limited to prescription status by an approved NDA. 21 U.S.C. § 353(b)(1).

² 62 Fed. Reg. 17431 (March 30, 2001). The Citizen Petition does not mention Zyrtec Syrup, but FDA has indicated its response to the petition will address both Pfizer products. Memorandum to Nonprescription Drugs Advisory Committee and Pulmonary Allergy Drugs Advisory Committee Members, Consultants, and Guests, from OTC Antihistamine Review Team (April 5, 2001).

301(j) of the FD&C Act and the Trade Secrets Act, and effect a taking in violation of the Fifth Amendment to the United States Constitution.

I. **A New Drug Application Contains Confidential and Proprietary Information, and Its Approval Confers a Private License to the Applicant.**

Section 505(a) of the FD&C Act provides that no new drug may be marketed prior to FDA approval of a new drug application containing full reports of clinical and animal investigations demonstrating that the product is safe and effective (or, after the first NDA is approved and all patent and marketing exclusivity has expired, approval of an abbreviated new drug application (ANDA) showing bioequivalence to the already-approved product).³ FDA regulations in 21 C.F.R. part 314 specify the required contents of a new drug application. These include: a description of pharmacology and toxicology studies in animals and the laboratory; a description of human pharmacokinetic and bioavailability studies; a description of human pharmacology studies; a description of controlled and uncontrolled clinical studies of safety and effectiveness; statistical evaluation of the clinical data; pediatric use information; information on the drug's chemistry and the manufacturing and analytical testing processes; and proposed labeling with recommended indications for use, dosages, warnings, prescription status, and other information.⁴

³ 21 U.S.C. § 355(a). A "new drug" is one that is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested by the manufacturer in its labeling. FD&C Act § 201(p), 21 U.S.C. § 321(p).

⁴ 21 C.F.R. § 314.50.

The information in an NDA is highly confidential and would be of tremendous value to competitors if disclosed. Since 1980, the average number of clinical trials conducted to support an NDA has more than doubled, and the number of patients in clinical trials per NDA has increased threefold.⁵ A typical NDA reaches hundreds of thousands of pages, and discusses dozens of clinical trials involving thousands of patients. Average drug development time has increased from eight years in the 1960s to nearly fifteen. Competitors might use the information in a company's NDA to guide their own research efforts for the development of competing drugs and use the data to support their own NDAs. For example, competitors could determine which study designs were successful and which were not, thereby saving the time and money invested by the original applicant. Maintaining the confidentiality of information in an NDA is thus essential to prevent competitors from free-riding on the data developed at great expense by the sponsor.

FDA's role, when it receives an NDA, is to review the submission and determine whether the product is safe and effective under the conditions prescribed or recommended by the manufacturer in the proposed labeling. Congress, FDA officials and staff, and the federal courts have confirmed the basic proposition that a manufacturer is the "owner" of its new drug application. When Congress enacted the FD&C Act in 1938, it emphasized this point by explaining that a new drug could not be marketed

⁵ Pharmaceutical Research and Manufacturers Association, Pharmaceutical Industry Profile 2000 <www.pharma.org/publications/publications/profile001> (visited May 5, 2001) (Industry Profile).

"unless the manufacturer has submitted full information showing that the drug has been adequately tested and has not been found to be unsafe for use under the conditions prescribed in the labeling."⁶ A 1976 House Report, discussing a proposal that FDA approve a particular product for a particular indication even though the Agency had not received an NDA for that use, explained: "when Congress enacted the new drug provisions of the Act, it desired to place the responsibility for initiating the NDA process solely on the drug manufacturer."⁷

In 1992, when discussing the limits on FDA's ability to require manufacturers to seek pediatric indications, Commissioner David Kessler remarked, "I need to acknowledge the limits of FDA's authority. It is our job to review drug applications for the indications suggested by the manufacturer. We do not have the authority to require manufacturers to seek approval for indications which they have not studied."⁸ Another FDA official wrote previously that:

⁶ H.R. Rep. No. 75-2139, at 9 (1938); see also H.R. Rep. No. 87-2464, at 8 (1961) (explaining that under the 1938 law a "new drug" is one "which is not generally recognized among qualified experts as safe for use under the conditions recommended in its labeling") (emphasis added); H. R. Rep. No. 87-2464, at 3 (1962) (revised provision section 355 "would require all new drugs to be proved effective as well as safe for use under the conditions prescribed, recommended or suggested in the labeling, before they may be marketed") (emphasis added).

⁷ H.R. Rep. No. 94-787, at 37 (1976).

⁸ Remarks by David A. Kessler, MD, at the Annual Meeting of the American Academy of Pediatrics (October 14, 1992), at 1. Although FDA subsequently promulgated a rule purporting to require manufacturers to perform pediatric testing, 63 Fed. Reg. 66632 (December 2, 1998), a legal challenge to that rule is pending in federal court. Association of American Physicians and Surgeons v. FDA (#00-CV-2898) (D.D.C., filed December 4, 2000).

It should be noted that the burden of proving the safety and effectiveness of a new drug – or of new uses of an already approved drug – rests on the manufacturer. It is the manufacturer who chooses the indications to be investigated and determines the dosage level for which he will seek FDA approval. It is the duty of the Food and Drug Administration under the law to decide that proposed dosages and levels are both safe and effective, based on the data submitted by the manufacturer.⁹

The federal courts have confirmed that FDA is limited to assessing the safety and effectiveness of a new drug under the conditions proposed by the manufacturer in the drug's labeling. Thus the United States Court of Appeals for the D.C. Circuit wrote, in a decision sustaining FDA's refusal to assert jurisdiction over cigarettes, that: "The manufacturer of the article, through his representation in connection with its sale, can determine the use to which the article is to be put."¹⁰

When FDA approves a new drug application, it grants the sponsor a license to market the product in question, provided the product is manufactured and labeled in accordance with the NDA. In a 1940 interpretation of the FD&C Act, Ashley Sellers, who as the staff attorney for the Department of Agriculture's Office of the Solicitor was responsible for advising on implementation of the Act, described NDAs as licenses, the "distinguishing characteristic" of which "is the presence of some form of prior approval before a private party may engage in a particular activity or utilize a

⁹ John Jennings, MD, "The Rx Label: Basis for All Prescribing Information," 1 FDA Papers 15-16 (November 1967).

¹⁰ Action on Smoking and Health v. Harris, 655 F.2d 236, 238-239 (D.C. Cir. 1980), quoting S. Rep. No. 74-361 at 4 (1935).

particular thing for a certain purpose."¹¹ Ever since, FDA has consistently characterized approved applications as licenses. For example, in its final FOI regulations published in 1974, FDA distinguished between food additives and new drugs on the basis that the former are subject to "public regulations rather than private licenses."¹²

II. Before FDA May Modify an NDA for a Prescription Drug to Require Labeling for Nonprescription Sale without the Owner's Agreement, FDA Must Provide the NDA Owner an Opportunity for a Formal Evidentiary Hearing.

Section 505(e) of the FD&C Act prescribes the procedure FDA must follow to modify or withdraw an approved new drug application. This provision expressly requires an opportunity for a formal evidentiary hearing. Even if there were no section 505(e), general principles of administrative law and constitutional due process would require FDA to offer the NDA owner a formal evidentiary hearing before modifying the NDA without its consent.

A. Section 505(e) of the FD&C Act requires FDA to provide an NDA owner an opportunity for a formal evidentiary hearing before the Agency modifies the NDA without the owner's consent.

Section 505(e) of the FD&C Act governs any FDA action to modify or withdraw an approved new drug application. This provision requires FDA to afford "due

¹¹ Ashley Sellers & Nathan D. Grundstein, Administrative Procedure and Practice in the Department of Agriculture Under the Federal Food, Drug, and Cosmetic Act of 1938 62 (1940).

¹² 39 Fed. Reg. 44602, 44631-44632 (December 24, 1974).

notice and opportunity for hearing" to the NDA holder, before withdrawing approval "of an application with respect to any drug" subject to section 505.¹³

When section 505(e) was originally enacted in 1938, contemporaneous Agency interpretation explained that hearings are required whenever the Agency adjudicates the status of an individual license. Ashley Sellers (who, as noted above, advised the Department of Agriculture unit responsible for implementing the Act) explained that Section 505 imposes a hearing requirement in proceedings affecting NDA licenses because of the particular nature of the inquiry and the particular impact on the NDA holder.

The point that the hearing is obviously quasi-judicial in character needs no belaboring since the proceeding is concerned with the refusal of a license. The order issued following a hearing has no general effect, but is confined to the parties to the new drug application involved in the proceedings. The statutory provisions for due notice and hearing are intended to furnish a basis of fact upon which the order of refusal is to be issued. Even if these procedural formalities were not required by Section 505, there is ground to believe that they would be necessary because of the constitutional requirements of "due process of law" Were it otherwise the procedure would be a rule making rather than an adjudication.¹⁴

¹³ 21 U.S.C. § 355(e). When enacted in 1938, Section 505(e) authorized FDA to suspend "[t]he effectiveness of an application with respect to any drug . . . after due notice and opportunity for hearing to the applicant." 52 Stat. 1040, 1053.

¹⁴ Sellers & Grundstein, *supra* note 11, at 102-03. Contemporaneous and longstanding interpretations of a statute are entitled to great weight. E.g., NRLB v. Boeing, 412 U.S. 67, 74-75 (1973); New Mexico Envtl. Improvement Div. v. Thomas, 789 F.2d 825, 831-32 (10th Cir. 1986).

