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August 25, 2000

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

Re: Docket No. 00N-1256: Over-The-Counter (OTC) Drug Products: Request for Comments; 65 *Fed. Reg.* 24704, April 27, 2000

Dear Sir or Madam:

On June 28 and 29, 2000, the Food and Drug Administration (FDA) held a public hearing about the agency's approach to regulating over-the-counter (OTC) drug products. According to FDA's notice of public hearing, the purpose "was to solicit information from, and the views of, interested persons, including scientists, professional groups, and consumers."

At the meeting, FDA elicited comment on general issues regarding the status of OTC drug products, including the criteria the agency should consider in rendering decisions on OTC availability of drugs, the classes of products, if any, that are not currently available OTC that should or should not be available OTC, how FDA can be assured that consumers understand the issues relating to OTC availability of drug products, how rational treatment decisions are affected by coexisting prescription and OTC therapies for a given disease, whether the current structure for marketing OTC products in the United States is adequate, and FDA's role in switching products from prescription to OTC status.

The Consumer Healthcare Products Association (CHPA) provided oral remarks at the June meeting on many of these matters. CHPA is the 119-year-old trade organization representing the manufacturers and distributors of national and store brand nonprescription medicines and dietary supplements. CHPA's membership includes over 200 companies involved in the manufacture and distribution of these self-care products and their affiliated services (e.g., raw material suppliers, research testing companies, contract manufacturing companies, advertising agencies, etc.). Over the years, CHPA

has worked collaboratively with consumers and the Food and Drug Administration on all aspects of OTC drug development, labeling, manufacturing and packaging.

The matter of Rx-to-OTC switch -- in both its conceptual and procedural ramifications -- represents an issue of great importance to CHPA member companies.

This submission represents CHPA's detailed written comments as follow-up to the June meeting and is intended to complement the Association's oral presentation. CHPA's comments are organized as follows:

Comments

I. Benefits of OTC Self Care: An OTC Perspective

Self-care with OTC medicines serves an important healthcare need. Consumers demand it; they are increasingly aware of self-care and want more control over self-care. The switch of drugs from prescription to nonprescription (Rx-to-OTC) has been phenomenally successful in creating new safe and effective self-care strategies for a variety of diseases and conditions. This success has stemmed from the collaborative efforts of the industry, consumers, and the FDA working in partnership to evaluate the specific merits of a case and to make a scientifically documented decision. Over the past 25 years, consumers, FDA, and industry have faced increasingly difficult challenges regarding OTC availability of Rx products. Together, FDA and industry have created novel solutions to difficult problems. Consumers have benefited from this collaboration and will continue to do so in the future.

The success of switch and its potential promise for the future is dependent on an OTC perspective being shared by all concerned parties, who recognize and accept the forces behind the self-care movement and understand the impetus for the development of new OTC products.

In considering the elements of this OTC perspective, it is first important to understand that consumers are extremely interested in their own healthcare. Evidence for this can be found in the explosion of health information that is available on the Internet as well as the thriving wellness movement among the population. This is particularly true of the baby-boomer generation who are determined not to go gently into middle age: sixty percent of adults follow news stories about health – more than those who follow business or even sports![1]

Second, consumers benefit from self-care. Access to self-medication options empowers consumers and effectuates their desire to take control of their own health. OTC medications provide convenience, cost and time savings. Consumers turn to OTC self-care for 38%[2] of all health problems they experience, yet for this vast volume, OTCs take up less than 2 cents of every healthcare dollar.[3] Ninety-two percent are satisfied with the medications they have used for self-care.[2] These benefits not only accrue to the individual, but to society as well. The resource savings to the healthcare system through responsible self-medication allows better allocation of limited healthcare resources and physicians' time to important issues beyond the scope of self-care.

Third, self-care with OTCs spans a broad range of conditions and diseases ranging from acute conditions such as analgesics for the treatment of headaches to the periodic use of GI products for heartburn. Some recurrent conditions will require an initial physician diagnosis, but can be very safely and effectively managed with OTC medications such as the antifungals for the treatment of recurrent vaginal yeast infections. Chronic disease prevention strategies will involve the use of sunscreens to prevent cutaneous solar damage and the development of skin cancer or the use of fluoride and triclosan for the prevention of caries and gingivitis. Finally, adjunctive treatment with OTC medications, coupled with life-style changes can make a real difference to patients who are attempting to quit smoking.

Next, industry experience has shown that consumers use the OTC label and responsibly self-medicate. A summary of actual use and attitude surveys show that 95%[4]

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1 "Consumer Use of Dietary Supplements" at 8, Prevention Magazine survey, 1999.

2 Heller Research Group for CHPA, 1992.

3 See AC Nielsen OTC sales estimates, 1999, and Health Care Financing Administration, Office of the Actuary, National Health Statistics Group, "National Health Expenditures Aggregate Amounts," January 2000.

4 See generally Heller Research Group for CHPA, 1992, Louis Harris & Assoc., 1991, Princeton Survey Research Assoc., 1992, and Princeton Survey Research Assoc.,

of consumers read the label prior to product use and that there is a high level of label comprehension. Importantly, "OTC" does not necessarily mean that the physician is out of the picture. In fact, for conditions such as vaginal yeast infections, for example, an important part of the OTC treatment program is the initial diagnosis of the condition by a physician.

Finally, the OTC industry and CHPA are proud of their leadership role in providing comprehensive, easily understood information on the package label – all the essential information for use of the product is readily available to the consumer.

The potential for further self-care empowerment of consumers is based upon a scientific paradigm which defines specific target populations, with readily recognizable conditions, previously diagnosed conditions, or self-diagnosable diseases, and determining which drugs at the appropriate dosage and with appropriate labeling can provide a reasonable expectation of benefit with a low potential for toxicity.

These new products are best determined on a case-by-case, data driven approach that is initiated by the drug manufacturer, in collaboration with the FDA in such a way that the individual, not comparative, merits of the switch candidate are assessed through the appropriate research methodologies.

This type of perspective has provided the consumer with a wide variety of products and truly some remarkable success stories for consumers. Over 80 ingredients, dosage forms and strengths have been switched from Rx status or introduced as new OTC drugs since the start of the OTC Review in 1972, accounting for over 700 marketed products.

To summarize this point, the OTC perspective or approach recognizes all of these features: (1.) consumers are interested in healthcare; (2.) consumers benefit from self-care; (3.) self-care is potentially applicable to a wide range of conditions; (4.) consumers read and use the informative OTC label and responsibly self-medicate; (5.) a scientific, research-based paradigm drives evaluation of new OTC products; (6.) new products should be evaluated on a case-by-case basis using sponsor-provided data from carefully designed research questions; (7.) the process allows changes to labeling as further information develops. Success will ensue from such a perspective being jointly pursued by the FDA and industry in a collaborative fashion to benefit the consumers who use these products.

II. Approval Issues

A. Switch Criteria

1993, finding 93%, 97%, 98%, and 95% of consumers reporting reading the label either before first use or on purchasing OTC medicines, respectively.

As part of the questions raised in preparation for the public meeting, FDA asked: What criteria should the agency use for switch? CHPA interprets switch criteria to mean standards for making the benefit/risk decision for OTC availability. As such, switch criteria should be the current statutory and regulatory criteria that have been the basis for the many successful switches undertaken since the start of the OTC Review. [5]

The foundational statutory criterion is the demonstration that labeling can be written for consumers to use a product safely and effectively without a prescription. 21 USC §502(f). On this statutory basis, the regulatory definitions of safety, effectiveness and labeling were developed in 1972 as the scientific underpinning of the OTC Review; in practice, they have been used subsequently as the basis for evaluations of OTC New Drug Applications.

Specifically, the regulatory implementation of the statute interprets safety, effectiveness, and labeling in relative terms – meaning a "reasonable expectation of effectiveness," "a low incidence of side effects" and a "low potential for abuse," and *not therefore* an absence of toxicity or an expectation that 100% of the target population will have a 100% benefit 100% of the time. See 21 CFR §330.10(a)(4)(i) and (ii).

These regulatory criteria are fulfilled through the application of the basic principles of toxicology, clinical pharmacology and epidemiology, using the standard scientific/regulatory paradigm, which is the case-by-case, weight-of-the-evidence, data-driven, dialogue-driven approach scientists use to determine drug approvability.

Specifically, companies are well equipped to address the sorts of potential issues that typically arise in the context of OTC availability. Companies[5] consider:

- Potential safety issues, with respect to:
  - Potential toxicity, which is often already worked out for the switch candidate in the Rx drug's New Drug Application.
  - Potential therapeutic hazards, including issues associated with misdiagnosis, potential treatment failure, incorrect use, and drug interactions.
- Key effectiveness issues, based on the nature and the severity of the condition, are considered (e.g., relating to: choice of dose relative to effective treatment or prevention; dosing interval; age specific dosages.)
- Core communication objectives of proposed labeling to help ensure safe and effective use of the product by consumers, which is in essence the basic statutory criterion.
- A compulsory benefit/risk assessment, which integrates safety, effectiveness, and labeling considerations within the question: Is the benefit of self-care through OTC availability worth the risk of access without a prescription?

