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CONSUMER HEALTHCARE PRODUCTS ASSOCIATION®

CHPA Presentations at
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OTC Part 15 Hearing
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Over-the-Counter Medications: A Success Story

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Legal Perspective

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Scientific/Regulatory Perspective on Rx-to-OTC Switch

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Over-the-Counter Medications: A Success Story

Michael D. Maves, MD, MBA

President

Consumer Healthcare Products Association

June 28, 2000

Good morning, my name is Dr. Michael Maves and I am the President of the Consumer Healthcare Products Association, headquartered in Washington, DC, and a practicing otolaryngologist at the Georgetown University Medical Center. I want to thank the Food and Drug Administration for allowing CHPA to share our views on the questions and issues compiled in the Federal Register announcement of this meeting. CHPA intends to file comprehensive comments on these issues by the comment deadline.

Consumer Healthcare Products Association

- **Michael Maves, MD, President -- Introduction/Policy Issues**
- **Eve Bachrach, Esq., Sr. VP, General Counsel & Secretary -- Legal Issues**
- **R. William Soller, Ph.D., Sr. VP and Director, Science & Technology – Technical/Regulatory Process**

Our presentation will be in three parts. I will be addressing the overall policy issues of importance to the industry, including the OTC perspective. Ms. Bachrach will speak to selected legal issues as they impact the FDA questions and issues. Dr. Soller will lastly

address the scientific and regulatory perspective on technical and process issues. We will all be available for questions following these presentations.

Consumer Healthcare Products Association

- **119-year-old association**
- **200 members -- 90% retail sales**
- **Active partner with FDA and consumers:**
 - OTC drug development
 - Labeling
 - Manufacturing
 - Packaging

CHPA is the 119-year-old trade organization representing the manufacturers and distributors of nonprescription medicines and dietary supplements. The Consumer Healthcare Products Association has over 200 members across the manufacturing, distribution, research, testing, advertising and supply sectors of the self-care industry. CHPA members represent over 90% of retail sales in the OTC marketplace. We have worked collaboratively with consumers and the Food and Drug Administration over the years on all aspects of OTC drug development, labeling, manufacturing and packaging.

Conclusions

❶ Self-care with OTCs is here to stay!

- Consumers demand self-care
- Consumers are increasing knowledge of self-care
- Consumers want more self-control over self-care

❷ Rx-to-OTC switch has been phenomenally successful!

- Collaborative effort -- initiated by manufacturer, with FDA/consumers
- Specific case merits
- Scientifically documented benefit/risk decision

❸ Past is prologue to the future!

Let me begin my presentation where I will end. Self-care with OTC medicines is here to stay! Consumers demand it; they are increasingly aware of self-care and want more control over self-care.

Secondly, the switch of drugs from prescription to nonprescription has been phenomenally successful. 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.

Finally, if past is prologue to the future, over the past 25 years, **consumers, FDA, and industry** have faced increasingly difficult challenges regarding OTC availability of Rx products. **Together**, we have created novel solutions to difficult problems. **Consumers** have benefited from this collaboration and will continue to do so in the future.

OTC Perspective

Consumers Are Interested in Their Own Healthcare:

- **Explosion of information on Internet**
- **Wellness movement among population**
- **60% adults follow news stories about health**
 - More than business
 - More than sports

We talk about an OTC perspective within the OTC industry. This perspective, which must be shared by all concerned parties, recognizes the forces behind the self-care movement and captures the impetus for the development of new OTC products. I want to spend some time reviewing the elements of this perspective.

As I am sure you are aware, 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

¹*Prevention Magazine* survey, 1999

OTC Perspective

Consumers Benefit from Self-Care:

- **Empowerment**
- **Convenience, cost, time savings**
- **OTC self-care for 38% of health problems, yet less than 2% of healthcare dollar**
- **92% satisfaction with medication for self-care**
- **Societal/governmental costs**

Secondly, consumers benefit from self-care. Access to self-medication options empowers consumers and effectuates their desire to take control of their own conditions. OTC medications provide convenience, cost and time savings. Consumers turn to OTC self-care for 38%¹ of all health problems they experience, yet for this vast volume, OTCs take up less than 2 cents of every healthcare dollar.² Ninety-two percent are satisfied with the medications they have used for self-care.³ 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.