When Congress amended the FD&C Act in 1951, it confirmed the requirement that individual licensing proceedings require adjudicatory processes. Congress added section 503(b)(3) to the statute to give FDA the authority to use rulemaking procedures to switch active ingredients in narrowly described circumstances – i.e., where the same active ingredient is marketed by different manufacturers for both prescription and nonprescription sale.¹⁵ Members of Congress pointed out repeatedly that the only alternative under the FD&C Act would have been for FDA to initiate a proceeding for misbranding against the individual drugs in question.¹⁶

In enacting the Drug Amendments of 1962, Congress again confirmed the requirement that FDA may proceed against an individual NDA only after providing the

¹⁵ As explained below on pages 22-28, section 503(b)(3) was not intended to be used and has never been used to switch a single drug subject to an NDA over the objection of the NDA holder.

¹⁶ E.g., 97 Cong. Rec. 9241 (July 31, 1951) (on the introduction of the bill) ("The Federal Security Administrator has authority under present law to proceed against one or the other of the manufacturers in the case the gentleman just referred to, proceed for mislabeling.") (Rep. Bennett); *id.* ("If he were proceeding there would be many, many proceedings at this time . . . it is because of the multitude of proceedings that would have to be instituted almost right now that we are undertaking to help straighten out this problem.") (Rep. Beckworth); 97 Cong. Rec. 9322 (August 1, 1951) ("Under the present law the Food and Drug Administration brings a suit for misbranding and in the course of such suit the court determines whether a particular drug is a prescription drug or an over-the-counter drug. Why is it desirable to change the law in this respect and to give the Federal Security Administrator power to determine which are prescription drugs and which are over the counter drugs? There are approximately 30,000 drug items which could require 30,000 lawsuits to determine under the present law which are prescription drugs and which are over-the-counter drugs.") (Rep. Wolverton); *id.* at 9347 ("If you are going back to the question of letting criminal procedures and seizures and injunctions determine it, you have 80 district courts in this country. You know and I know, with the jury system, it is utterly impossible to insure any consistency through that procedure. You will have one case decided one way and another decided in another way, and we would never have an end to it.") (Rep. Heselton).

holder an opportunity for a formal evidentiary hearing. Congress redefined "new drug" as one that is not generally recognized by experts as safe "and effective" for its intended use, and replaced premarket notification with premarket approval for all drugs. It also re-enacted and reaffirmed the hearing requirement in section 505(e). The withdrawal provision was revised to include additional substantive grounds for withdrawal, but the hearing requirement was left in place. On the few occasions the withdrawal provision was discussed, the requirements of a formal hearing and an administrative order were always reaffirmed.¹⁷

FDA's implementation of the Act's new effectiveness standard in the Drug Efficacy Study Implementation (DESI) program confirmed the Agency's understanding of the evidentiary hearing requirement. The 1962 Amendments required FDA to review the effectiveness of all new drugs introduced into the United States market under pre-

¹⁷ E.g., 107 Cong. Reg. 5641 (Daily Ed., Senate, April 12, 1961) ("Paragraph (e) provides for a public hearing upon objections by an applicant or licensee to a refusal to license or the suspension or revocation of a license within 30 days after notice by the Secretary of such action by him.") (Sen. Kefauver, introducing S. 1552); 108 Cong. Rec. 15238 (Daily Ed., House, August 13, 1962) ("This bill authorizes the Secretary, when he finds that there is substantial doubt as to a new drug's effectiveness or safety, to give the applicant due notice and opportunity for a hearing on the question of withdrawing approval of the application by order.") (Speech on H.R. 11581 by John L. Harvey, Deputy Commissioner, Food and Drug Administration, read into the record at the request of Rep. Harris); 108 Cong. Rec. 16304 (Daily Ed., Senate, August 23, 1962) ("Withdrawal of approval of any new drug application on the basis for the foregoing grounds would be preceded by a hearing and an order with findings on the basis of the record.") (Sen. Eastland, discussing S.1552 as reported by the Committee on the Judiciary on July 19, 1962); see also 108 Cong. Rec. 19891-19892 (Daily Ed., House, September 27, 1962) (Rep. Harris, explaining that amendment of the withdrawal provision entailed the addition of a new ground for withdrawal).

1962 NDAs.¹⁸ Pursuant to a contract with FDA, the National Academy of Sciences (NAS) reviewed the safety, effectiveness, and appropriate labeling of nearly 4000 drugs with NDAs that had become effective prior to 1962.¹⁹ In addition to the products with effective NDAs, thousands of similar or "me too" formulations had entered the market as "old drugs." Their manufacturers had concluded independently that the drugs were "generally recognized as safe" (GRAS) either because an NDA was in effect for a version manufactured by another company or because they had obtained FDA's agreement that the drug was GRAS.

In 1968, FDA announced that it would apply the NAS findings not only to the pioneer drugs subject to NDAs, but also to subsequently-marketed "me too" drugs. In other words, it chose to proceed against the pioneer and follow-on drugs together as one "class." When a few manufacturers successfully challenged the Agency's withdrawal of approval for their NDAs without providing an opportunity for a formal evidentiary hearing,²⁰ FDA responded by promulgating regulations that defined the showing that an NDA holder or the manufacturer of any generic copy would have to make to avoid summary judgment. The Agency's response acknowledged its obligation to provide a

¹⁸ 76 Stat. 781, 788.

¹⁹ See National Academy of Sciences, Drug Efficacy Study: Final Report to the Commissioner (1969).

²⁰ E.g., USV Pharmaceutical Corp. v. Secretary of HEW, 466 F.2d 455 (D.C. Cir. 1972) (overturning FDA withdrawal of approval for bioflavonoid drugs); Upjohn Co. v. Finch, 303 F.Supp. 241 (W.D. Mich. 1969) (enjoining FDA from withdrawal approval of Panalba without first ruling on firm's request for a formal evidentiary hearing); American Home Products v. Finch, 303 F.Supp. 241 (W.D. Mich. 1969) (same).

formal evidentiary hearing to any class member who could demonstrate a genuine dispute of material fact.²¹

B. General principles of administrative law and constitutional due process require FDA to provide an opportunity for an evidentiary hearing before it modifies an NDA over the owner's objection.

The switch of any NDA'd drug from prescription to nonprescription status constitutes modification of the license for that drug. Accordingly, general principles of administrative law and constitutional due process would require FDA to provide notice and to offer to hold a formal evidentiary hearing.

Due process analysis begins with two questions. First, a court will determine whether the claimant has a cognizable property right. As discussed above, an approved NDA is a license to market a drug product on the terms agreed to by the license holder. Government-issued licenses are property.²² Second, the court will determine whether the government's proposed action represents a deprivation of property. Government-initiated modification (or revocation) of a license is a cognizable "deprivation" of property for due process purposes.²³ If the government threatens to

²¹ FDA required any manufacturer seeking such a hearing to submit at least two adequate and well-controlled clinical investigations. This would constitute a threshold showing of "substantial evidence of effectiveness" and entitle the manufacturer to a formal evidentiary hearing. 34 Fed. Reg. 14595 (September 19, 1969).

²² E.g., Barry v. Barchi, 443 U.S. 55 (1979) (horse trainer's license); Bell v. Burson, 402 U.S. 535 (1971) (driver's license); Industrial Safety Equip. Ass'n, Inc. v. EPA, 837 F.2d 1115, 1122 (D.C. Cir. 1988) ("There is no question that appellants possess cognizable property interests in their respirator certifications.").

²³ Committee for Effective Cellular Rules v. FCC, 53 F.3d 1309, 1318 (D.C. Cir. 1995) ("Obviously, the FCC cannot, merely by invoking its rulemaking authority, avoid the adjudicatory procedures required for granting and modifying individual licenses.").

deprive a pharmaceutical manufacturer of its protected property right in an approved NDA, therefore, due process applies.

In determining what process is due, courts begin with the framework set out by the Supreme Court early in the last century in Londoner v. Denver²⁴ and Bi-Metallic Inv. Co. v. State Bd. of Education.²⁵ In Londoner, the city of Denver undertook municipal improvements and the city council apportioned the cost of those improvements among the property owners specially benefited. Although the city council allowed the affected taxpayers to file written complaints, it enacted an ordinance of assessment without any hearing after complaints had been filed. One taxpayer challenged the tax imposed on his property, claiming that the failure to afford him a hearing violated the fourteenth amendment.²⁶ The Supreme Court found that the taxpayer was entitled to a hearing, because the city had designated the specific amount of the tax that he and other named property owners would pay, in light of a specific benefit they received. The council's decision was not a general tax assessed on all residents of the city.²⁷

In Bi-Metallic, decided a few years later, the Colorado Tax Commission and State Board of Education increased the valuation of all taxable property in Denver by forty percent. An owner of real estate brought suit under the fourteenth amendment due

²⁴ 210 U.S. 373 (1908).

²⁵ 239 U.S. 441 (1915).

²⁶ 210 U.S. at 373.

²⁷ Id.

process clause, demanding a hearing prior to the assessment of the city-wide tax.²⁸ The Court found that because of the general applicability of the tax, no single individual was entitled to an adjudicatory hearing.²⁹ Justice Holmes distinguished the Court's earlier decision: "In Londoner v. Denver, a local board had to determine 'whether, in what amount, and upon whom' a tax for paving a street should be levied for special benefits. A relative small number of persons was concerned, who were exceptionally affected, in each case upon individual grounds, and it was held that they had a right to a hearing. But that decision is far from reaching a general determination dealing only with the principle upon which all the assessment in a county had been laid."³⁰

The Supreme Court clarified and reaffirmed the distinction again in a 1973 case: Londoner and Bi-Metallic "represent a recognized distinction in administrative law between proceedings for the purpose of promulgating policy-type rules or standards, on the one hand, and proceedings designed to adjudicate disputed facts in particular cases on the other."³¹ A decision that one particular drug subject to an NDA must be switched from prescription status to nonprescription status is more analogous to the action at issue in Londoner than the action at issue in Bi-Metallic. It is a decision about the status of a specific party's property – an NDA – reached on the basis of the unique features of that property – the safety and effectiveness profile of the drug.