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[5] See Soller, R.W.: OTCness. DIA Journal 32 555-560, 1997.

Because the switch process is case-specific, it often requires substantial data development. This is best developed through a company-initiated approach (see Section II.B.) that includes early and frequent dialogue with the agency during the OTC R&D process. Case specificity is universal to switch, often necessitating a data-intensive approach and close company-agency interaction. For example:

- Quit rates for Nicotine Replacement Therapy (NRT) were much better in high-support settings vs. lower-support settings, yet the limitation of access to prescriptions was actually thwarting usage of NRT and therefore limiting total quit attempts on a population basis. OTC access resolved this.
- Pediatric ibuprofen involved the largest trial in the company's history to assess the relative risk of rare side effects when the drug was used as a fever reducer.

In summary, the statutory and scientific/regulatory framework for Rx-to-OTC switch decisions is well established and is responsible for the remarkably successful track record for switch over the past 30 years. There is every expectation that future switches can be encompassed by this framework – i.e., a case-by-case, data-driven, dialogue-driven, and company-initiated process that creates new self-care options in a two-class distribution system. The following sections further amplify certain aspects of this framework.

1. The Need to Avoid Negative Switch Lists

In preparation for the meeting FDA also asked: What types of drugs/class of products should not be available OTC?

This question suggests that FDA may be interested in creating presumptive negative lists. Such an approach is inconsistent with the statutory and scientific/regulatory framework for switch as discussed above. FDA should not create presumptive negative lists.

As a conceptual matter, no drug or category of drugs should be listed as "off limits" to scientific research when we cannot predict technological developments, the results of future studies, or novel measures to help enhance consumer use of specific switch candidates. To do so would be in conflict with the statutory criterion for switch and the associated case-by-case, data-driven scientific/regulatory paradigm.

For example, eleven years ago at a national switch symposium[6], it was predicted that H2 blockers "will never go OTC." Yet today, through collaborative efforts by companies and FDA, H2 blockers are a major part of the OTC antacid/acid reducer-controller category. The point is, presumptive negative lists should be avoided, as they stifle innovation.

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[6] DIA/CHPA Symposium on Switch. Washington, DC (1989).

2. Comparative Assessments of Safety and Effectiveness

FDA requested comment on comparative assessments: "Within a therapeutic class, should the first drug to enter the OTC market be the 'best' drug, in terms of the benefit-to-risk ratio? How should the availability of a better OTC product, in terms of efficacy or safety, affect the status of products already on the OTC market for treatment of the same condition? Should older therapies that may provide less benefit or more risk be removed from the OTC market, or should the labeling be revised? Suppose the more effective drug is more difficult to use and must remain prescription – might that encourage use of the less satisfactory drug?" 65 Fed. Reg. at 24705.

As explained below, the Federal Food, Drug, and Cosmetic Act (FD&C Act) dictates that drugs are to be approved on their own merits. Comparative effectiveness is *not* a criterion under the Act, and comparative safety is relevant only in the rare situations where there is a clearly safer alternative to a drug with very serious or fatal side effects.

Drugs should be evaluated on their individual merits. The FD&C Act was carefully and deliberately written to provide that drugs should be made available to consumers if FDA concludes that they are safe, effective, and properly labeled. If a drug meets these criteria for OTC use, FDA must and should approve the application, regardless whether the agency believes that other products are "better" in one respect or another. Once approved, a product can be withdrawn only on a finding that it is no longer safe or effective. The availability of a "better" drug is not a criterion for withdrawal. The safety and effectiveness standard in the FD&C Act is not a comparative standard. As the Director of the Center for Drug Evaluation and Research commented recently, "there is no relative safety or effectiveness standard in the statute."[7]

The legislative history of 1962 drug amendments demonstrates that effectiveness is not a comparative standard. Testifying before Congress in favor of the bill that would become the 1962 amendments, the Secretary of Health, Education, and Welfare explained:

> "Let me make it absolutely clear that we are not dealing here with what some have called 'relative efficacy.' The claim has been made before this subcommittee that the proposed amendment would enable us 'to decide the relative or comparative efficacy of a new drug in terms of drugs already on the market,' or allow us to refuse clearance for a new drug merely because, in the Food and Drug Administration's opinion, it is 'not the most

[7] See "An Interview with CDER Director Janet Woodcock, M.D." in *U.S. Regulatory Reporter* (May, 2000) at 1. [Attachment A]

> efficacious drug for the purpose intended or was not as efficacious as one might ideally wish.'
>
> "The bill furnishes no basis for such apprehensions. The proposed amendments would merely require a showing that the new drug described in the application is safe for use and is effective in use, under conditions prescribed, recommended, or suggested in the labeling thereof. This would not require a showing of relatively greater efficacy than that of other drugs. It would merely require that a drug claimed to be effective for a particular purpose has been demonstrated by sound scientific procedures to be effective for that purpose. In short, it must live up to the claims made for it."[8]

Senator Carroll sought clarification on this point:

> "SENATOR CARROLL. Coming back, again, I repeat, I am disturbed about this question of giving the authority and the power to the Secretary of HEW to determine the relative efficacy of drugs.
>
> "And you do not seek that authority at all?"
>
> "SECRETARY RIBICOFF. We do not seek it. We do not want it. And my testimony indicated we do not intend to pass on it, and I think all we contend that we should have, it should be an authority that makes the manufacturer prove the effectiveness of the claims he himself makes. In other words, if he claims it is going to have this effect or this cure, that the representation he makes be true.
>
> "Now, we do not want to pass on relative efficacy. We do not want to say that drug A is better than drug B or B is greater than C.
>
> "We are not looking for that at all, and we do not think it is necessary."[9]

Moments later, Secretary Ribicoff added:

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[8] "Drug Industry Antitrust Act," *Hearings before the Subcommittee on Antitrust and Monopoly of the Committee on the Judiciary, U.S. Senate*, 87th Cong., 1st Sess. 2585 (1961) (statement of Abraham Ribicoff).

[9] *Id.* at 2605.

> "I think we have made our position clear. The bill is clear. If there would be any doubt on it, the language should be stronger. But we would not and do not intend and do not want to pass on relative efficacy. This is no power we seek and no power we desire."[10]

FDA Commissioner Larrick made the same point: that determination of effectiveness would not involve consideration of the relative efficacy of one drug compared with another.[11]

In isolated instances involving very serious adverse events, the safety of a drug can be a comparative issue. As the Director of CDER explained, "[f]or mortality . . . we have always taken the stance that that is an important issue obviously, and that where one drug has a fatal side effect that that could be a lethal lesion for that drug getting approved." Note 7, supra, *Woodcock Interview* at 1. Thus, for instance, FDA withdrew approval of Seldane® (terfenadine) when Allegra® (fexofenadine hydrochloride) was approved. This decision was based on the facts that fexofenadine is the active metabolite of terfenadine that is responsible for the desired beneficial properties of terfenadine, and that fexofenadine hydrochloride appears to lack its parent's risk of serious cardiovascular adverse events 62 *Fed. Reg.* 1889, January 14, 1997. Thus, comparative safety issues may come into play where a drug's toxicity that is acceptable at the time of approval, becomes unacceptable in light of additional alternatives that become available, or where new scientific information comes to light, *i.e.*, a potentially lethal drug/drug interaction becomes known after approval. Note 7, supra, *Woodcock Interview* at 4. Such instances are rare and would be even less likely to arise in the OTC context than with prescription drugs, because OTC drugs by definition have a wide margin of safety and a safety profile that has been well-characterized before approval of the product for nonprescription use.

Moreover, comparative safety and effectiveness would not be workable in practice. "[S]afety," Dr. Woodcock explained in May 2000, "is always a relative concept." *Id.* Thus, "FDA has traditionally not adopted, and I think that it would be very, very hard, even though people have urged us to adopt some kind of relative safety standard overall, because for most side effects, comparing them and determining which are worse is impossible. Is nausea worse than having a headache?" *Id.* "Safety," she pointed out, "is a very personal issue." *Id.* at 2. Effectiveness, too, is a very personal issue. Individuals – consumers, patients, and physicians – vary in their responses to and preferences for different treatments. This can lead to individual differences in compliance that may further vary the response to treatment. Because of individual variability and preferences, what is "best" for one person may not be "best" for another.

Finally, comparative assessments would waste agency resources. When genuine safety or effectiveness issues are presented by a marketed drug product, industry has a

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10 *Id.* at 2606; *see also* S. Rep. No. 1744, 87th Cong., 2d Sess. 16 (1962).