¹ Heller Research Group for CHPA, 1992

² See ACNielsen OTC sales estimates, 1999, and HCFA health expenditure estimates, 1999

³ Heller Research Group for CHPA, 1992

OTC Perspective

Self-Care Applies to a Wide Range of Conditions/Diseases:

- **Acute conditions without a prior diagnosis:**
 - Analgesics -- headache
 - Dermatological products -- rash
 - Gastrointestinal products -- heartburn
- **Acute recurrent conditions with an initial diagnosis:**
 - Antifungals -- vaginal yeast infection
- **Disease prevention strategies:**
 - Sunscreen -- skin cancer
 - Fluoride/Triclosan -- dental caries/gingivitis
- **Adjunctive treatment with life-style changes**
 - Nicotine replacement therapy -- smoking cessation

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 managed with OTC medication 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.

OTC Perspective

Consumers Use the OTC Label and Responsibly Self-Medicate:

- **95% consumers read the label prior to use**
- **High rates of consumer label comprehension**
- **OTC does not mean the physician is out of the picture**
 - Vaginal antifungals
- **All essential information in a usable form**

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%¹ 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 MD 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 easily available to the consumer.

¹ See generally Heller Research Group for CHPA, 1992, Louis Harris & Assoc., 1991, Princeton Survey Research Assoc., 1992, and Princeton Survey Research Assoc., 1993, finding 93, 97, 98, and 95 percent of consumers reporting reading the label either before first use or on purchasing OTC medicines.

OTC Perspective Scientific/Regulatory Paradigm

Reasonable expectation of benefit:

- **Specific target populations**
- **Readily recognizable conditions, previously diagnosed conditions, or self-diagnosable diseases**
- **Medications at the appropriate dosage and with comprehensible labeling**
- **Low potential for toxicity**

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.

OTC Perspective

New Products for Consumers Are Best Determined:

- **Case-by-case, specific to product**
- **Data-driven approach**
- **Initiated by the manufacturers**
- **Collaboration with FDA**
- **Individual, not comparative, merits**

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.

OTC Switch Successes!

- **Over 80 ingredients, dosages forms and strengths**
- **700 marketed products**
- **Examples**
 - Nicotine replacement therapy
 - Fluoride/Triclosan
 - Antifungals
 - Analgesics
 - Cough/cold remedies

This type of perspective has provided the consumer with a wide variety of products and truly some remarkable success stories for all of us. 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. I spoke about some examples earlier in the context of where self-care takes place. Several categories are listed again here.

OTC Perspective/Approach

Recognize:

- **Consumers are interested in healthcare**
- **Consumers benefit from self-care**
- **Self-care applies to a wide range of conditions**
- **Read OTC label and responsibly self-medicate**
- **Scientific paradigm to evaluate new OTCs**
- **New products -- case by case, data driven process**
- **A process to further develop labeling**
- **Success from a collaborative effort --
FDA/industry/consumers**

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 driven 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.

FDA Question:

Can prevention claims promote ill-advised behavior?

CHPA Answer:

- **Not specific to OTC products**
- **If this does happen, what is the public health risk/benefit to consumers**
- **Case-by-case analysis with specific data**

I would like to now address three aspects of FDA questions. My colleagues, Ms. Bachrach and Dr. Soller, will provide commentary on other aspects of FDA's questions.

FDA asks whether prevention claims can promote ill-advised behavior.

Let's step back. How patients and consumers behave rests with them irrespective of our best intentions. This is not unique or limited to OTC products. The more relevant questions are if this does happen, to what extent does it occur and how would OTC availability provide a similar or greater public health benefit to consumers than prescription alternatives. Again, we would feel that such an inquiry is best answered on a case-specific basis with data.

FDA Question:

Impact of co-existing treatments, including how to determine appropriate self-selection of OTC and Rx treatments?

CHPA Answer:

- **Already have availability of Rx and OTC products with the same active ingredients, but in different doses**
- **Nothing in law precludes co-existence of Rx and OTC**
- **Physician's Desk Reference: Many conditions have OTC and Rx options available:**
 - Pain
 - Contact dermatitis
 - GI conditions
 - Cough suppression
- **Appropriate to provide products for self-care and physician directed care**

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. We already have availability of both Rx and OTC products 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 X 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.

FDA Question:

What about the availability of a “better” OTC product in terms of efficacy or safety should affect the status of products already on the OTC market for treatment of the same condition?

CHPA Answer:

- **Individual response, preference, or compliance with treatment**
- **Medical policy backs wide armamentarium of options**
- **Consumers should have same choice**

FDA asks also about how the availability of a “better” OTC product would affect the status of products already on the OTC market for treatment of the same condition.