²⁸ 239 U.S. at 445.

²⁹ Id.

³⁰ Id. at 445-446 (citation omitted) (emphasis added).

³¹ United States v. Florida East Coast Ry. Co., 410 U.S. 224, 245 (1973).

In applying Londoner and Bi-Metallic, courts have identified several factors to be considered in determining whether an administrative body must provide an adjudicatory hearing. An agency must generally provide a hearing if its decision: (1) requires a review and analysis of facts that are unique and specific to a particular entity or event; (2) applies only to, or targets, a particular entity or group; or (3) places a particularized burden on a specific entity or group. A decision that a prescription new drug must be relabeled for nonprescription sale over the objection of the sole marketer of the drug owner would: (1) require review and analysis of facts pertaining only to that drug, (2) apply only to that NDA, and (3) impose a particular burden on the NDA owner.

Factual Inquiry Specific to a Particular Drug. The decision to switch a drug subject to an NDA from prescription to nonprescription status would require review and analysis of facts pertaining uniquely to that drug. In assessing whether a hearing is required, courts focus on whether the agency's decision requires the determination of adjudicatory facts – facts that are "peculiar to" an individual or entity. In Air Line Pilots Assoc. v. Quesada,³² the Second Circuit sustained an FAA decision to forbid pilots over the age of 60 from flying for commercial airlines. The court explained that the decision could be made through rulemaking rather than adjudication, because it was generally applicable.³³ By contrast, the decision would have required adjudicatory procedures if it

³² 276 F.2d 892 (2d Cir. 1960).

³³ Id. at 896.

had been "directed to an individual airman and concerned with conduct or other facts peculiar to that airman."³⁴

A decision to modify an NDA to require labeling for nonprescription sale would be based on the drug's distinctive safety and effectiveness profile. Indeed, FDA has instructed the advisory committee considering the petition at issue here to consider, for each of the three drugs:

- whether it has special toxicity in its class,
- whether it has a large margin of safety,
- whether its frequency of dosing affects its safe use,
- whether its safety profile has been defined at high dose,
- whether it has been used for a sufficiently long time on the prescription market to enable a full characterization of its safety profile,
- its worldwide marketing experience,
- the results of use data pertaining to its marketing,
- a vigorous risk analysis of the drug,
- whether there is a full understanding of the pharmacodynamics of the drug,
- whether the minimally effective dose for the drug is known, and
- whether possible interactions between the drug and other drugs have been characterized.³⁵

³⁴ Id. at 897.

³⁵ Memorandum to Nonprescription Drugs Advisory Committee and Pulmonary Allergy Drugs Advisory Committee Members, Consultants, and Guests, from OTC Antihistamine Review Team (April 5, 2001).

Effectiveness trials, safety data, actual use trials, and label comprehension trials – pertaining specifically to each drug – would have to be considered to support the switch.³⁶ The Second Circuit explained in Quesada that adjudication involves "the application of a statute or other legal standard to a given fact situation involving particular individuals."³⁷ The decision to switch any of the three drugs in the Blue Cross petition would be the essence of adjudication. It would involve the application of a statute – the standard in section 503(b)(1) of the FD&C Act – to a particular set of facts – the safety and effectiveness information pertaining to a specific drug.

Applicability to One Entity. A decision to switch a drug subject to an NDA from prescription to nonprescription status would be directed to the individual NDA owner. FDA would be directing one party – the NDA owner – to amend its labeling and to market its product for nonprescription sale. In American Airlines, Inc. v. Civil Aeronautics Board, the United States Court of Appeals for the D.C. Circuit explained that decisions which are individual in impact are inherently adjudicatory.³⁸ The Civil Aeronautics Board (CAB) issued licenses to cargo and commercial carriers specifying the type of cargo the carrier was permitted to carry. In this instance, it also issued a regulation declaring that only non-commercial all-cargo planes could sell blocked space service. The plaintiffs, commercial carriers, argued that by restricting the

³⁶ Id.

³⁷ Quesada, 276 F.3d at 879. See also Interport Pilot Agency, Inc. v. Sammis, 14 F.3d 133, 143 (2nd Cir. 1994) (holding an action to be adjudicative when a decision is based on a determination of facts about the parties and their activities, businesses, and properties, and finding thus that due process applies).

cargo of commercial airlines, the CAB regulation effectively altered their licenses, which it could do only by adjudication. The D.C. Circuit disagreed. Given the general application of the regulation to all commercial carriers, the court concluded, the agency had exercised rulemaking authority.³⁹ It distinguished the proceeding from one "that in form is couched as rulemaking, general in scope and prospective in operation, but in substance and effect is individual in impact and condemnatory in purpose."⁴⁰ As explained by the court, "Where the agency is considering a general regulation, applicable to all carriers, or to all carriers within an appropriate class, then each carrier is protected by the fact that it cannot be disadvantaged except as the Board takes action against an entire class."⁴¹ However, adjudicatory process is required "where an agency is considering an order against a particular carrier or carriers."⁴²

The Supreme Court therefore required adjudicatory procedures when the CAB sought to amend Delta's certificate of public convenience. In September 1958, the Board awarded a certificate of public convenience and necessity to Delta to extend an existing route northwest so as to provide service from Miami to Detroit, and to add Indianapolis and Louisville as intermediate points on its existing Chicago-to-Miami route. In May 1959, the CAB issued a new order amending Delta's certificate, barring Delta's operations between ten pairs of intermediate cities unless the flights initiated at

³⁸ 359 F.2d 624 (D.C. Cir. 1966)

³⁹ Id.

⁴⁰ Id.

⁴¹ Id. at 631.

Atlanta or points further south. The effect was to bar certain flights Delta was then operating. Delta had no formal notice and no opportunity for a hearing. The Supreme Court ruled, in Civil Aeronautics Board v. Delta Airlines, that because of the specificity of the regulation, which was directed to a single carrier, the CAB's action really amounted to amendment of Delta's license.⁴³ Delta was therefore entitled to a hearing.

Under the reasoning in the Delta and American Airlines decisions, the switch of a drug's marketing status would require adjudicatory procedures. It would direct one party – the NDA owner – to amend its labeling and to market its proprietary product for nonprescription sale. Even if the proceeding were in form "couched as rulemaking, general in scope and prospective in operation," the decision to require labeling for nonprescription sales for any of these three drugs would be, in substance and effect, individual in impact. No other manufacturers may legally market any of these formulations. Like the CAB decision in Delta Airlines, FDA's decision would be specific and directed to a single NDA owner. The Agency therefore must provide each of the three manufacturers an opportunity for a hearing.

Burden on the NDA Owner's License. Finally, an FDA decision to switch a drug subject to an NDA from prescription to nonprescription status would place a burden on the NDA owner. Due process requires a hearing if the impact of an agency action falls disproportionately on particular individuals or entities.⁴⁴ The 9th Circuit

⁴² Id.

⁴³ 367 U.S. 316, 331-32 (1961).

⁴⁴ Cf. American Airlines, 359 F.2d at 631.

decision in Harris v. County of Riverside elaborates this principle.⁴⁵ The County had specifically targeted Harris's property for a zoning change, after publishing notice of a General Plan Amendment regarding a larger area. The court concluded that the County's decision to alter its proposed General Plan Amendment "specifically to rezone Harris' land constituted a decision which was distinct from, rather than a part of, approval of the General Plan Amendment." This decision, unlike the County's approval of the General Plan Amendment, "concerned a relatively small number of persons . . . rather than the entire population of the West Coachella Valley." Furthermore, it "'exceptionally affected' Harris 'on an individual basis' by severely altering the permissible uses of Harris' land." Due to the "exceptional effect" of the decision on Harris as a specific, identifiable individual, the County's decision to rezone his land was subject to due process constraints.⁴⁶ A decision that any of the three drugs mentioned in the Blue Cross Petition should be sold over the counter rather than by prescription would alter the terms of marketing of that drug product and "exceptionally affect" the NDA owner on an "individual basis."

* * * *

For the foregoing reasons, under general principles of administrative law and constitutional due process, FDA may not modify an NDA to require labeling for nonprescription use over the objection of the NDA owner, without providing the opportunity for a formal evidentiary hearing. The Administrative Procedure Act codified

⁴⁵ 904 F.2d 497 (9th Cir. 1990).

this general requirement of administrative law by providing that licensing procedures be adjudicative in nature. Section 558(c) of the APA provides: "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 – (1) notice by the agency in writing of the facts or conduct which may warrant the action; and (2) opportunity to demonstrate or achieve compliance with all lawful requirements."⁴⁷ Indeed the courts have added that "an amendment of licensing . . . under the [APA] . . . results in even more rigorous procedural requirements than apply to initial licensing."⁴⁸

C. No provision of the FD&C Act authorizes FDA to dispense with adjudication procedures when modifying an NDA over the objection of the owner.

Only one provision of the FD&C Act – section 503(b)(3) – mentions the possibility of another process to effectuate the switch of drugs. Section 503(b)(3) was not intended for, and has never been used for, the switch of one proprietary drug product subject to an approved NDA over the objection of the manufacturer. The language of section 503(b)(3), the legislative history of the provision, FDA's own descriptions of the provision, and FDA's practice for forty years confirms that the provision was intended to be used when identical products are labeled inconsistently by multiple manufacturers. In contrast, Blue Cross asks FDA to adjudicate the status of three different drugs, each

⁴⁶ 904 F.2d at 502-503.