11 S. Rep. No. 1744, at 57.

long history of working cooperatively with FDA in the public interest, through labeling changes and, where appropriate, withdrawal of the product from the market. It would be an enormous waste of resources for FDA to institute a comparative review of marketed products.

Consumers benefit from the widest possible availability of drug products that are safe, effective, and properly labeled. It is good public health policy for consumers to have access both to new switch drugs and to older drugs that may be appropriate choices. The process of comparing one drug to another is a decision for the consumer. It would not be appropriate for FDA to refuse to switch a drug simply because it thought a "better" one might come along later, or for FDA to review existing marketed products with an eye towards removing older ones from the market.

B. Company Initiation of Rx-to-OTC Switch

FDA's hearing notice raised the issue whether the agency should propose to switch a drug without the support of the sponsor or otherwise should be more active in initiating switches. As explained in our testimony and comments provided at the June hearing, it would be poor public policy for FDA to initiate switches without the support of the sponsor. In any event, the agency lacks the legal authority to initiate a switch over the objection of the holder of the approved new drug application (NDA) for prescription use of the drug, at least without providing a formal evidentiary hearing.

The NDA holder – the company that developed the drug for prescription use -- knows the most about the drug and is in the best position to determine whether it would be appropriate to request a switch. Of course, FDA can and should consult with the NDA holder about whether the switch process should be initiated, but switches pursued over the NDA holder's objection run the risk of prematurely or inappropriately removing prescription safeguards, to the detriment of the public health. In the only case in which FDA did switch a drug without the prior support of the sponsor (metaproterenol), extensive adverse comment ensued, and the agency moved quickly to rescind its decision. See 48 *Fed. Reg.* 24925 (June 3, 1983).

Modern switches require extensive supporting data to demonstrate that the drug can be used safely and effectively, with proper labeling, on a nonprescription basis. These data can include reports of clinical studies, actual use studies, label comprehension studies, and epidemiological studies. With rare exceptions, the only way that these data will be developed is by the NDA sponsor through the submission of an NDA or NDA supplement. If FDA switched a drug over the sponsor's objection by relying on data in the sponsor's NDA without following the procedures set forth in the Hatch-Waxman Amendments, this would violate the sponsor's proprietary rights to its data. Since virtually any switch would have to be based at least in part on data in the prescription

NDA, this is an additional legal restriction on the agency's ability to switch a drug without the sponsor's consent.[12]

The switch regulation procedure set forth in section 503(b)(3) of the Act is ill-suited to the development and review of such data and, in any event, is an anachronism that has not been used since 1971. Switch petitions by third parties, unsupported by data comparable to what FDA requires in a switch NDA, must be summarily rejected. Moreover, the switch regulation process was never used by FDA to switch a drug over the objection of the sponsor. It would be inconsistent with FDA's historic practice to revive this mechanism and use it in a manner that is totally at odds with its use during the entire time in which the agency actively relied on it.

Regardless of whether FDA wished to resuscitate the switch regulation process, the agency could not switch a drug over the objection of the NDA holder without providing a formal evidentiary hearing. A switch would alter the fundamental conditions of approval by removing the Rx legend from a drug's labeling. FDA cannot do this over the sponsor's objection without following the hearing process established in section 505(e) of the Act and proving that the inclusion of the legend renders the drug's labeling false or misleading in accordance with that statutory provision and the agency's regulations (21 C.F.R. §§ 314.150, 314.200).

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[12] Further, if FDA were to switch a drug over a sponsor's objection by relying on data in the sponsor's NDA, it could only do so in the limited circumstances permitted under the Hatch-Waxman Amendments and pursuant to the protections established by that law. For example, FDA could not legally approve an abbreviated new drug application (ANDA) to provide for OTC use of a listed drug that is limited to prescription use, because the labeling of the ANDA drug would not be the same as the labeling for the listed drug. 21 USC § 355(j)(4)(G). A supplement to the ANDA similarly could not be approved, because the labeling of the ANDA drug must remain the same as that of the listed drug even after approval; otherwise, the ANDA is subject to withdrawal. *See* 21 CFR § 214.150(b)(10); 57 Fed. Reg. 17950, 17970 (April 28, 1992). Nor could FDA release safety and effectiveness data from the prescription NDA, because these constitute confidential commercial information exempt from release under the Freedom of Information Act, and the NDA holder's opposition to switch presents "extraordinary circumstances" justifying withholding under the Hatch-Waxman Amendments. *See* 5 USC §552(b)(4); 21 USC §355(l); 21 CFR § 314.430. Finally, any attempt to switch a drug through the ANDA or section 505(b)(2) process would have to honor the exclusivity and patent protections established by the Hatch-Waxman Amendments. Whether or not these protections may have expired, FDA could not use the Hatch-Waxman process (either through an ANDA or a section 505(b)(2) application) to approve an OTC version of an approved prescription drug without first going through the hearing process described below to change the labeling of the NDA. Under the Durham-Humphrey Amendment, the same drug, at the same dose and for the same indication, cannot simultaneously be available on a prescription and nonprescription basis. Under Durham-Humphrey, FDA would be barred from approving an application for OTC use of an approved prescription drug without addressing the prescription status of that drug—which would be subject to the NDA holder's section 505(e) hearing rights.

Congress did not intend the switch regulation process established in section 503(b)(3) to override a sponsor's hearing rights under section 505(e). Section 503(b)(3) was enacted as part of the Durham-Humphrey Amendment in 1951. This amendment enabled FDA to bring order to situations in which different companies marketed the same drug on Rx and OTC bases, by establishing that a particular drug (in the same dosage form and strength, and labeled for the same indication) must be marketed either as a prescription or nonprescription drug, but not both. There is no suggestion that Congress intended FDA to apply the provision in a way that overrides the hearing rights of an NDA sponsor when only one company currently is marketing the drug. Moreover, Congress amended the NDA provisions, including section 505(e), in 1962, more than ten years after passage of the Durham-Humphrey Amendment. Since it was modified later, section 505(e) should control over section 503(b)(3).

In any event, section 503(b)(3) does not specify what procedure is to be followed in issuing a switch regulation. While FDA reasonably may use informal rulemaking when a sponsor does not object, or when a large class of NDAs would be affected, fundamental principles of administrative law and due process require that FDA use a formal hearing process for switch rules issued under this section that affect a single or small number of NDA holders, regardless of the applicability of section 505(e), because the switch regulation constitutes an individual adjudication requiring a formal hearing. See, e.g., *Air North America* v. *DOT*, 937 F.2d 1427 (9th Cir. 1991) (agency must comply with both the Administrative Procedure Act and its organic statute); *Committee for Effective Cellular Rates* v. *FCC*, 53 F.3d 1309, 1318 (D.C. Cir. 1995) (an agency "cannot, merely by invoking its rulemaking authority, avoid the adjudicatory procedures required for granting and modifying individual licenses"); *Civil Aeronautics Bd.* v. *Delta Airlines*, 367 U.S. 316 (1961) (regulation forcing modification of a single license required a hearing); *American Airlines, Inc.* v. *CAB*, 359 F.2d 624, 631 (D.C. Cir. 1966) (agency cannot undertake an "individual action . . . masquerading as a general rule").

Thus, the case law establishes "a recognized distinction . . . 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." *United States* v. *Florida East Coast Ry. Co.*, 410 U.S. 224, 245 (1973). The switch of one or a small number of drugs falls clearly into the latter category rather than the former and therefore requires a hearing to resolve any dispute with the NDA holder. A hearing similarly is required under principles of procedural due process, because of the NDA holder's property rights in its approved NDA. See generally, e.g., *Barry* v. *Barchi*, 443 U.S. 55 (1979); *Ingraham* v. *Wright*, 430 U.S. 651 (1977).

FDA thus would face virtually insurmountable procedural obstacles to initiating switches over the objection of drug sponsors. If it pursued this path, it would find itself tied up in lengthy and burdensome hearings, quite possibly for years. It makes far more sense – not just legally, but practically as well – for FDA to continue to undertake its switch activities with the cooperation of sponsors. This way, drugs will be switched

more quickly (where appropriate), more safely, and with more supporting data, all to the benefit of the public health.

C. Prevention Claims

FDA asks whether prevention claims can promote ill-advised behavior. Placing this in perspective, how patients and consumers behave rests with them irrespective of the best intentions of the medical professional, the manufacturers, or the agency. This question is true both for Rx and OTC products.

The more relevant questions in the context of switch are: what is the nature and extent of ill-advised behavior associated with prevention claims, is this balanced by the benefits associated with prevention claims, and how would OTC availability provide a similar or greater public health benefit to consumers than prescription alternatives. Such an inquiry is best answered on a case-specific basis with data.

D. Co-existing Treatments

FDA asks about the impact of co-existing treatments, including how to determine appropriate self-selection of OTC and Rx treatments.