It’s well known that individuals – consumers, patients and physicians – vary in their responses and preferences for different treatments. This can lead to individual differences in compliance that may further vary the response to treatment. Therefore, the definition of “better” is not easily defined for this purpose. For that matter, on the Rx side, medical practice welcomes a wide armamentarium where many “older” drugs play a critical role. Consumers should have this same choice. Ms. Bachrach will amplify on this point in her comments.

Conclusions

❶ Self-care with OTCs is a phenomenon here to stay!

- Consumers demand self-care
- Consumers are increasing knowledge of self-care
- Consumers want more self-control over self-care

❷ Rx-to-OTC switch has been phenomenally successful!

- Collaborative effort -- initiated by manufacturer, with FDA/consumers
- Specific case merits
- Scientifically documented benefit/risk decision

❸ Past is prologue to the future!

In concluding my portion of our remarks, let me emphasize that self-care is here to stay! Consumers demand it; they are aware of it, and want more control over self-care.

Secondly, the switch of drugs from prescription to nonprescription has been phenomenally successful. 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.

Finally, if past is prologue to the future, over the past 25 years, **FDA/industry** have faced increasingly difficult challenges regarding availability of Rx products. **Together**, we have created novel solutions to difficult problems. **Consumers** have benefited from this collaboration and will continue to do so into the future. Thank you.

Eve E. Bachrach

Eve E. Bachrach

Senior Vice President, General Counsel and Secretary

Consumer Healthcare Products Association

June 28, 2000

I am Eve Bachrach, Senior Vice President, General Counsel and Secretary of the Consumer Healthcare Products Association. CHPA believes that FDA should continue to foster a regulatory environment under which consumers have greater access to safe and effective medicines that can be appropriately used and labeled for self-care. By following well-established legal principles, this public health goal can be met. We are pleased that the agency has provided this open forum to discuss important questions about the regulation of OTC drugs because we have concerns with some of the questions FDA has raised in its hearing notice.

Four Issues

- **Who should initiate switch?**
- **Role of comparative assessments**
- **Use of a single brand name to identify a family of products**
- **Two-class system of U.S. drug distribution**

I will focus on four areas that involve combined policy and legal issues. *First*, who should initiate an OTC switch; *second*, the role of comparative assessments in making decisions to switch drugs, approve them, or withdraw them from the market; *third*, the use of a single

brand name to identify a line of OTC products; and *fourth*, the two-class system for distributing drugs in the United States.

FDA Questions:

Should FDA propose OTC switches without drug company support?

Should FDA be more active in initiating switches?

CHPA Answer:

In public interest for NDA company to initiate switches

- **Most comprehensive knowledge about drug**
- **In best position to design, conduct, analyze studies**
- **Switches without NDA company could be inappropriate**

– Metaproterenol

FDA asks if it should propose OTC marketing “in the absence of support from the drug sponsor” and, more generally, if FDA should be “more active in initiating switches.”

Today, virtually every switch is accomplished through the new drug approval (NDA) process. This makes public health sense. The company that developed the drug in the first place and obtained the NDA for the Rx drug knows the most about the drug. The company also is in the best position to design and perform the studies necessary to establish whether a drug can be adequately labeled for OTC use and, where necessary, to establish that the drug is safe and effective for the proposed OTC indication and dose.

Where FDA believes that a drug should be considered for OTC use, the agency should consult with the company about this. However, the suggestion that FDA might switch a drug without the company’s active participation, or worse, over its opposition, could lead to the switch of drugs that should remain prescription, based on full knowledge about their properties, including emerging data.

The only instance where FDA undertook to switch a drug to nonprescription status without the active support and participation of the company was metaproterenol. The agency soon reversed its decision, acknowledging that it had not taken into account all of the pertinent information and views.* Valuable lessons were learned from that experience, and the switch process has evolved to a collaborative approach between the NDA company and FDA. This has been a successful approach that has benefited consumers.

* 48 Fed. Reg. 24926 at 24927-28 (June 3, 1983).

Switch without company consent requires due process, protection of data

- **FDA notice and hearing**
- **Proprietary NDA data**

If a switch were undertaken without consent of the NDA company, the Act requires that due process be followed. The “Rx legend” is part of the approved NDA. To remove it over the objection of the company, FDA would have to follow notice and hearing requirements.

Neither the “switch regulation” procedure under section 503(b)(3) of the Act nor OTC Review rulemaking could be substituted for statutory hearing rights. In any event, the switch regulation procedure is an anachronism in today’s environment, because it only provides for removal of the Rx legend, not for development of the extensive data and labeling needed to support OTC use, which is critical to effective consumer self-care.