⁴⁷ 5 U.S.C. § 558(c).

⁴⁸ American Airlines, 359 F.2d at 631.

marketed by a single company pursuant to an approved license. FDA's practice in such situations has been to use the individualized and adjudicative process prescribed by section 505(e).

1. **Congress enacted section 503(b)(3) to give FDA a tool to address a then-existing problem: multiple manufacturers marketing identical products for prescription and nonprescription sale.**

In the years following the enactment of the new drug provisions of the FD&C Act, NDAs became effective for several hundred drug products. In addition, many thousands of similar formulations entered the market as "old drugs." Manufacturers of these products concluded independently that their products were "generally recognized as safe." Most of these "me too" products reached the market without notice to FDA. As a result, by 1951 dozens of drugs containing the same active ingredient were on the market but often bearing quite different labeling. Some brands were labeled for prescription sale, others for nonprescription sale.

Congress passed the Durham-Humphrey Amendments in 1951 in order to give FDA the authority to bring order to this chaos. Section 503(b)(3) permits FDA to "by regulation remove drugs" from the prescription requirements in section 503(b)(1) "when such requirements are not necessary for the protection of the public health."⁴⁹ The

⁴⁹ The plain language of section 503(b)(3) confirms that the provision applies to active ingredients marketed by multiple manufacturers. The section applies to "drugs" rather than to "a drug." The FD&C Act uses the term "drug" in more than one way. In section 503(b)(1), where the statute addresses a drug that is limited "by an approved application under section 505," the word refers to a specific drug product. An approved application covers a particular product. The exemption provision, in contrast, refers to "drugs" in the sense of active ingredients or generic "drugs."

legislative history accompanying the Durham-Humphrey Amendments establishes unequivocally that Congress was concerned about drugs that were identical in composition but labeled differently by different manufacturers. A House Report in the summer of 1951 described several examples, including dehydrocholic acid, acetophenetidin, and precipitated chalk.⁵⁰ "Many products of identical composition, placed on the market by different manufacturers, were shown to the committee in a practical demonstration of the druggists' dilemma," the report explained. "One would bear the prescription legend while another of the same composition would provide directions for use."⁵¹ Discussion on the floor in the House at the end of July 1951 shows that the House was motivated by the problem of multiple manufacturers marketing identical products differently.⁵² Several witnesses before the Senate Subcommittee on

⁵⁰ H.R. Rep. No. 700, 82d Cong., 1 Sess. 5 (1951).

⁵¹ Id.

⁵² E.g., 97 Cong. Rec. 9241-9242 (introduction of H.R. 3298); id. at 9242 ("The thing I am trying to point out is that the same commodity sold to druggists by different firms bears different legends.") (Rep. Beckworth); id. at 9242 ("On that point will the gentleman recognize the testimony that was in the record that some drug manufacturers sell to the druggist for over-the-counter sale; some of them sell to druggists for resale by prescription.") (Rep. O'Hara); id. at 9324 (discussing precipitated chalk example) (Rep. Williams); id. at 9332-9333 ("In order that we might see what we are doing here, let us see what the present law is and just what we want to do. In the first place, under the present act there is confusion in the administration of this law even among the manufacturers, because some of them put out a drug that is to be dispensed only on the prescription of a doctor, whereas on that same identical drug, if it is made by another manufacturer, it can be sold over the counter. Now, this confusion must be righted here.") (Rep. Rogers); id. at 9344 ("I have before me two drugs. These are manufactured by different manufacturers, yet they are identical in chemical make-up, they are identical in quantity, they are exactly the same product. One product is manufactured by the Davies-Rose Co., of Boston, Mass. On this drug – this is quinidine sulfate – you will find this legend: *Caution: To be dispensed only by or on the prescription of a physician.* Here is the same drug manufactured by the Ely Lilly Co., of Indianapolis. There is no

Labor and Public Welfare in September 1951, which would report the House bill out in essentially the form that became law, testified to the confusion on the market. George Larrick, FDA Deputy Commissioner, gave the Subcommittee several examples of drugs sold both on prescription and nonprescription, including quinidine sulfate, theobromine with sodium salicylate, dehydrochloric acid, iron tablets, and tincture of hyoscyamus.⁵³ The legal counsel for the National Association of Retail Druggists gave the Subcommittee thirty examples and provided photocopies of the labels in question.⁵⁴

This legislative history confirms two points. First, when it enacted section 503(b)(3), Congress was concerned about the drugs on pharmacy shelves in 1951 that had reached those shelves without FDA review or approval. Second, Congress intended the new provision to be used when multiple manufacturers marketed products of identical composition.

legend on this drug. . . . On this drug is written the simple language: *Adult dose: One tablet as directed by the physician.*") (Rep. Williams); *id.* at 9344 (giving example of phenacticin marketed both with and without the prescription legend) ("This is what we are seeking to eliminate with this bill.") (Rep. Williams).

⁵³ "A Bill to Amend Section 503(b) of the Federal Food, Drug and Cosmetic Act of 1938, as Amended," Hearings before the Subcommittee on Labor and Public Welfare, United States Senate, 82d Cong., 1st Sess. 6-7 (September 11, 1951) (testimony of George P. Larrick, Deputy Commissioner of Food and Drugs).

⁵⁴ *Id.* at 84 (written statement of Herman S. Waller, Legal Counsel for the National Association of Retail Druggists).

2. FDA relied on section 503(b)(3) to switch pre-1951 active ingredients that were marketed by multiple manufacturers with different labeling.

FDA used section 503(b)(3) in precisely the circumstances that Congress intended: to create uniform marketing conditions for the dozens of identical pre-1951 drugs manufactured and marketed differently by different manufacturers.

FDA's regulation implementing section 503(b)(3) states that the Agency may switch a drug "limited to prescription use under section 503(b)(1)(C) of the Act"⁵⁵ if it finds that prescription-dispensing requirements are "not necessary for the protection of the public health by reason of the drug's toxicity or other harmful effect, or the method of its use, and [it] finds that the drug is safe and effective for use in self-medication as directed in proposed labeling."⁵⁶ Switches pursuant to section 503(b)(3) entail the use of informal (notice and comment) rulemaking. At the conclusion of the process, FDA issued a regulation exempting the ingredient and formulation from the prescription dispensing requirements. FDA used section 503(b)(3) to switch 28 active ingredients, beginning with acetaminophen in May 1955.⁵⁷ Twenty-five of those switches occurred in

⁵⁵ There is no section 503(b)(1)(C) of the FD&C Act. All three drugs referenced in the Blue Cross petition are limited to prescription dispensing under section 503(b)(1)(B) of the Act.

⁵⁶ 21 C.F.R. § 310.200(b) presupposes that the manufacturer (not FDA) proposes labeling that directs self-medication.

⁵⁷ See 20 Fed. Reg. 3499 (May 19, 1955) (acetaminophen, sodium gentisate); 20 Fed. Reg. 5635 (August 5, 1955) (isoamylhydrocupreine with zolamine hydrochloride); 20 Fed. Reg. 7166 (September 24, 1955) (phenyltoloxamine dihydrogen citrate, oxtetracycline with polymyxin B sulfate); 20 Fed. Reg. 7927 (October 21, 1955) (diamtazole dihydrochloride); 20 Fed. Reg. 8189 (November 1, 1955) (meclizine hydrochloride); 21 Fed. Reg. 420 (January 20, 1956) (dicyclomine hydrochloride, neomycin sulfate); 21 Fed. Reg. 768 (February 3, 1956) (hexadenol); 21 Fed. Reg. 1417

the 1950s. Section 503(b)(3) was used only three times after 1959: in 1963 for biphenamine hydrochloride, in 1966 for the combination of tyloxapal and bezalkonium chloride, and in 1971 for tolnaftate. Section 503(b)(3) regulations are in effect now for only 18 drugs, the most recent of which was switched 35 years ago.⁵⁸

FDA has conceded that section 503(b)(3) is intended for use when more than one manufacturer markets the same ingredient. In 1983, Commissioner Arthur Hull Hayes testified before Congress about the use of the NDA process for switches, contrasting it with use of section 503(b)(3). "Examples of prescription drugs switched to OTC use under supplemental NDAs," he explained, "include Benylin cough syrup (diphenhydramine) and Actifed antihistamine / nasal decongestant (triprolidine / pseudoephedrine)." He added, "Conversion of prescription drugs to OTC status without using the rulemaking procedure of [section 503(b)(3)]" – in other words, using the NDA process – "is appropriate when there are only one or a few manufacturers of a drug and

(March 3, 1956) (sodium fluoride); 21 Fed. Reg. 3247 (May 17, 1956) (sulfur dioxide); 21 Fed. Reg. 3672 (May 30, 1956) (doxylamine succinate); 21 Fed. Reg. 4341 (June 21, 1956) (dextromethorpan hydrobromide); 22 Fed. Reg. 2314 (April 6, 1957) (tuaminoheptane sulfate, a different neomycin sulfate preparation); 22 Fed. Reg. 3435 (May 16, 1957) (vibesate); 22 Fed. Reg. 6911 (August 28, 1957) (pramoxine hydrochloride); 22 Fed. Reg. 8812 (November 1, 1957) (carbetapentane citrate); 23 Fed. Reg. 324 (January 17, 1958) (diphemanil methylsulfate); 23 Fed. Reg. 479 (January 24, 1958) (pamabrom); 23 Fed. Reg. 10436 (December 30, 1958) (dyclonine hydrochloride); 24 Fed. Reg. 5827 (July 22, 1959) (chlorethen citrate); 24 Fed. Reg. 6805 (August 21, 1959) (chlorcyclizine hydrochloride, methoxyphenamine hydrochloride); 28 Fed. Reg. 7426 (July 20, 1963) (biphenamine hydrochloride); 31 Fed. Reg. 9992 (July 22, 1966) (tyloxapal with benzalkonium chloride); 36 Fed. Reg. 824 (January 19, 1971) (tolnaftate).