This is not a new issue to both self-care and physician-directed care. Both Rx and OTC products are already available for the same conditions, some with the same active ingredients, but with different formulations, strengths, or indications. In fact, a casual perusal of the PDR reveals many conditions, which have both Rx and OTC options available to the patient and to the consumer. OTC products typically contain usage limitations, i.e., if the condition persists beyond a specified number of days, see a physician. Many conditions exist across a spectrum of severity and symptomatology where it is entirely appropriate to provide products for both self-care and physician-directed care.

E. Consumer Understanding & Request for Further Dialogue

On the subject of consumer understanding, FDA asked: How can the agency be assured of consumer understanding of the benefits and risks of specific OTC drug products and the ability of consumers to use OTC products safely and effectively?

FDA can continue to gain assurance by using the established switch process and the consumer behavioral research studies that have been refined in the last decade to address case-specific switch questions. Consumer behavioral research includes attitudinal and comprehension as well as observational research. Examples include:

- Actual use studies
- Label comprehension studies
- Research defining potential OTC target populations;

- Research on educational programs/materials that form part of the labeling of the switch candidate.

Any and all of these studies can be essential to the OTC benefit/risk decision. FDA's question suggests a need for further dialogue on this matter. We asked for this orally at the time of the June meeting and are taking steps to follow-up on this matter, initially through a joint workshop with FDA and industry at the CHPA Research & Scientific Development Conference scheduled November 8 and 9, 2000.

III. Marketing Issues

A. Brand Name Line Extensions

FDA requested comment on the use of brand name line extensions, and inquired in particular about the possibility of consumer confusion when the active ingredients generally associated with a brand are not present in some of the brand's extended product line. 65 Fed. Reg. at 24705. As explained below, brand name line extensions provide accurate and useful information to consumers. Moreover, the use of brand name line extensions is essential for manufacturers in developing useful new products for consumers. Finally, FDA may not prohibit the use of an extended brand name unless it is inherently misleading and no other measure (such as clarification in the labeling) will eliminate consumer confusion. Prohibiting the use of a brand name on a product in an extended product line is tantamount to trademark excision, which is ordinarily reserved for situations where use of the brand name would be so misleading as to constitute an outright lie.

1. Brand Name Line Extensions Provide Accurate and Material Information to Consumers and are Essential for the Continued Availability of New OTC Drug Products.

The function of a trademark or brand name is twofold: to identify to consumers the source of a product, and to secure for the manufacturer a return on its investment in research, development, and advertising, by differentiating its product from other products.

Brand name line extensions are useful to consumers. Consumers confronted with many products offering similar benefits need and seek criteria for narrowing the field of products available to the single product they will ultimately select. A brand name line extension conveys the message that the product on which the brand name appears is available from the same company as an already-marketed product with which the consumer may be familiar. This accurate message assists the purchasing decision by identifying the source of a product. It allows the consumer to locate a family of products in which he or she has trust, and to choose from among them the one most appropriate to a current need. In short, brand line extensions provide information to consumers that is both accurate and useful to the purchasing decision.

Brand name line extensions are also critical to the market success of OTC drug products. Brand names are the principal repository of the good will that leads to repeat purchases of products. They are also the principal mechanism by which a company distinguishes its product from that of others. See, e.g., *American Steel Foundries* v. *Comm'r of Patents*, 269 U.S. 372 (1925); *Estate of Beckwith* v. *Comm'r of Patents*, 252 U.S. 538 (1919). Use of an established company trademark on a second company product identifies the source of the product and communicates to consumers a particular standard of quality.

The inherent value of brand names is augmented by the fact that they are costly to create. The value of a brand name is only as significant as the images it inspires in the minds of consumers. These images are hard to fashion in a powerful and memorable way, and the start-up costs of producing a successful brand name are high. A company often invests significant sums in advertising the safety, effectiveness, and quality of a product. The company similarly invests in its product development and manufacturing operations to ensure that those advertising claims are supported in practice. Brand names thus become extremely valuable business assets.

A limit on line extensions would raise the costs of introducing new products, thereby reducing competition and ultimately increasing consumer prices. Such a limitation also would restrict consumer choice because the expense of establishing new brand names could reduce the number of new products introduced to the market.

2. FDA May Not Preclude the Use of Brand Name Line Extensions on OTC Drug Products.

FDA's authority over a company's use of its trademark stems from the statutory provision deeming a drug to be misbranded if its labeling is false or misleading and from the related provision authorizing FDA to refuse to approve an NDA proposing labeling that is false or misleading. 21 U.S.C. §§ 352(a) and 355(d)(7). The legislative history of the latter provision makes it clear that a product is misbranded in this way only if there are "objective facts of record which make the proposed labeling demonstrably false or demonstrably misleading." See 108 *Cong. Rec.* 21066 (1962). Similarly, under the Federal Trade Commission Act, use of a trademark can be prohibited only if additional labeling will not clarify the confusion. See, e.g., *FTC* v. *Royal Milling Co.*, 288 U.S. 212, 217 (1932) (trade names are misleading where purchasers are deceived into purchasing an article which they do not wish or intend to buy, and which they might or might not buy if correctly informed as to its origin).

The First Amendment requires the same conclusion. It has been clear since at least the early 1980s that product labeling is commercial speech entitled to the protection of the First Amendment. See *Bolger* v. *Young Drug Prods. Corp.*, 463 U.S. 60, 67-68 (1983); *Pearson* v. *Shalala*, 164 F.3d 650, 655 (D.C. Cir. 1999) (applying First Amendment and striking FDA regulation that governed health claims on the labels of dietary supplements). It is also well settled that trademarks are commercial speech. See

Friedman v. *Rogers*, 440 U.S. 1, 11 (1979) (adoption of a symbol as a trademark is a form of commercial speech); J. Thomas McCarthy, "Important Trends in Trademark and Unfair Competition During the Decade of the 1970s," 71 Trademark Rep. 93, 119 (1981) ("[A] company's trademark is the most important element of commercial speech . . . ."); Marla J. Caplan, Comment, "Antidilution Statutes and the First Amendment," 21 S.W.U. L. Rev. 1139, 1163 (1992).

Commercial speech that is neither misleading nor illegal may be regulated or prohibited only if (1) the asserted government interest is substantial, (2) the regulation directly advances the government interest, and (3) the fit between the means and the ends is reasonable. *Central Hudson Gas & Elec. Corp.* v. *Public Serv. Comm'n*, 447 U.S. 557 (1980). The fit between means and ends is per se unreasonable if the government chooses suppression when a disclaimer would adequately serve its interest. See *Pearson*, 164 F.3d at 656-57. Moreover, the courts have tended to apply the First Amendment strictly when government seeks to regulate a company's right to use its mark. See, e.g., *Berkey Photo* v. *Eastman Kodak*, 603 F.2d 263 (2d Cir. 1979), *cert. denied*, 444 U.S. 1093 (1980) (reversing trial court decree that Kodak sell color print paper without its backprint at the option of the purchaser).

Line extensions are not inherently misleading. The *Central Hudson* Court explained that speech is inherently misleading only if it is "more likely to deceive the public than to inform it." 447 U.S. at 563. Line extensions, by way of contrast, reduce customer confusion by providing accurate information that helpfully categorizes products by source. They provide patients and physicians with helpful information, by allowing them to associate a new product with a known manufacturer or distributor. Because line extensions are not inherently misleading, the FDA may not prohibit them unless it can articulate a substantial government interest in doing so, demonstrate that preventing them directly advances that government interest, and show that some sort of explanatory information in the labeling would not serve its interest. *Cf. Washington Legal Foundation* v. *Friedman*, 13 F. Supp.2d 51, 72-74 (D.D.C. 1998), *appeal dismissed and vacated in part on other grounds*, 202 F.3d 331 (D.C. Cir. 2000); *see also Nutritional Health Alliance* v. *Shalala*, 953 F. Supp. 526 (S.D.N.Y. 1997).

FDA has suggested it may have an interest in preventing the customer confusion that may result if products in the same line use different active ingredients. However, the Agency's own regulations require the inclusion of sufficient information to ensure complete and accurate consumer understanding of all items purchased. OTC drug products must be labeled with their ingredients, indications, and directions for use. 21 C.F.R. §§ 201.5, 201.10, 201.66. Thus FDA regulations already ensure that consumers know precisely what is being purchased. Indeed, in the final rule on OTC labeling, FDA required active ingredients to be listed first in the "Drug Facts" panel, remarking that this placement "will help to ensure proper product selection, especially for product line extensions." 64 *Fed. Reg.* 13254, 13260 (March 17, 1999). Accordingly, under the *Central Hudson* test, FDA may not prohibit the use of brand names in OTC product line extensions.