In addition to due process, almost any switch would also have to rely in part on data submitted as part of the original NDA for the prescription drug. The company has proprietary rights in its NDA data, which could not be used without its consent, regardless of the regulatory switch option used. *

For all these reasons, FDA should continue to rely on the NDA company to initiate the switch process.

*Historically, FDA has used three mechanisms for switching drugs. First, following enactment of the Durham-Humphrey Amendment in 1951, FDA switched a number of drugs to OTC status using a rulemaking approach

referred to as the “switch regulation,” which was authorized under section 503(b)(3) of the Act. This rulemaking process made sense in the 1950s and 1960s as a way for the agency to gain control over a variety of drugs that were marketed by different companies under different conditions, some Rx and some OTC, some with NDAs and others without. The very same drug, with identical dosage and indications, might be sold Rx by one company and OTC by another. Of course, that situation does not exist today, and FDA has not used this process to switch a drug for almost 30 years (the last time being in 1971).

Second, beginning in the early 1970s, FDA relied on the OTC Drug Review as the principal vehicle for switching drugs to OTC status. This, too, made a great deal of sense for its time, since it was part of the agency’s comprehensive review of the safety, effectiveness, and labeling of OTC drugs. FDA switched approximately 32 drugs through the OTC Drug Review in the 1970s and 1980s. The OTC Drug Review, however, has largely run its course, and it is not the focus of switch activity today.

FDA entered the third, and current, switch era in the mid-1980s when it began switching drugs through the NDA process. With very few exceptions, every switch today is accomplished through approval of an NDA or NDA supplement. And again, this makes eminent sense in today’s environment. FDA comprehensively regulates new drugs, both Rx and OTC, through the NDA process, which gives the agency the maximum degree of authority over all aspects of a drug and provides the means by which manufacturers may invest in the development of proprietary data for submission to FDA in support of approval.

FDA Questions:

Should the “best” drug in a class be switched 1st?

Should older OTCs be taken off market when “better” ones are introduced?

CHPA Answer:

- **Consumers benefit from broadest choice of drugs**
- **“Best” and “better” are relative**
- **Drug comparison is for the consumer**

FDA asks about comparative assessments. Should the “best” prescription drug in a class be switched first? Should older OTC therapies be taken off the market after “better” ones are introduced?

Consumers benefit from the widest possible availability of drug products that are safe, effective, and properly labeled. Because of individual variability and preferences, what is “best” for one person may not be for another.

The process of comparing one drug to another is a decision for the consumer. FDA should not foreclose potentially useful options. It therefore would not be appropriate for FDA to refuse to switch a drug because it thought a “better” one might be coming along later, or for FDA to review existing marketed products with an eye toward removing older ones from the market.

Drugs Should Be Evaluated on Their Individual Merits

- **Criteria for FDA approval in the Act**
- **“Better” switch candidate not a criterion**

FDA should evaluate drugs on their individual merits. The statute 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 of whether the agency believes that other products are “better” in one respect or another.

Drugs Should Be Evaluated on Their Individual Merits

- **Criteria for FDA withdrawal**
- **“Better” drugs not a criterion**

Once approved, a product can only be withdrawn based on a finding that it is no longer safe or effective. The availability of “better” drugs is not a criterion for withdrawal.

When genuine safety or effectiveness issues are presented with a marketed product, industry has a long history of working cooperatively with FDA in the public interest, through labeling changes and, where appropriate, by taking products off the market. It would be an enormous waste of resources for FDA to institute a comparative review of marketed products across-the-board, with no promise of any benefit to consumers.

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. For that reason, there is nothing in the statute that permits the FDA to make the sort of comparative assessments contemplated by the questions in the hearing notice.

FDA Question:

How can we be sure consumers understand benefits/risks of a product when same brand name used for line of OTCs with different active ingredients?

CHPA Answer:

- **Consumers benefit from brand name families**
 - Identified trusted product sources
 - Company development of useful new products
 - Labels help ensure proper OTC selection

FDA asks how to assure that consumers understand the benefits and risks of particular products when the same brand name is used for a line of OTC products.

Use of a single brand name to identify a family of consumer products is a well-established practice. From a policy standpoint, the use of a family brand name for a line of drug products benefits consumers, who use the brand name to identify trusted product sources. Manufacturers are able to develop useful new products based on an established brand heritage, thus expanding the range of consumer self-care choices.