⁵⁸ 21 C.F.R. § 310.201 (1), (2), (3), (4), (8), (11), (12), (16), (18), (19), (20), (21), (22), (23), (24), (26), (27), and (28). Tolnaftate was subsumed in the OTC Drug Review

they all have NDAs."⁵⁹ In its response the following year to a citizen petition requesting that FDA devise a "cohesive and comprehensive policy governing the conditions and criteria for switching prescription drugs to OTC status," the Agency explained that existing procedures – the OTC Drug Review, section 503(b)(3), and the NDA process – were adequate. Section 503(b)(3), FDA elaborated, "enables the agency to provide public notice of a proposed switch, to solicit comment, and to establish uniform marketing conditions where more than one manufacturer markets the drug."⁶⁰

Regulatory and legislative developments since 1971 governing generic drugs – the paper NDA policy and enactment of sections 505(b)(2) and 505(j) of the FD&C Act in 1984 – have rendered section 503(b)(3) an anachronism. New drugs are no longer brought to market without FDA approval. Manufacturers of follow-on drugs proceed through section 505(b)(2) or section 505(j) of the Act. Generic drugs must bear the same labeling as the pioneer drugs to which they are bioequivalent. There are no "identical products" on the market today labeled differently by different manufacturers. It is no surprise that FDA has not used section 503(b)(3) in thirty years.

in 1993. 58 Fed. Reg. 49890 (September 23, 1993) (final monograph for topical antifungal drug products).

⁵⁹ "FDA's Prescription to Over-the-Counter Drug Switch," Hearing before the Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce, House of Representatives, 98th Cong., 1st Sess. (June 6, 1983), at 11 (testimony of Arthur Hull Hayes, Jr., Commissioner, Food and Drug Administration).

⁶⁰ Letter to Charles N. Jolly, Chattem, Inc., denying Citizen Petition 77N-0094 (May 18, 1984), at 6.

3. When FDA switches a drug marketed exclusively by a single company pursuant to an approved license, it uses the NDA process.

In contrast with the situation Congress faced in the 1950s, FDA now confronts a petition that seeks the adjudication of the status of three individual drugs. Each drug is marketed by a single manufacturer, pursuant to a license approved by the NDA, based on data supplied by the manufacturer. FDA has switched a number of such drugs from prescription to nonprescription status. In each instance it did so with the consent and cooperation of the manufacturer and in each instance it used the NDA process.

To initiate such a switch, the manufacturer submits an NDA, a supplemental NDA, or an NDA under section 505(b)(2) of the FD&C Act. FDA makes an individualized decision about the prescription or nonprescription status of the specific drug covered by that NDA, based on the singular safety and effectiveness profile of that product. A number of drugs have been switched in this way— all with the agreement of the NDA owner – including Advil (ibuprofen) in 1984, Nix (permethrin) in 1990, Naprosen (naproxen sodium) in 1994, Visine (pheniramine maleate with naphazoline hydrochloride) in 1994, Vasacon-A (antazoline phosphate with naphazoline hydrochloride) in 1994, Femstat (butoconazole nitrate) in 1995, Nicorette (nicotine polacrilex) in 1996, Nicoderm (nicotine transdermal system) in 1996, Rogaine (minoxidil) in 1996, Imodium Advanced (loperamide/simethicone) in 1997, Vagistat-1 (tioconazole) in 1997, Zantac (ranitidine) in 1998, and Pepcid AC (cimetidine suspension) in 1999.

III. A Forced Switch of a Prescription Drug that is Subject to an NDA Would Violate the Confidentiality Provisions of the FD&C Act and the Trade Secrets Act and Violate the Takings Clause of the U.S. Constitution.

A decision to modify an NDA to require labeling for nonprescription sale must necessarily take account of the drug's specific and unique safety and effectiveness profile. In order to make the findings that will support nonprescription marketing for a drug, FDA would need to rely on confidential data and information in the drug's NDA. The fact that FDA would need to review and rely on this information confirms the argument we make in Part II, namely, that the switch of a drug represents an adjudication of its status.

If FDA sought to effect the switch by regulation, not only would it violate the sponsor's procedural rights, it would appropriate the confidential information in the NDA. To promulgate such a regulation, FDA would also be obliged to disclose the basis of its decision in the Federal Register. This use and disclosure of the NDA owner's proprietary information would violate section 301(j) of the FD&C Act and the Trade Secrets Act and would effect a taking in violation of the Fifth Amendment to the U.S. Constitution.

A. FDA could not switch a drug subject to an approved NDA from prescription to nonprescription status without considering and relying on confidential information in the NDA.

FDA could not switch a drug without reviewing the contents of the NDA. In order to determine that a drug no longer meets the standard in section 503(b)(1) for a prescription legend, FDA must find that prescription-only dispensing requirements are

not required by the drug's "toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use."⁶¹ This would entail a review of safety data, including data from preclinical and clinical studies, epidemiological studies, actual use studies, and consumer label comprehension studies. It would require consideration of factors such as whether the drug has special toxicity, whether it has a large margin of safety, whether its frequency of dosing affects its safe use, whether its safety profile has been defined at high dose, and whether there is a full understanding of its pharmacodynamics.⁶² In particular, to assess the safety of the drug for nonprescription use, FDA would need to review the preclinical pharmacology and toxicology studies in the NDA. Rarely is any of this information public.⁶³

The memorandum that established FDA's Paper NDA policy in 1978 confirms that FDA may not ordinarily rely on unpublished information in a sponsor's NDA. In the original memorandum setting out the Paper NDA policy, the Associate Director for New Drug Evaluation wrote that "Depending upon the quality of the clinical

⁶¹ The Blue Cross petition does not purport to present scientific evidence to support such a finding.

⁶² See above, page 16.

⁶³ The memorandum that established FDA's "Paper NDA" policy in 1978 confirms that a review of animal data is essential to an assessment of the safety of a drug. In this memorandum, the Associate Director for New Drug Evaluation explained that "pertinent animal information" should be included in any paper NDA, including data from pharmacologic, toxicologic, reproduction, and carcinogenicity studies. Memorandum to Division Directors from Marion J. Finkel, Associate Director for New Drug Evaluation (July 31, 1978), 46 Fed. Reg. 27396 (May 19, 1981). Moreover, as she noted, "Often there will be little in the way of animal toxicity and reproduction data in the published literature and such data as may be available may be inadequately described for in-depth analysis." *Id.* at 27397.

data submitted and the FDA medical reviewers' own knowledge from the published literature of the clinical safety of the drug at issue, clinical information can be substituted for full reports of animal data should such reports not be available in the published literature or in any unpublished data submitted by the duplicate sponsor."⁶⁴

In the December 1980 Federal Register document announcing and defending the policy, FDA emphasized the point.⁶⁵ For example, when some pointed out that "FDA has consistently recognized that the information contained in a manufacturer's NDA file is trade secret data that may not be publicly disclosed or used to support an NDA of another applicant without the express permission of the original NDA holder," FDA responded that the issue was "not relevant here, for paper NDAs are based on published literature."⁶⁶ This response would not have been necessary, if FDA could rely on the proprietary material in a sponsor's NDA. Enactment of the Hatch-Waxman Amendments in 1984 further confirms the point: legislation permitting the Agency to approve abbreviated new drug applications on the basis of material in the pioneer NDA would not have been necessary, had the Agency had the authority to rely on proprietary information in the first instance.⁶⁷

⁶⁴ 46 Fed. Reg. at 27397.

⁶⁵ 45 Fed. Reg. 82053, 82056, 82058-82060 (December 12, 1980).

⁶⁶ Id. at 82058.

⁶⁷ 98 Stat. 1585 (1984).

B. When promulgating regulations, FDA must publicly disclose the data and information on which it relies.

Under the Administrative Procedure Act, FDA must disclose publicly the data upon which any proposed rule is based. In United States v. Nova Scotia Food Products Corp., the United States Court of Appeals for the Second Circuit concluded that FDA's promulgation of a regulation establishing a time-temperature-salinity prescription for processing smoked whitefish was procedurally erroneous, because the Agency had failed to notify interested parties of the scientific research on which it was relying.

"When the basis for a proposed rule is a scientific decision," the court explained, "the scientific material which is believed to support the rule should be exposed to the view of interested parties for their comment."⁶⁸

FDA's own regulations require the Agency to publish the factual basis for any proposed regulations. Section 10.40(b) of FDA's regulations states that any notice of proposed rulemaking must summarize the facts underlying the proposal and include "references to all information on which the Commissioner relies."⁶⁹

FDA's uniform practice is to release publicly the information on which proposed and final regulations rely. For example, the Agency took this approach in the OTC Drug Review. In 1972, the Agency began a review of the hundreds of thousands of

⁶⁸ 568 F.2d 240, 252 (2d Cir. 1977). See also Endangered Species Committee of the Building Industry Association of Southern California v. Babbitt, 852 F. Supp. 2d 32, 36 (D.D.C. 1994) ("Where an agency relies upon data to come to a rulemaking decision, it generally has an obligation under the APA to provide such data for public inspection.").