The recent spate of federal court decisions rejecting FDA's attempts to suppress truthful commercial speech suggests the Agency should tread lightly in the area of brand name line extensions. These cases have confirmed the fundamental proposition -- that is definitive in this area -– that FDA may not prohibit truthful speech simply to protect consumers from confusion, when further speech will remedy any possible confusion. In *Pearson*, for instance, FDA argued "that it is never obligated to utilize the disclaimer approach, because the commercial speech doctrine does not embody a preference for disclosure over outright suppression." 164 F.3d at 657. The Court of Appeals unequivocally rejected this argument: "Our understanding of the doctrine is otherwise." *Id.* Quoting the Supreme Court, the Court of Appeals wrote that "'the preferred remedy is more disclosure, rather than less.'" *Id.*, *quoting Bates* v. *State Bar of Arizona*, 433 U.S. 350, 376 (1977). Indeed, in "recent cases, the [Supreme] Court has reaffirmed this principle, repeatedly pointing to disclaimers as constitutionally preferable to outright suppression." *Id.* at 657. See also *Washington Legal Foundation*, 13 F. Supp.2d at 72-74 (describing "Supreme Court's preference for combating potentially problematic speech with more speech," rejecting Guidance Document restrictions on off-label speech, and noting "the most obvious alternative [which] is full, complete, and unambiguous disclosure by the manufacturer"); *Western States Medical Center* v. *Shalala*, 69 F. Supp.2d 1288 (D. Nev. 1999), *appeal pending*, No. 99-17424 (9th Cir.).

3. Trademark Excision is Permissible Only when Use of the Brand Name is Tantamount to a Lie.

Longstanding FDA policy permits trademark excision only when qualifying language would not adequately correct likely consumer misperceptions. Twenty years ago, FDA proposed a rule providing that a change in the formulation of a drug would not require the excision of a trade name, if the change did not significantly alter the product's use or active ingredients. The proposed rule was not adopted, due to administrative backlog, but the Notice of Proposed Rulemaking in question made it quite clear that the agency recognized this was already its existing policy and the rule announced by the courts. FDA stated that "It is the policy of the Food and Drug Administration, in accordance with principles laid down in the courts, to require excision of a brand name only where nothing less than excision would eliminate the possibility of deception, and to permit retention of a brand name where either permanent qualification of the name or prominent public disclosure of the change in the product for a significant period of time is sufficient to inform the public of the change in the product or its use." 39 Fed. Reg. 11298 (March 27, 1974).

Cases in which excision have been found appropriate present extreme circumstances where the brand name was so misleading as to constitute an outright lie. See, e.g., *FTC* v. *Algoma Lumber*, 291 U.S. 67 (1934) (sustaining FTC determination that no method short of trade name excision would protect the public from being misled into purchasing "yellow pine" that was advertised as the superior and more expensive "California White Pine"); *Indiana Quartered Oak* v. *FTC*, 26 F.2d 340 (2d Cir. 1928) (finding excision the only appropriate remedy where "Philippine Mahogany" wood was not mahogany). In these instances, "white pine" was not white pine, and "mahogany"

was not mahogany. No amount of clarification could render these brand names non-misleading. Compare *Jacob Siegel* v. *FTC*, 327 U.S. 608, 613 (1946) ("[T]he policy of the law to protect [trade names] as assets of a business indicates that their destruction 'should not be ordered if less drastic means will accomplish the same result.'"). These cases have no application to line extensions: while a trade name may be associated with products containing a particular ingredient, the trade name is not the active ingredient name, and it is not inherently misleading to use the same trade name for a variety of products, each accurately labeled with its active ingredients.

In sum, the courts permit excision only when a brand name rises to the level of a lie. There is no way that brand name extensions on OTC drug product lines could be deemed to rise to this level; to the contrary, they accurately convey useful information about the source of a product, as described above. FDA prohibition of a brand name line extension would violate the food and drug law, FDA policy, and the First Amendment.

B. The OTC Drug Distribution System

FDA asked if the current structure for marketing OTC products in the United States is adequate and what lessons can be learned from different systems, such as those countries where some nonprescription drug products are sold "behind the counter."

The subject of a third class of drugs available only from a pharmacist has been exhaustively studied and repeatedly rejected in the United States on the ground that no public health need has been demonstrated. FDA has acknowledged that FDA has no legal authority to mandate a pharmacy-only class of drugs. The developing trend in other countries is to follow America's lead by expanding unrestricted access to OTC drugs. Against this background, it would be a backward step and contrary to sound public health policy for the United States to consider restrictions on OTC availability.

1. The Third Class Idea Has Been Repeatedly Rejected for Over a Century.

The subject of a third or pharmacist-only class of drugs has been exhaustively debated and rejected repeatedly for over a century. The U.S. General Accounting Office (GAO) conducted the definitive modern study on the subject. The title of its 1995 Report tells the story: *Nonprescription Drugs: Value of a Pharmacist-Controlled Class Has Yet to Be Demonstrated.*[13] GAO conducted a three-year investigation of 10 countries plus the European Union, and concluded that experiences in these countries, all of which have a restricted class of nonprescription drugs, "do not support a fundamental change in the drug distribution system of the U.S."[14] On the contrary, GAO found that "The evidence

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13 (GAO/PEMD-95-12, August 1995).

14 Id. at 79.

that does exist tends to undermine the contention that major benefits are being obtained in countries with a pharmacist or pharmacy only class."[15]

Whether termed third class, pharmacy-only, pharmacists' monopoly, restrictive sales, or transition class, the conclusion has always been the same: A restriction on consumer choice and access, with higher costs, and no demonstrated public health benefit to the consumer. Formal appeals to establish a third class of drugs have been consistently rejected in the states, by FDA, by the Department of Justice, by Congress, and the courts.[16] The concept of placing prescription-to-nonprescription switch drugs in a

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[15] Id. at 80.

[16] For states, see CHPA, "State Legislation/Regulations Involving Third Class," July 24, 2000 (listing 558 proposals since 1915). FDA rejections are examined in more detail later, and include, for example, letter from Frank Young, Commissioner of Food and Drugs, to Charles M. West, NARD (December 1984). For the Department of Justice, see letter from Thomas E. Kauper, Assistant Attorney General, Antitrust Division, to hearing clerk, Department of Health, Education and Welfare, February 4, 1974 (concluding a pharmacist-only proposal would have severe anticompetitive effects and inhibit the efficient distribution of OTC drug products to the consumer); and letter from Lawrence E. Walsh, Deputy Attorney General, to Rep. John L. McMillan, Chairman, District of Columbia Committee, U.S. House of Reps., May 3, 1960 (stating preventing supermarkets and other stores from selling pharmacist-only drugs would substantially lessen competition and unduly inconvenience consumers by limiting access, and noting "courts in several states have viewed the health justification for such a measure as a sham"). For the courts, see, for example, Board of Pharmacy of the State of New Jersey v. Anderson, 40 N.J. 40, 190 A.2d 664 (1963) (finding the state's pharmacy practice act was not intended to regulate the sale of "patent or proprietary medicines"); State v. Childs, 32 Ariz. 222, 257 Pac. 366 (1927), Noel v. The People, 167 Ill. 587, 58 N.E. 616 (1900), State v. Wood, 51 S.D. 485, 215 N.W. 487 (1927) (finding an exemption from pharmacy practice acts for "proprietary" medicines was necessary to avoid being construed as an unjustified grant or privilege to one class of merchants to the detriment of another). One of the earlier cases put it most bluntly: "Now, it is a matter of common knowledge that what are called 'patent' or 'proprietary' medicines are prepared ready for immediate use by the public. . . . There is nothing that calls into use any skill or science on the part of the one who sells them. One man can do it just as well as another, if he can read the label on the package and make change with the purchaser. The fact that the seller is a pharmacist, of itself, furnishes no protection to the public. The articles might as well be sold by a grocer or dry goods merchant." State v. Donaldson, 41 Minn. 74, 442 N.W. 781 (1889). Some cases in the 1930s through the 1950s *did* find the OTC medicine exemption in state pharmacy practice acts did not encompass *all* OTC medicines, but based on confusion over the meaning of "proprietary," not based on the merits of the case. All of these cases were either later over-turned; or the state legislature acted to clarify that unrestricted general sale of OTC medicines would remain the standard. For further history on these cases, see Edmondson and Weigel, "Recent Developments in the Law Relating to the Retail Sale of Drugs," Food Drug Cosmetic Law Journal, at 469, August 1965, and Weigel, "State Legislation Restricting the Sale of Drugs," Food Drug Cosmetic Law Journal, at 48, January 1958.

"transitional" category dates back over 35 years and has also met with repeated rejection on public health policy and legal grounds.[17] Over the years, the concept of a third class of drugs has been studied, debated, and rejected by organizations outside of government as well, such as medical groups, consumer groups, state chambers of commerce, retailers, labor unions, organizations representing the elderly, and farm groups.[18] All have reached consistent conclusions that no public health benefit has been shown and/or that consumers would be unnecessarily deprived of access to important OTC products, without a countervailing health benefit.