FDA recently addressed the issue of product selection through its OTC label format rule, which requires active ingredients to be identified first in the “Drug Facts” section of the labeling. The agency remarked that this placement “will help to ensure proper product selection, especially for product line extensions.” And 95% of consumers report that they do read the label prior to product use, as Dr. Maves stated.

Thus, brand name line extensions are beneficial to the healthcare system, by contributing to the growth and vitality of the OTC armamentarium. We also believe that any attempt by FDA to restrict brand name line extensions generally would violate the First Amendment protection for truthful and nonmisleading commercial speech, and would violate the property rights of manufacturers in their trade names. FDA precedent also makes trade name restrictions a matter of last resort. We will be providing an extensive written analysis of the legal issues following the hearing.

FDA Question:

What can we learn from other countries where OTCs are sold “behind the counter”?

CHPA Answer:

- **U.S. two-class drug system benefits consumers**
- **U.S. 3rd class has been rejected for 120 years: No public health benefit**
- **The rest of world is starting to follow U.S.**

FDA asks if we can learn from countries where nonprescription drugs are sold “behind the counter.”

Convenience and access are hallmarks of the effective self-medication system in the United States. A third class of drugs would reduce both convenience and access without providing a benefit to consumers.

A third or pharmacist-only class of drugs in the U.S. has been exhaustively studied for 120 years, and rejected. The definitive study was undertaken by the U.S. General Accounting Office. A three-year investigation of 10 countries plus the European Union,* resulted in a 1995 GAO report, whose title tells the story: “Nonprescription Drugs: Value of a Pharmacist-Controlled Class Has Yet to Be Demonstrated.” GAO concluded that experience in these countries, all of which have a restricted class of nonprescription drugs, “do[es] not support a fundamental change in the U.S. system.” On the contrary, GAO remarked that “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.”

Since 1974 FDA has repeatedly rejected a third class of nonprescription medicines on the grounds that a public health benefit has not been demonstrated. Both the agency and the Department of Justice have acknowledged that FDA lacks statutory authority to establish any such class.

In short, the U.S. system of unrestricted OTC drug distribution works and other countries are starting to follow America’s lead.

*Australia, Canada, Denmark, France, Germany, Italy, The Netherlands, Sweden, Switzerland, and the U.K.

Conclusion

- **NDA company should initiate switches -- most knowledgeable**
- **Consumers benefit from wide availability of OTC choices**
- **Consumers benefit from brand name families**
- **Consumers benefit from two-class drug system**

In conclusion, the public interest and the public health support switches initiated by the company with the NDA, the party with the most comprehensive knowledge about the drug.

The public interest and public health are best served by having the broadest range of safe and effective OTC therapies available. The law supports this principle by directing that each drug be reviewed on its individual merits.

Use of a brand name to identify a line of products is well-accepted and benefits American consumers by facilitating product choice, and enabling manufacturers to develop and bring to market useful new products, further broadening the range of useful self-care choices.

Finally, a third class of drugs has been exhaustively studied and rejected for over a century on the ground that no public health benefit has been demonstrated. It would be a backward step for the United States to consider restrictions on OTC availability as the rest of the world is starting to follow America's lead by expanding unrestricted access to OTC drugs.

Scientific/Regulatory Perspective on Rx-to-OTC Switch

R. William Soller, Ph.D.

Senior Vice President and

Director of Science & Technology

Consumer Healthcare Products Association

June 28-29, 2000

My name is Dr. Bill Soller, Senior Vice President and Director of Science & Technology.

I have been involved in the OTC industry and switch for over twenty years, including consultation with CHPA members on many of the switches undertaken over that time.

Areas of Comment

- **Switch Criteria**
- **Consumer Understanding**
- **Category Exemptions**

I plan to concentrate on three areas of FDA's questions -- Switch Criteria, Consumer Understanding, and Category Exclusions -- by describing the Rx-to-OTC switch process.

Switch Criteria

- **FDA Question:**
 - What criteria should the agency use for switch?
- **CHPA Answer: The current statutory and regulatory criteria**

Question: FDA asks: What criteria should the agency use for switch? [We interpret switch criteria to mean standards for making the benefit/risk decision for OTC availability.]

Answer: 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.

(See Soller, R.W.: OTCness. DIA Journal 32 555-560, 1997.)