⁶⁹ 21 C.F.R. § 10.40(b).

pre-1962 nonprescription drugs on the market that had not been the subject of NDAs.⁷⁰ After dividing these nonprescription drugs into twenty-six therapeutic categories, FDA asked panels of experts to review and evaluate data and information pertinent to products in each category.⁷¹ Each panel submitted a report to FDA containing its recommendations "with respect to the conditions under which OTC drugs falling within the category . . . are generally recognized as safe and effective and not misbranded."⁷² The conditions included: active ingredients, labeling indications, warnings and adequate directions for use, and prescription or nonprescription status.⁷³ After reviewing the panel's report, FDA published the report as a proposed monograph in the Federal Register.⁷⁴ After review of the comments submitted, FDA published a tentative final monograph, allowed further public comment, and in some cases scheduled an oral hearing.⁷⁵ Following this, FDA published a final monograph for the therapeutic

⁷⁰ 37 Fed. Reg. 9464 (May 11, 1972).

⁷¹ 21 C.F.R. § 330.10(a)(2). The therapeutic categories were: antacids, laxatives, antidiarrheal products, emetics, antiemetics, antiperspirants, sunburn prevention and treatment products, vitamin-mineral products, antimicrobial products, dandruff products, oral hygiene aids, hemorrhoidal products, hematinics, bronchodilator and antiasthmatic products, analgesics, sedatives and sleep aids, stimulants, antitussives, allergy treatment products, cold remedies, antirheumatic products, ophthalmic products, contraceptive products, miscellaneous dermatologic products, dentifrices and dental products, and miscellaneous drug products. 37 Fed. Reg. at 9475. The initial twenty-six categories were later subdivided into 88 subcategories, each the subject of a separate rulemaking.

⁷² 21 C.F.R. § 330.10(a)(5).

⁷³ Id.

⁷⁴ 21 C.F.R. § 330.10(a)(6).

⁷⁵ 21 C.F.R. § 330.10(a)(7) and (8).

category.⁷⁶ If an ingredient/formulation was found to be generally recognized as safe and effective, it was deemed an "old drug." Any manufacturer would be entitled to bring a product to market under the conditions specified in the regulation for that ingredient/formulation, without filing an NDA. Supporting information for that regulation was made publicly available. In a 1985 article about the marketing of drugs proposed for switch through the monograph process, the Director of the Division of OTC Drug Evaluations explained that the "public availability of data is necessary to general recognition [of safety and effectiveness] for purpose of the OTC review."⁷⁷

To give another example, in 1974 FDA determined that the safety and effectiveness data in food additive petitions – unlike the safety and effectiveness data in new drug applications – would be made available to the public when notice of the filing of the petition was published in the Federal Register. These petitions "result in public regulations rather than private licenses," FDA explained.⁷⁸ Such a regulation is generally applicable – it "permits all persons to manufacture and market the ingredient" in question.⁷⁹ Accordingly, the Agency concluded, the facts on which it is based must be released to the public.

⁷⁶ 21 C.F.R. § 330.10(a)(9).

⁷⁷ William E. Gilbertson, "The OTC Drug Review – Switch Without Regulation or Application," 19 Drug Information Journal 101, 107 (1985).

⁷⁸ 39 Fed. Reg. 44602, 44631-44632 (December 24, 1974) (final regulations).

⁷⁹ 38 Fed. Reg. 9128, 9130 (May 5, 1972) (proposed regulation); see also Peter Barton Hutt, Assistant General Counsel for Food, Drugs, and Product Safety, Department of Health, Education, and Welfare, "Public Information and Public Participation in the Food and Drug Administration," 36 Quarterly Bulletin of the Association of Food and Drug Officials of the United States 212, 215 (October 1972) ("Since food additives, color

The fact that FDA must publish the facts underlying any generally applicable regulation – including an OTC drug monograph – means that use of the OTC Drug Review to switch any of the three drugs Blue Cross wants reclassified would create an anomaly. To be sure, FDA switched several drugs during the OTC Drug Review. The panels were asked to consider all drugs that should be available over the counter, including any ingredients and formulations only available as prescription.⁸⁰ Any interested person could submit data and views suggesting that a prescription drug be moved to nonprescription status. A panel could – and many panels did – recommend that prescription ingredients be switched to nonprescription status. Between 1976 and 1992, FDA switched 32 active ingredients and formulations through the OTC Drug Review,⁸¹ including hydrocortisone acetate (an anti-pruritic) in 1979 and sodium fluoride (for oral care) in 1980.⁸² However, all drugs that were switched through the monograph process became, by virtue of that switch, "old drugs." The monograph was generally applicable and the data and information underlying the monograph were made public. There have

additives, and antibiotics are subject to public regulations rather than private licenses, and thus permit any person to engage in their manufacture, it is proposed that the scientific data underlying those regulations would promptly be released to the public upon request the moment that the regulation is promulgated.").

⁸⁰ 37 Fed. Reg. at 9474.

⁸¹ See Consumer Healthcare Products Association, *Ingredients and Dosages Transferred from Rx-to-OTC Status (or New OTC Approvals) by the Food and Drug Administration (October 17, 2000)*, available at <www.chpa-info.org>. The CHPA chart lists 82 ingredients and dosages transferred from prescription to nonprescription status or approved directly as over-the-counter products. Thirty-two were switched as part of the OTC Drug Review. Fifty are listed as NDAs.

⁸² 44 Fed. Reg. 69768 (December 4, 1979) (hydrocortisone acetate); 45 Fed. Reg. 20666 (March 28, 1980) (sodium fluoride).

been no switches in the OTC Drug Review in nearly ten years, and FDA has never used the OTC Drug Review to switch a drug over the manufacturer's objection. By contrast, the drugs Blue Cross wants reclassified are new drugs subject to NDAs containing proprietary information. If FDA were to switch any of these drugs to nonprescription status through the OTC Drug Review, the Agency would be required either to (1) repudiate the entire premise of the monograph system by placing a "new drug" subject to an NDA into a monograph that otherwise establishes general conditions of marketing for old drugs, or (2) issue a generally applicable regulation for the ingredient and formulation in question and effectively invite third parties to infringe the patents of the NDA owner.

C. Unauthorized disclosure of the proprietary information in an NDA would violate the FD&C Act and the Trade Secrets Act.

As explained above, if FDA were to issue a regulation effecting a switch in the NDA, whether under section 503(b)(3) of the FD&C Act or through the OTC Drug Review, it would be required to disclose to the public the information underlying its decision. This disclosure would violate federal law and the U.S. Constitution. FDA may not disclose the proprietary information in an NDA without the owner's permission. Section 301(j) of the FD&C Act and the Trade Secrets Act preclude the public disclosure of the confidential commercial information in NDAs and investigational new drug (IND) applications.

1. Disclosure of the safety and effectiveness information in an NDA would violate section 301(j) of the FD&C Act.

Section 301(j) of the FD&C Act prohibits the disclosure of trade secrets and confidential commercial information obtained by the Agency through the IND and NDA processes. The provision precludes FDA employees, and FDA itself through regulations, from revealing "any method or process which as a trade secret is entitled to

protection."⁸³ The phrase "trade secret" in section 301(j) is coextensive with the phrase as used in the Restatement of Torts. The Restatement of Torts in turn defines a trade secret as "any formula, pattern, device or compilation of information which is used in one's business, and which gives him an opportunity to obtain an advantage over competitors who do not know or use it."⁸⁴ This includes sensitive commercial information – including preclinical data, such as the results of toxicological studies in animals. FDA has adopted the Restatement definition of "trade secret" when interpreting section 301(j).⁸⁵ As the FDA Commissioner explained in 1977, since the FD&C Act was enacted FDA has interpreted "'method or process which as a trade secret is entitled to protection' in section 301(j) as encompassing animal and human testing data."⁸⁶

⁸³ 21 U.S.C. § 331(j).

⁸⁴ Restatement of Torts, § 757 cmt. b; see also Ruckelshaus v. Monsanto Co., 467 U.S. 986, 1001 (1984).

⁸⁵ 39 Fed. Reg. 44602, 44613 (December 24, 1974) (final FOI regulations); 37 Fed. Reg. 9128, 9129, 9130 (May 5, 1972) (proposed FOI regulations) ("The Commissioner proposes to adopt the Restatement of Torts definition of 'trade secrets.'"); see also Carson Products Co. v. Califano, 594 F.2d 453, 460-61 (5th Cir. 1979) (applying Restatement definition when reviewing FDA's determination whether information was trade secret); H.R. Rep. No. 94-853, at 48-49 (1976) (drawing from Restatement definition during consideration of Medical Device Amendments of 1976) (quoted in Public Citizen Health Research Group v. FDA, 539 F. Supp. 1320, 1325 (D.D.C. 1982)). Also, when promulgating its confidentiality regulations in 1974, FDA wrote that the scope of the Trade Secrets Act and section 301(j) were "identical." 39 Fed. Reg. at 44612. As explained below, the Trade Secrets Act extends to both classic trade secrets and confidential commercial information. While FDA has narrowed its interpretation of "trade secrets" as that phrase appears in Exemption 4 of the FOI Act, 59 Fed. Reg. 531 (January 5, 1994), it has not narrowed – nor does it have the authority to narrow – the scope of the phrase in section 301(j).

⁸⁶ "Business Record Exemption of the Freedom of Information Act," Hearings Before a Subcommittee of the House Committee on Government Operations, 95th Cong. 93 (1977) (statement of Dr. Donald Kennedy, FDA Commissioner).