2. Limited State Approaches to Drug Distribution Do Not Provide a Useful Model for a Federal Pharmacy-Only Class of Nonprescription Drugs

Some proponents of a pharmacist-only third class of drugs have offered as precedent certain restrictive drug distribution models in the United States. Upon closer examination, however, these examples do not provide a basis for pharmacist-only third class distribution of nonprescription drugs.

Florida has experimented with a pharmacist class of *prescription* drugs. Under the state law, pharmacists may prescribe/dispense certain prescription drugs without the written order of a physician. *See Fla. Stat.* s.465.186. Physicians may continue to prescribe the drugs as well, thus, pharmacists do not hold a monopoly on the drugs' availability. The Florida experiment has been largely unsuccessful because pharmacists and/or the stores who employ them have been unwilling to assume the liability risks attached. *See GAO* at 71-72. GAO noted that the effect of the Florida law has been minimal because few pharmacists were using their prescribing authority; record keeping

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[17] Apple, "Statement of the American Pharmaceutical Association," before the Subcommittee on Reorganization and International Organizations of the Committee on Government Operations, U.S. Senate, 88th Cong., 1st Sess., September 12, 1963 ("This 'available only through pharmacists' category of drugs should include: (1) all drugs for a period of ten years subsequent to removal of the Rx legend. . . .").

[18] See letter from the American Association of Healthcare Consultants to FDA, Sept. 15, 1993 (opposing a third or transitional class); resolution of the American Legislative Exchange Council, July 9, 1988 (supporting continued unrestricted sale of OTC medicines); American Medical Association Report of the Board of Trustrees, 1994 (opposing establishment of a pharmacist-only class of drugs); letter from the Interamerican College of Physicians and Surgeons to FDA, May 12, 1993 (supporting the two class system of drug distribution); letter from the National Council on Aging to FDA, August 11, 1993 (opposing adding a third class of drugs); letter from the California National Retired Teachers Assn./American Assn. of Retired Persons to a California Assemblyman, Feb. 15, 1978 (opposing a pharmacist-only bill); letter from AFSCME to a Mass. Senator, March 22, 1975 (opposing druggist monopoly bill); memo from Illinois Retail Merchants Association to the Illinois House of Representatives (co-signed by 22 organizations), May 6, 1985 (opposing a pharmacy-only bill); letter from National Grange to NDMA (now CHPA), August 27, 1991 (supporting the U.S. two class of drug system and opposing legislation that would restrict competition).

and information gathering from patients created time problems; and because of the liability concerns. At a time when there is a shortage of pharmacists, the added time-pressures that a pharmacy-only class of nonprescription drugs would add make such a plan even less appealing. No other state has adopted a plan similar to the Florida law.

Another model advanced in support of a pharmacist-only class of nonprescription drugs is the doctor-pharmacist dependent prescribing protocol that exists in a number of states. Under this model, which varies among the states, pharmacists in retail settings can exercise dependent prescribing authority.[19] A pharmacist is permitted to prescribe/dispense certain prescription drugs if he follows a written protocol of questions for the patient established by the licensed physician(s). In some states, the collaborative protocol is restricted to institutional settings such as hospitals and clinics where physicians are readily available. Typical of the prescription drugs subject to the dependent pharmacist prescribing protocols is the emergency contraceptive (EC) pill, whose effectiveness is enhanced the sooner it is administered following unprotected intercourse. The emergency contraceptive situation is unique in that a physician "diagnosis" is not required in the traditional sense, since the woman best knows whether she has had unprotected intercourse and thus may be a candidate for EC treatment. Even in the collaborative protocol situation, the physician is not removed from the picture in favor of the pharmacist. The physician has developed the detailed written protocol, which the pharmacist must strictly follow in order to dispense the drug. In effect, the protocol is a detailed prescription. The pharmacist has no independent authority to prescribe the drug absent adherence to the protocol. Further, the drugs subject to the protocols are prescription drugs rather than OTCs, and may continue to be prescribed by a physician such that the pharmacist does not hold a monopoly on their availability. Collaborative agreements fall squarely within the realm of professional health care.[20] Accordingly, state collaborative prescribing protocols do not offer a useful model for a pharmacist-only class of nonprescription drugs.

Some states restrict consumer access to Schedule V nonprescription controlled substances to pharmacies. These restrictions were imposed under state controlled substance laws, not federal law, state food and drug laws or state pharmacy practice acts. The original intent of the restrictions was to prevent abuse, but many states that had originally placed Schedule V nonprescription drugs behind the counter discovered that the restrictions did not achieve their intended purpose. Instead, roughly half of the states

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[19] See Kimberly A. Galt, "The Key to Pharmacist Prescribing: Collaboration," 52 Am. J. Health-Sys Pharmacists, 309 (1995); National Association of Boards of Pharmacy, *1998-1999 Survey of Pharmacy Law*, at 66, listing 12 states with some form of prescribing authority, be it dependent, based on collaborative practice agreements, or independent based on a limited formulary (as in Florida). See also Deborah Boatwright, "Legal Aspects of expanded prescribing authority for pharmacists," 55 Am. J. Health-Sys Pharmacists, 585 (1985)(identifying a trend toward dependent prescribing authority arrangements and some of the liability issues involved).

[20] See Boatwright, supra.

placed such substances on prescription status under their controlled substances laws.[21] GAO found that use of a pharmacy only class to prevent abuse met with similarly poor results in other countries. In a German study, for example, children between 10 and 14 were sent to pharmacies to ascertain how easily they could purchase medicines containing alcohol. In all 54 pharmacies visited, the children were allowed to purchase the drugs, and in only one instance was the child questioned intensively. The German pharmacy association called the results of this consumer association study "lamentable."[22]

Federal regulations issued under the authority of the Controlled Substances Act (CSA) restrict the distribution of non-narcotic OTCs to pharmacy sale under strict record keeping requirements. The purpose of the restrictions is to prevent the abuse of controlled substances under conditions of widespread availability. Under the CSA regulation a pharmacist may dispense a non-narcotic OTC drug that is listed in Schedules II, III, or IV without a doctor's prescription if he maintains a bound record book containing information about the purchaser, the quantity of the controlled substance purchased, and the date purchased. 21 CFR § 1306.26. The pharmacist's role is narrowly circumscribed to provide this security function. The security purpose of the CSA regulation is fundamentally different from the purpose of the Federal Food, Drug, and Cosmetic Act (FDC Act) to assure safe and effective use of drugs. The CSA regulation does not and indeed could not require pharmacist counseling of purchasers about the safe and effective use of affected OTC drugs as a precondition to their sale. In passing the Controlled Substances Act, Congress made clear that "nothing in the CSA . . . shall be construed as in any way affecting, modifying, repealing, or superseding the provisions of the Federal Food, Drug, and Cosmetic Act."[23] As discussed below, FDA lacks the legal authority under the FDC Act to create a mandatory restricted or pharmacy-only class of nonprescription drugs. Thus, the restrictive sale of scheduled OTCs does not provide a model for a pharmacy-only class of nonprescription drugs under the FDC Act.

3. International Experience Does Not Support a Change in the U.S. Two-Class System and the World Trend is To Follow America's Lead and Expand Unrestricted Access to Nonprescription Drugs.

The existence of third or pharmacist-only classes of drugs in other countries does not support establishing such a class in the United States. No public health advantages have been identified to justify importing the foreign systems. The existence of those systems can generally be traced to historical social, cultural, and economic traditions, and not to any public health rationale. For example, sales restrictions may be relics of

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21 Among others, these include California, Colorado, Louisiana, Montana, Nebraska, New Hampshire, North Dakota, Oregon, Rhode Island, and Texas. Full state summary chart, with citations, on file at CHPA.

22 GAO, supra, at 28.

23 H.R. Rep. No. 1214, 90th Cong., 2d Sess. 2 (1968).

centuries-old European guilds. American principles that favor open competition do not have equivalents in many nations.

The U.S. General Accounting Office (GAO) devoted three years to the investigation of third class systems in other countries, and concluded in its August 24, 1995 report that experiences in these countries "do not support a fundamental change in the U.S. system."[24] GAO stated:

> "The evidence that does exist tends to undermine the contention that major benefits are being obtained in countries with a pharmacist or pharmacy only class."[25]

The GAO report offered the following additional conclusions:

- Drug distribution: Third class systems in other countries are "not being used to facilitate the movement of drugs to sale beyond pharmacies." Instead, they are generally viewed as fixed classes into which drugs are permanently placed.[26]
- Switch and OTC drug availability: The existence of a third class does not make regulatory officials more or less likely to approve new OTC products or switch prescription drugs to unrestricted nonprescription status (i.e., Rx-to-OTC switch).[27]
- Pharmacy practice: Pharmacists in the U.S. and elsewhere often do not perform the roles on which the benefits of third class are premised – even when such roles are expected or required. These roles include appropriate and complete counseling, reporting adverse drug events, and maintaining patient profiles. GAO concludes, "the theory of pharmacy practice diverges from the reality."[28]

At a time when community pharmacies are frequently challenged by workloads and manpower shortages, pharmacy counseling requirements are increasingly difficult to

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24 GAO, supra, at 80. GAO was asked by Rep. John Dingell (D-MI) to determine if there were significant benefits or costs from a third class of drugs based on experience in the European Union and 10 countries – Australia, Canada, Denmark, France, Germany, Italy, the Netherlands, Sweden, Switzerland, and the U.K. – countries restrict some or *all* nonprescription medicines to pharmacy-only sale.