Statutory & Regulatory Switch Criteria

- **Foundational statutory criterion for OTC availability is the demonstration that :**
 - *Labeling can be written for consumers to use a product safely and effectively without a prescription.*
- **Regulatory Definitions:**
 - Safety
 - Effectiveness
 - Labeling

The foundational statutory criterion is the demonstration that labeling can be written for consumers to use a product safely and effectively without a prescription.

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”
- not an absence of toxicity or an expectation that 100% of the target population will have a 100% benefit 100% of the time.

Fulfillment of Regulatory Switch Criteria

- **Disciplines of toxicology, clinical pharmacology and epidemiology, well-equipped to address:**
 - Potential **safety** issues
 - Toxicity
 - Carcinogenicity, reproductive toxicity, side effects
 - Therapeutic hazards
 - Misdiagnosis -- self-selection, self-diagnosis
 - Treatment failure -- delayed professional treatment
 - Incorrect use -- long-term self-monitoring, overdose, misuse
 - Drug interactions
 - Potential **effectiveness** issues, based on nature/severity of condition
 - Choice of dose, dose interval, age restrictions, etc.
 - Ability of **label** to convey core communication objectives
 - Benefit/risk assessment

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 we use as scientists to determine drug availability.

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

Potential safety issues, with respect to:

- Potential **toxicity**, which are 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.)
- And, companies consider the ability of the **label** to convey the core communication objectives of safe and effective use of the product by consumers. After all, this is the basic statutory criterion.
- Based on this framework, the compulsory **benefit/risk assessment** 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?

Switch Process

- **Case-specific**
- **Substantial data development**
- **Best developed through company- initiated approach**

Because the switch process is case-specific, it often requires substantial data development. This is best developed through a company-initiated approach that includes early and frequent dialogue with the agency during the OTC R&D process.

Examples of Case-specificity of Switch

- **NRT:**
 - Quit rates in high-support Rx environment vs. OTC setting, projecting more quits when OTC
- **Pediatric ibuprofen:**
 - Rare side effects
- **Vaginal antifungals:**
 - Initial physician diagnosis
- **Cimetidine:**
 - Drug interactions

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, 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 used as a fever reducer

Vaginal antifungals posed the question of the ability of women to recognize symptoms of recurrent vaginal candidiasis after a physician diagnosis.

A core issue for **OTC Cimetidine** related to potential drug-drug interactions.

We can expect therefore that every future switch will have its own unique set of issues, that can only be resolved by a data-driven dialogue-driven approach.

Consumer Understanding

- **FDA Question:**

- How can FDA be assured of consumer understanding of the benefits and risks of specific drug products and the ability of consumers to use products safely and effectively were the drug products to be marketed OTC?

- **CHPA Answer:**

- Use the **established switch process and the consumer behavioral study designs** to address case-specific switch questions.

- **Need:**

- An ongoing dialogue.

On the subject of consumer understanding, FDA asks:

How can it 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, and we ask for this today.

Category Exclusions

- **FDA Question:**

- What types of drugs/class of products should not be available OTC?

- **CHPA Answer:**

- In the context of the statutory criteria for OTCness and the established switch process, FDA should not create presumptive negative lists.

FDA also asks: What types of drugs/class of products should not be available OTC?

Answer: FDA should not create presumptive negative lists.

Does this mean that every drug is potentially OTCable in the future?

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 or the results of future studies. To do so would be in conflict with the statutory criterion for switch and the associated case-by-case, data-driven scientific/regulatory paradigm.

Remember, eleven years ago at a national switch symposium, it was predicted that H₂ blockers would never “go OTC.” Yet, today, through collaborative efforts by companies and FDA, they are a major part of the OTC antacid/acid reducer category.

The point is, presumptive negative lists should be avoided.

Summary

- **Switch has been successful, providing benefits to consumers.**
- **FDA must use the statutory switch criterion.**
 - Continue to use the established regulatory definitions
 - Practice the scientific/regulatory paradigm
 - Review drugs on an individual basis
 - Avoid presumptive negative category/ingredient lists
- **CHPA seeks additional dialogue on switch.**
- **Switch should remain company-initiated.**
- **GAO finds no benefit for third class.**
- **Collaborative approach needed for the future!**

In summary to our remarks:

- The switch process has been very successful in providing significant therapeutic benefits to 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 an individual basis, and avoid presumptive negative lists.
- We seek additional dialogue on consumer behavioral research.
- Switch should be initiated by the NDA company who has the most knowledge about the drug.
- 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, we should seek collaborative, not confrontational, approaches for the company-agency dialogue that is vital to creating a thorough, yet reasonable, OTC R&D program to test future switch proposals.