Congress has ratified FDA's interpretation of the phrase "trade secret" in section 301(j). Congress is fully aware of FDA's broad interpretation of the phrase and has not amended the statute or indicated that it intends a different meaning. Indeed, Congress has amended section 301(j) over ten times since the enactment of the FD&C Act,⁸⁷ most recently in 1997 – the year that Congress reformed many of FDA's policies through the FDA Modernization Act.⁸⁸ It has never modified the provision's treatment of trade secrets.

Section 301(j) extends to the confidential data and information in an NDA. In 1963, House hearings explored what was by then "FDA's 25-year-long interpretation" that all information relating to the new drug approval process was confidential and could not be publicly disclosed.⁸⁹ Several witnesses criticized FDA's confidentiality policy and supported an interpretation of FD&C Act section 301(j) that would be "strictly limited to

⁸⁷ 111 Stat. 2296, § 125(a)(2)(A) (1997) (striking "356, 357" from the text); 110 Stat. 1489, § 403 (1996) (inserting "or the violating of section 346a(i)(2) of this title or any regulation issued under that section"); 107 Stat. 2044, § 3(c)(1) (1993) (substituting "379, or 379e" for "379e, or 379"); 106 Stat. 4491, § 107(2)-(3) (1992) (substituting "379e" for "376"); 104 Stat. 1388 (1992) (adding sentence: "This paragraph does not authorize the withholding of information from either House of Congress or from, to the extent of matter within its jurisdiction, any committee or subcommittee or such committee or any joint committee of Congress or any subcommittee of such joint committee."); 94 Stat. 1190, § 5(c) (1980) (adding reference to section 350a); 90 Stat. 539, § 3(b)(3) (1976) (adding references to sections 360, 360c, 360d, 360e, 360f, 360h, 360i, 360j, and 379); 82 Stat. 342, § 103(2) (1968) (adding reference to section 360b); 74 Stat. 397, § 104 (1960) (adding reference to section 376); 72 Stat. 1784 (1960) (adding reference to section 348); Act of March 10, 1947 (adding references to sections 356 and 357).

⁸⁸ 111 Stat. 2296 (1997).

⁸⁹ "Interagency Coordination in Drug Research and Regulation," Hearings Before the Subcommittee on Reorganization and International Organizations, Senate Committee on Government Operations, 88th Cong. 1891 (1963).

manufacturing methods and processes."⁹⁰ FDA Commissioner George Larrick responded that the Agency's policy on the confidentiality of new drug data and information was based on section 301(j) of the FD&C Act as well as the Trade Secrets Act. FDA explained that it would be up to Congress, and not the Agency, to change that policy: "A requirement that all research performed in connection with a new drug be made public would involve far reaching considerations of national policy which go beyond the administrative considerations with which we are concerned and involve judgments we are not in a position to make."⁹¹

The courts have confirmed that section 301(j) of the FD&C Act prohibits the disclosure of data and information in INDs and NDAs. In Pharmaceutical Manufacturers Ass'n v. Weinberger, for instance, the U.S. District Court for the District of Columbia explained that FDA receives information "of a very sensitive nature" from manufacturers, and that FDA agrees manufacturers "do maintain a property interest in certain sensitive information" particularly because if that information were disclosed, "a substantial loss could be incurred by the drug company."⁹² "The importance of maintaining the confidentiality of such information," the court wrote, "is reflected in two

⁹⁰ Id.

⁹¹ Id. at 1900.

⁹² Pharmaceutical Manufacturers Ass'n v. Weinberger, 401 F. Supp. 444, 445 (D.D.C. 1975).

statutes which prohibit disclosure of certain information by the FDA" – section 301(j) of the FD&C Act and the Trade Secrets Act.⁹³

2. Disclosure of the safety and effectiveness information in an NDA would violate the Trade Secrets Act.

The Trade Secrets Act prohibits any federal employee from disclosing "trade secrets, processes, operations, style of work, or apparatus."⁹⁴ The Supreme Court has characterized the Act as "a general criminal statute that provides a penalty for any employee of the United States Government who discloses, in any manner not authorized by law, any trade-secret information that is revealed to him during the course of his official duties."⁹⁵ However, the Trade Secrets Act is "more than an 'anti-leak' statute aimed at deterring Government employees from profiting by information they receive in their official capacities."⁹⁶ It applies not only to individual acts of disclosure, but also to disclosure pursuant to agency decisions and regulations. FDA has accordingly described the statute as a "general Federal prohibition against disclosure of trade secret information" under which "[d]isclosure of information . . . constitutes a criminal offense."⁹⁷

⁹³ Id.; see also Webb v. DHHS, 696 F.2d 101, 103 (D.C. Cir. 1982) ("Premature disclosure of NDA data is further discouraged by the existence of criminal sanctions for FDA officials who release trade secrets without the submitter's consent. These sanctions are contained in both the Food, Drug, and Cosmetic Act and the Trade Secrets Act.").

⁹⁴ 18 U.S.C. § 1905.

⁹⁵ Ruckelshaus v. Monsanto Co., 467 U.S. 986, 1008 (1984).

⁹⁶ Id.

⁹⁷ 39 Fed. Reg. 44602, 44612 (Dec. 24, 1974).

Like section 301(j) of the FD&C Act, the Trade Secrets Act extends to both classic trade secrets and confidential commercial information.⁹⁸ It prohibits the disclosure of any material falling within the scope of Exemption 4 of the FOI Act. Exemption 4 permits a federal agency to protect from disclosure "trade secrets and commercial or financial information obtained from a person [that is] privileged or confidential."⁹⁹ The D.C. Circuit held in 1987 that the Act is "at least co-extensive with" the scope of Exemption 4 of the FOI Act.¹⁰⁰ The Department of Justice describes the Trade Secrets Act as "an extraordinarily broadly worded criminal statute" which "prohibits the disclosure of much more than simply 'trade secret' information and instead prohibits the unauthorized disclosure of all data protected by Exemption 4."¹⁰¹ The court of appeals has explained that the Trade Secrets Act embodies "a congressional judgment

⁹⁸ In National Parks & Conservation Ass'n v. Kleppe, the D.C. Circuit explained that the Trade Secrets Act is "a general prohibition against unauthorized disclosures of confidential commercial or financial information." 547 F.2d 673, 687 n.50 (D.C. Cir. 1976).

⁹⁹ 5 U.S.C. § 552(b)(4). In 1983, the D.C. Circuit narrowed the definition of "trade secret" within the Exemption 4 context. Specifically, in Public Citizen Health Research Group v. FDA, 704 F.2d 1280 (D.C. Cir. 1983), the court of appeals concluded that adverse reaction data are not trade secrets under Exemption 4 of the FOI Act, but held that such data are nonetheless confidential commercial information. The court did not discuss the broader provisions of the Trade Secrets Act, which applies to both "trade secrets" and "confidential commercial information." See also Anderson v. HHS, 907 F.2d 936, 944 (10th Cir. 1990).

¹⁰⁰ CNA Financial Corp. v. Donovan, 830 F.2d 1132, 1151 (D.C. Cir. 1987).

¹⁰¹ Department of Justice, Freedom of Information Act Guide Exemption 4 (May 2000) <www.usdoj.gov/oip/exemption4.htm> (visited March 9, 2001). The D.C. Circuit has recognized the Department of Justice (DOJ) Guide as an authoritative resource, explaining that the DOJ "has established procedures for agencies to follow in evaluating FOIA requests that include the separate review under the Trade Secrets Act." Gulf Oil Corp. v. Brock, 778 F.2d 834, 841 (D.C. Cir. 1985).

that private commercial and financial information should not be revealed by agencies that gather it, absent a conscious choice in favor of disclosure by someone with power to impart the force of law to that decision."¹⁰² Because the Trade Secrets Act is co-extensive with Exemption 4, the Act effectively mandates that FDA protect the confidentiality of materials falling within the exemption.

Information required to be submitted to the government – for example in an NDA – falls within Exemption 4 of the FOI Act if its disclosure would cause substantial competitive harm to the submitter.¹⁰³ In National Parks & Conservation Ass'n v. Morton, the D.C. Circuit explained that this requires a showing of both actual competition and a likelihood of substantial competitive injury.¹⁰⁴

The material in an NDA meets this test. First, it is well established that competition in the pharmaceutical industry is intense. Development of a new drug takes an average of nearly fifteen years and can cost hundreds of millions of dollars.¹⁰⁵ Only three out of ten approved drugs recovers average research and development costs. Second, significant competitive harm would result from public disclosure of the data and information in an NDA. FDA has repeatedly conceded this very point. Over twenty-five years ago, FDA noted that drug safety and effectiveness information has "enormous

¹⁰² CNA, 830 F.2d at 1141.

¹⁰³ See National Parks, 498 F.2d at 770; Critical Mass, 975 F.2d at 878-80.

¹⁰⁴ CNA, 830 F.2d at 1140 (citing Gulf & W. Indus. v. United States, 615 F.2d 527, 530 (D.C. Cir. 1979)).

¹⁰⁵ Industry Profile, supra note 5; see also FDA Special Report, From Test Tube to Patient: Improving Health Through Human Drugs (1999 ed.).

economic value."¹⁰⁶ In a recent FOI Act case in federal court, FDA acknowledged the extensive competitive harm that can result from the disclosure of confidential information.¹⁰⁷ FDA resisted producing even an index of materials encompassed within Exemption 4, recognizing that an index would enable competitors to decipher the research and development strategies of the submitter.¹⁰⁸ Information regarding the nature and number of clinical studies, the nature and number of amendments to a sponsor's application, and the data and information used to support drug approval, the Agency explained, would reveal confidential information used to support a sponsor's application as well as the sponsor's "thought processes" in assembling the application.¹⁰⁹ FDA concluded that "even the most cursory description of the contents of an NDA would enable a competitor to determine [a company's] research and development strategies."¹¹⁰

The courts agree that unpublished data and information in INDs and NDAs fall within the scope of Exemption 4. In 1999, the D.C. Circuit held that four

¹⁰⁶ 39 Fed. Reg. at 44634.