25 Id.

26 Id., at 75.

27 See Id., at 42-43, 78.

28 Id., at 57-59, 65, 79.

satisfy in the prescription drug area. Adding a pharmacist-counseling requirement for a third class of nonprescription drugs would further burden an already burdened system.[29]

International experience with a pharmacy class does not relate well to U.S. experience or needs. In Europe the pharmacy monopoly system is rooted in historic practice. In France, a pharmacy monopoly on the sale of medicines pre-dates the French Revolution.[30] Restrictive business practices related to pharmacy-only systems in Europe -- practices such as uniform retail prices, geographic limitations on where pharmacies can be set up, limits or bans on retail chains, requirements that only pharmacists may own pharmacies, and restrictions on what goods may be sold in a pharmacy -- are widespread in Europe, but run counter to the U.S. competitive system.[31]

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[29] See American Pharmaceutical Association submission to the Health Resources and Services Administration, "Study Regarding Shortages of Licensed Pharmacists, 65 Fed. Reg. 14288 [March 16, 2000]," May 1, 2000, providing background for the HRSA study on pharmacist shortages, and including discussion of a paper, "Implementing Effective Change in Meeting the Demands of Community Pharmacy Practice in the United States," to outline responses to meeting the pharmacy manpower need and meeting the workload challenge. Similarly, the National Association of Chain Drug Stores has noted that the HRSA study "could serve as the basis for further federal action to alleviate the pharmacist shortage. "Action Alert: Federal Study of Pharmacist Shortage – Your Response Needed!" March 30, 2000, www.nacds.org/news/how.html. The HRSA was mandated by Congress "to determine whether and to what extent there is a shortage of licensed pharmacists." Pub.L. 1060-129, sec.5. See also Katherine K. Knapp, "Charting the demand for pharmacists in the managed care era," 56 *American Journal of Health-System Pharmacy,* 1309 (1999), forecasting increasing demand for pharmacists and finding little reason to expect the work force predictions of the Pew Commission Report. But see *Critical Challenges: Revitalizing the Health Professions for the Twenty-First Century*, 3d report of the Pew Health Professions Commissions (December 1995), which suggests an over-supply of pharmacists within the next several years. At the same time, the Pew Commission recognized the uneven supply needs and based its conclusion on increasing centralization in dispensing medicines.

[30] See AESGP, Self-Medication and the Pharmacist, at 33 (June 1993); J. Brodon and Georges Viala, "France," in International Pharmaceutical Services: The Drug Industry and Pharmacy Practice in Twenty-Three Major Countries of the World (Spivey, Wertheimer, and Rucker, eds., 1992), at 220-21.

[31] On uniform retail prices, see Bachynsky, "Denmark," in International Pharmaceutical Services, at 135; AESGP, Economic and Legal Framework for Nonprescription Medicines, at 137, on uniform retail prices for medicines available only in pharmacies in Germany; and at 337, on retail price maintenance for OTC medicines in the U.K. (May 2000). On geographic limitations, see, for example, Case 168/85 Commission v. Italy, 1986 E.C.R. 2945; and Brudon, "France," International Pharmaceutical Services, supra, at 204. On pharmacy ownership and chain bans or limitations, see Santiago Tapia, "Developing Self-Medication in France, Italy, and Spain," in AESGP, proceedings, Pharmacy – Growing Self-Medication: The Marketing Challenge, at 35-36 (January 26, 1993); Peter Kielgast, "Self-Medication and the Pharmacist," in AESGP, proceedings, at 47-48; AESGP, Economic and Legal

Since the 1995 GAO report was issued, there has been a developing world trend toward the U.S. approach of wider availability of nonprescription medicines. In the mid-1990s, the Netherlands broadened OTC availability by allowing "drugstores" as well as "pharmacies" (Netherlands "pharmacies" are different than "pharmacies" elsewhere in continental Europe) to sell nonprescription medicines.[32] The Netherlands Health Ministry is currently considering a recommendation of the Dutch Medicines Evaluation Board to allow general sale of all nonprescription medicines.[33] In Finland, the national competition authority has suggested exploration into general sale availability for nonprescription medicines.[34] In 1998, Japan re-classified a number of categories of nonprescription medicines as "quasi-drugs," and now allows their sale outside of pharmacies.[35] The European Commission noted in a 1998 "Single Market Communication" that a way to develop the underdeveloped nonprescription market in Europe would be for Member States to relax restrictions on the place of sale of medicines.[36] And while European Union (EU) seeks to harmonize regulation of medicines among Member States through suasion rather than mandated change, the EU body itself recognizes two classes of drugs: prescription and nonprescription.[37] There is no global or European trend in the more restrictive direction.

4. FDA Lacks the Legal Authority to Create a Third Class of Drugs.

Framework for Nonprescription Medicines, at 135, on pharmacist ownership of pharmacies in Germany; and Amendment to Recital 6a submitted by the EC Commission to the Council, 1984 O.J. c 40/4, on why a directive recognizing access to the practice of pharmacy among Member States did not extend to the establishment of new pharmacies or the takeover of existing pharmacies. On goods restrictions, see Sitzius-Zehender, "Germany," International Pharmaceutical Services, at 246.

[32] See AESGP, Economic and Legal Framework for Nonprescription Medicines, supra, at 219.

[33] See "Dutch druggists dispute distribution proposals," OTC Bulletin, at 14-15 (May 12, 2000); "General-sale issue ignites heated debate in Holland," OTC Bulletin, at 21 (March 29, 2000); "Dutch agency suggests a general-sale category," OTC Bulletin, (March 13, 2000).

[34] "Finnish OTC deregulation call," Scrip, at 7 (November 5, 1999).

[35] "Sales restrictions for some OTCs eased in Japan," Scrip, at 17 (June 10, 1998); Proprietary Association of Japan, PAJ Guide, at 10 (March 1999).

[36] See "Pharmacy monopoly and RPM could go says EC," OTC Bulletin, at 1 (November 30, 1998).

[37] See Council Directive 92/26/EEC, 1992 O.J. L 113/1; see also Case C-369/88 Re Delattre, 1991 E.C.R. I-1487, where the European Court of Justice noted the EU "acknowledges the existence of a pharmacists' monopoly in member states, but does not, in view of the fact that it is not a European Community concept, give any definition to it."

FDA lacks the legal authority to create a third class of nonprescription drugs that is available only from pharmacists. FDA Acting Commissioner Mark Novitch stated in 1984:

> "The current law does not authorize such a restriction. . . . Further, the American Pharmaceutical Association successfully challenged the 1972 FDA regulations which established a closed distribution system for methadone [*APhA v. Weinberger*, 377 F. Supp. 824 (D.D.C. 1974)]. … The court held that FDA lacked statutory authority to impose or authorize the imposition of certain post-approval controls on methadone and declared the regulations invalid to the extent that they prohibited or restricted shipment to, or receipt or dispensing by, a duly-licensed pharmacy. Although that case involved a drug which was subject to the new drug provisions of the Federal Food, Drug, and Cosmetic Act, and was a prescription drug, the opinion does raise serious questions concerning the Agency's authority to establish a third class of drugs. Because the Act requires that a drug either be limited to prescription dispensing or available OTC with adequate directions for use by a layman, this opinion appears to preclude the Agency from establishing a class of drugs whose labeling needs to be supplemented by a pharmacist's instructions."[38]

Since then, other FDA Commissioners and senior officials have consistently reiterated the position. For example:

- "[T]he agency believes it is questionable whether the distribution of lawfully marketed OTC drugs can be restricted as you request under current statutory provisions."-- Commissioner Frank Young.[39]
- "FDA has also concluded that it is questionable whether the distribution of lawfully marketed OTC drugs can be restricted through creation of this intermediate class of drugs."-- Acting Commissioner James Benson.[40]
- "We also reiterate that it is questionable whether FDA has legal authority under current law to establish a transitional or other intermediate class of

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[38] Letter from Mark Novitch, Acting Commissioner of Food and Drugs, to Rep. Albert Gore (D-TN), July 9, 1984.

[39] Letter from Frank Young, Commissioner of Food and Drugs, to Charles M. West, National Association of Retail Druggists, December 3, 1984. [Docket No. 84P-0028]

[40] Attachment to letter from James Benson, Acting Commissioner of Food and Drugs, to Rep. Ron Wyden (D-OR), November 5, 1990.

> drugs or to require distribution only through licensed pharmacists with education and consultation."-- Associate Commissioner Ronald Chesemore.[41]

The legislative history of the Durham-Humphrey amendments to the FDC Act supports the two-class system. The purpose of the prescription-nonprescription distinction in the amendments was to protect the public from abuses in the sale of potent prescription drugs, and to relieve pharmacists and the public from burdensome and unnecessary restrictions on the dispensing of safe OTC medicines.[42] The House report on the amendments that notes that "the Federal Food, Drug and Cosmetic Act, as enacted in 1938, recognized the right of self-medication . . . it was not the purpose of the Act to restrict self-medication, but to make it safe."[43] While an intermediate class of drugs was suggested during debates on the amendments, Congress specifically adopted a two-class system.[44]

In considering the Drug Regulation Reform bill of 1978, the Secretary of HHS (then Health Education and Welfare (HEW)) acknowledged that FDA lacked legal authority to create a third class of drugs. HEW Secretary Joseph A. Califano, Jr. stated: "Under current law, FDA has no authority to impose [distribution] restrictions. . . . The reform bill remedies this defect in current law by authorizing FDA to restrict the distribution of a drug if it finds that the restrictions are needed to make the drug safe because other measures are not adequate to make the drug safe."[45] While the bill did not pass, the Secretary's acknowledgement remains pertinent.

5. FDA Has Repeatedly Stated that a Public Health Need for a Third Class of Drugs Has Not Been Demonstrated.

FDA has consistently concluded that a public health need for a third class of drugs has not been demonstrated. FDA addressed this subject comprehensively early in the OTC Review. In the antacid monograph, FDA stated:

> "The Commissioner has spent a great deal of time reviewing the comments and discussing [the issue of a third class] with various groups, both in and out of the profession of pharmacy. The Federal Food, Drug, and Cosmetic Act

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41 Letter from Ronald Chesemore, FDA Associate Commissioner for Regulatory Affairs, to Frederick Mayer, Pharmacists Planning Service, Inc., October 26, 1993 [Docket No.93P-0185]

42 See S. Rep. No. 946, 82d Cong., 1st Sess. (1951).

43 H.R. Rep. No. 700, 82d Cong., 1st Sess. 110 (1951).

44 See hearings on S.1186 and H.R. 3295 before the Senate Subcommittee on Health of the Committee on Labor and Public Welfare, 82d Cong., 1st Sess. 14 (1951); H.R. Rep., supra, at 8-9, 11, 28.

45 Hearings on S.2755 before the Subcommittee on Health and Scientific Research of the Committee on Human Resources, 95th Cong., 2d Sess. 243 (1978).

> requires that OTC drugs be safe and effective for lay use. Although the act permits imposition of whatever limitations or restrictions are necessary to assure the safe use of any drug, including restrictions on the channels of distribution, no controlled studies or other adequate research data have been supplied to support the position that any class of OTC drugs must be dispensed only by pharmacists in order to assure their safe use. It would be inappropriate to restrict the sale of OTC drugs to pharmacies based on anything less than proof that a significant safety issue was involved.
>
> "There were a number of comments stating that creating a third class of drugs would create an economic monopoly and an anti-competitive situation. The Department of Justice opposed any such restriction on antitrust grounds.
>
> "The Commissioner believes that these concerns are valid. Restricting the sale of some or all OTC drugs only to pharmacies would decrease the number of outlets where the consumer could purchase OTC products, limit competition and raise some OTC drug prices, with no attendant public benefit. There is at this time no public health concern that would justify the creation of a third class of drugs to be dispensed only by a pharmacist or in a pharmacy. The 'third class of drugs' issue at this time is solely an economic issue. The Commissioner therefore categorically rejects the establishment of a third class of drugs at this time."[46]

Most recently, Commissioner Henney addressed the following remarks to the National Association of Boards of Pharmacy:

> "One last area that I know is of concern to your organization is the creation of a 'transition class' of pharmaceuticals that would be sold only under the supervision of a registered pharmacist, and only under certain conditions. First, it is a very good thing that we are constantly questioning the current system in an effort to find ways to increase patient access to medical products in a way that does not create unnecessary procedural hurdles,

[46] 39 Fed. Reg. 19862, 19880-81 (June 4, 1974). (The FDA assertion that the Act permits distribution restrictions came before APhA v. Weinberger, consideration of the 1978 Drug Regulation Reform bill, and FDA's own subsequent questioning of its legal authority; and it runs counter to the legislative history of the 1951 Durham-Humphrey amendments, as discussed in the preceding subsection of these comments.)

> yet provides adequate safeguards for patients and consumers. However, weighing the balance, we do not believe that the creation of another class of drugs is needed since there is a formal process in place to establish when a prescription product is appropriate for OTC use."[47]

Between the 1974 antacid monograph and Commissioner Henney's 1999 statement, FDA maintained its opposition to a third class of drugs. FDA formally rejected a third class in response to a series of citizen petitions filed by the Pharmacists Planning Service Inc. (PPSI) from 1991 to 1994. PPSI had opposed virtually all potential prescription-to-nonprescription switches during that time and sought a third class of drugs.[48] The Agency also rejected a third class of drugs in the tentative final monograph for combination cold, cough, allergy, bronchodilator, and antiasthmatic drug products because a public health need had not been demonstrated and because of the questionable legal authority to create such a class.[49]

The 1995 GAO report also found no public health need justifying a third class:

> "[T]here is no evidence to show that the role that U.S. pharmacists would have to play to support the appropriate use of an intermediate class of drugs (either fixed or transition) would be fulfilled reliably and effectively. The evidence indicates that at this time major improvements in nonprescription drug use are unlikely to result from restricting the sale of some OTCs to pharmacies or by pharmacists, nor are the safeguards for pharmacy- or pharmacist-class drugs that would have otherwise remained in the prescription class likely to be sufficient."[50]

6. Conclusion: The Two-Class System of Drug Distribution Serves Consumers Well.

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47 Speech to the National Association of Boards of Pharmacy Executive Officers Conference, Jane E. Henney, Commissioner of Food and Drugs, September 28, 1999.

48 See FDA letters of July 11, 1992 (Docket No. 91P-0470); January 25, 1993 (Docket No. 92P-0474); January 25, 1993 (Docket No. 78N-301H); July 1, 1992 (Docket No. 91P-0163); October 26, 1993 (Docket No. 93P-0185); January 25, 1993 (Docket No. 92P-0480); and December 3, 1993 (Docket No. 93P-0280). (This is not a comprehensive list.)

49 See 53 Fed. Reg. 30522, 30525 (August 12, 1988).

50 GAO, supra, at 80. (Note this discussion sets aside the issue of the quality of pharmacist counseling even where it is received. For a critical article on that point, see "Danger at the Drugstore," U.S. News & World Report, at 46 (August 26, 1996), asserting that "pharmacists are your last defense against risky drug interactions. Too many are blowing it.")

Convenience and access are fundamental to self-care and self-medication in the U.S. A third class of drugs would reduce consumer access to OTC medicines and increase costs without providing a tangible benefit to consumers or the healthcare system. No public health need for a change in that system has been shown to justify a third class, and the FDA lacks legal authority to establish such a class of drugs. The two-class system of prescription and nonprescription drugs works.

IV. Conclusion

In conclusion:

- The public is best served by having the broadest range of safe and effective OTC medicines available.
- The switch of drugs from prescription to nonprescription has been phenomenally successful in providing significant therapeutic benefits to consumers. This success has stemmed from the collaborative efforts of the industry and FDA working together to evaluate the specific merits of a case and to make a scientifically documented decision, and to the benefit of consumers.
- FDA must use the statutory criterion for switch, should continue to use the regulatory definitions of safety, effectiveness, and labeling, practice the scientific/regulatory paradigm, review drugs on their individual and not their comparative merits, and avoid presumptive negative lists.
- CHPA seeks additional dialogue on consumer behavioral research.
- Switch should be initiated by the NDA company, which has the most knowledge about the drug.
- Use of a brand name to identify a line of products facilitates product choice and enables manufacturers to develop and bring to market useful new self-care products.
- A third class of drugs has been thoroughly reviewed and rejected for over a century on the grounds that no public health benefit has been shown.

Most important, CHPA seeks collaborative approaches for the company-agency dialogue that is vital to creating a thorough, yet reasonable, OTC R&D program to test future switch proposals.

Submitted by:

_____ _____

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Attachments: A: *An Interview with CDER Director Janet Woodcock, M.D.*, U.S. Regulatory Reporter (May 2000)