¹⁰⁷ Federal Defendant's Motion to Dismiss Count II or, Alternatively, for Summary Judgment (Defendant's Motion) at 11-12, R&D Laboratories, Inc. v. FDA, Civ. Action No. 00-165 (D.D.C. Sept. 7, 2000).

¹⁰⁸ *Id.* at 12.

¹⁰⁹ Declaration of Betty B. Dorsey, Director of FDA Freedom of Information Staff ¶ 12, Defendant's Motion, R&D Laboratories, Civ. Action No. 00-165.

¹¹⁰ R&D Laboratories, Civ. Action No. 00-CV-0165, Court Memorandum at 13; see also Public Citizen Health Research Group v. FDA, 185 F.3d 898, 905 (D.C. Cir. 1999); Webb v. DHHS, 696 F.2d at 101; Citizens Commission on Human Rights v. FDA, 45 F.3d 1324 (9th Cir. 1995); Sokolow v. FDA, Food Drug Cosm. L. Rep. (CCH) ¶ 38,551 (E.D. Tex. 1998).

abandoned INDs fell within Exemption 4 of the FOI Act.¹¹¹ This ruling confirmed the D.C. Circuit's long-held view that disclosure of any information that would help a pharmaceutical company's competitors bring a competing product to market more quickly and less expensively is the essence of competitive harm. That judicial doctrine dates at least to 1983, when the D.C. Circuit concluded that manufacturers "have a commercial interest in" – and a desire to keep confidential – the "health and safety experience of their products."¹¹² In that case, the court held that manufacturers of intraocular lenses had adequately demonstrated that safety information submitted to FDA, if released, could be used by competitors, and thus that summary judgment under Exemption 4 was supportable with respect to the vast majority of the requested records.¹¹³ Similarly, the Ninth Circuit in 1995 affirmed a district court's ruling that safety and effectiveness information in the NDA for Prozac, a prescription antidepressant drug, was exempt from disclosure.¹¹⁴

¹¹¹ Public Citizen Health Research Group v. FDA, 185 F.3d 898 (D.C. Cir. 1999).

¹¹² Public Citizen Health Research Group v. FDA, 704 F.2d at 1290.

¹¹³ Id. at 1290-1291; see also R&D Laboratories, Civ. Action No. 00-CV-0165, Court Memorandum at 14 (holding that information contained in pending NDAs is confidential in toto).

¹¹⁴ Citizens Commission on Human Rights v. FDA, 45 F.3d 1325 (9th Cir. 1995); see also Anderson v. DHHS, 3 F.3d 1383 (10th Cir. 1993) (holding that safety and effectiveness information could be considered confidential commercial information and remanding for further fact-finding).

3. Longstanding FDA policy precludes the disclosure of the safety and effectiveness data and information in a new drug application.

For over sixty years, FDA has protected the confidentiality of the data and information in INDs and NDAs. FDA implemented a policy of protecting these materials in 1938, the year the FD&C Act was enacted, and has followed this policy ever since. In 1974, FDA formalized this already well-established policy in regulations implementing the Freedom of Information (FOI) Act.¹¹⁵ These regulations were based on FDA's interpretation of the Trade Secrets Act, section 301(j) of the FD&C Act, and Exemption 4 of the FOI Act. Based upon these three federal laws, FDA concluded that unpublished data and information relating to investigational drug products are confidential and may not be disclosed to the public, at least until the drug is completely abandoned or an NDA is disapproved and all appeals exhausted.¹¹⁶ FDA's interpretation of these statutes has been reiterated in preambles to Federal Register notices,¹¹⁷ in reports that have considered the matter,¹¹⁸ in court briefs filed by the Department of Justice on behalf of

¹¹⁵ 37 Fed. Reg. 9128, 9130-9131 (May 5, 1972); 39 Fed. Reg. 44602, 44612-44614, 44634-44638 (December 24, 1974).

¹¹⁶ See 21 C.F.R. §§ 20.60-20.91 (outlining exemptions from mandatory disclosure in accordance with FOI Act); 21 C.F.R. § 312.30 (providing for confidentiality of IND materials); 21 C.F.R. § 314.430 (providing for confidentiality of NDA materials).

¹¹⁷ E.g., 37 Fed. Reg. 9128, 9130-9131 (May 5, 1972); 39 Fed. Reg. 44602, 44612-44614, 44633-44638 (December 24, 1974); 40 Fed. Reg. 26142, 26148, 26160-26161 (June 20, 1975); 43 Fed. Reg. 12869, 12870 (March 28, 1978).

¹¹⁸ E.g., Review Panel on New Drug Regulation, Interim Report: An Evaluation of FDA's Trade Secrets and Freedom of Information Policies 2, 17-27 (November 1976).

the United States,¹¹⁹ and in testimony by FDA officials before congressional committees.¹²⁰ Under this longstanding policy of confidentiality, FDA may not disclose the data and information in an NDA without the express consent of the NDA owner. This precludes the use of rulemaking to switch the new drug subject to that NDA from prescription status to nonprescription status.

D. Unauthorized disclosure of the proprietary information in an NDA would violate the Fifth Amendment to the U.S. Constitution.

Trade secrets and confidential commercial information are "property" protected by the Fifth Amendment to the United States Constitution.¹²¹ With respect to such property, "the right to exclude others is central to the very definition of the property interest."¹²² In short, the essence of ownership of a trade secret or confidential

¹¹⁹ E.g., Briefs for FDA in: Morgan v. FDA, 495 F.2d 1075 (D.C. Cir. 1974); Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609 (1973); Weinberger v. Bentex Pharmaceuticals, Inc., 412 U.S. 645 (1973).

¹²⁰ E.g., "Interagency Coordination in Drug Research and Regulation," Hearings Before the Subcommittee on Reorganization and International Organizations, Senate Committee on Government Operations, 88th Cong. 1899-1900 (1963); "Competitive Problems in the Drug Industry," Hearings Before the Subcommittee on Monopoly, Senate Select Committee on Small Business, 90th Cong. 743-46, 748-49, 755, 761 (1967); "Small Business Problems in the Drug Industry," Hearings Before the Subcommittee on Activities of Regulatory Agencies, House Select Committee on Small Business, 90th Cong. 370, 383 (1967 & 1968); "Drug Listing Act, 1971," Hearing Before the Senate Committee on Labor and Public Welfare, 92d Cong. 31-32, 46, 50, 54, 59 (1971); "Drug Safety Amendments of 1976," Hearings Before the Subcommittee on Health and the Environment, House Committee on Interstate and Foreign Commerce, 94th Cong. 60 (1976).

¹²¹ Ruckelshaus v. Monsanto, 467 U.S. 986, 1003-1004 (1984).

¹²² Ruckelshaus, 467 U.S. at 1011.

commercial information is the right to exclude others. Therefore, once secrecy has been lost, the property has been irrevocably destroyed.

Government action constitutes a per se taking if it deprives the property owner of all economically beneficial use of his property, or if it constitutes an appropriation of one or more of the property owner's fundamental ownership rights in the property, including the right to exclude others from making use of the property.¹²³

Disclosure of trade secrets and confidential commercial information compiled during the testing of an investigational new drug and submitted in a new drug application would do both. It would allow a company's competitor to duplicate its research without the same expenditure of time and money or to avoid that research altogether, and would strip the company of its ability to use that information profitably in a commercial setting.

Even if public disclosure of material in an NDA were not a per se taking, it would be a compensable "regulatory taking." Although there is no precise formula for determining when a regulatory taking has occurred, the Supreme Court examines "the character of the governmental action, its economic impact, and its interference with reasonable investment-backed expectations."¹²⁴ Pharmaceutical companies invest millions of dollars in the research and development of new drugs. Disclosure of the toxicological and other information contained in an NDA would have a devastating economic impact on the NDA owner's ability to recoup that investment. These

¹²³ Lucas v. South Carolina Coastal Council, 505 U.S. 1003, 1015 (1992); Kaiser Aetna v. United States, 444 U.S. 164, 179-180 (1979).

¹²⁴ Ruckelshaus, 467 U.S. at 1005 (citations omitted).

investments were made with the understanding and expectation that FDA would continue to comply with the Trade Secrets Act and would continue to withhold from public disclosure data and information within Exemption 4 of the FOI Act. The NDA owner has a reasonable investment-backed expectation in the continued legal protection of the trade secret and confidential commercial information in the NDA. The reasonableness of this expectation is underscored by the fact that FDA has for nearly sixty years insisted the data and information in INDs and NDAs are confidential,¹²⁵ by the Department of Justice's position that the Trade Secrets Act extends to everything within Exemption 4 of the FOI Act,¹²⁶ and by the court cases confirming that INDs and NDAs fall within Exemption 4.¹²⁷

The takings clause thus prohibits FDA from disclosing the proprietary information in an NDA without the express consent of the NDA owner. This too precludes the use of rulemaking to switch the new drug subject to that NDA from prescription status to nonprescription status.

¹²⁵ See pages 45-46, above.

¹²⁶ See page 41, above.

¹²⁷ See pages 43-44, above.

CONCLUSION

For the reasons set forth above, FDA must provide notice and an opportunity for a formal evidentiary hearing in accordance with section 505(e) of the FD&C Act, if it intends to modify the NDA for Zyrtec to delete the prescription legend from the approved labeling of the drug.

Respectfully submitted,



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