UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

CPSC/OFFICE OF THE SECRETARY

2000 MAY 17 P 3:42

# Vote Sheet

**Date:** MAY 16 2000

**TO** : The Commission
Sadye E. Dunn, Secretary

**FROM** : Michael S. Solender, General Counsel MS
Stephen Lemberg, Asst. General Counsel SL
Harleigh Ewell, Attorney, GCRA (ext. 2217) HE

**SUBJECT** : Whether to Propose PPPA Rule for Oral Drugs Switched from Prescription to OTC Status

This vote sheet concerns options raised by the staff's briefing package on whether the Commission should propose to require child-resistant packaging under the Poison Prevention Packaging Act of 1970, as amended, ("PPPA") for products that are subject to the Commission's rule requiring special packaging for oral prescription drugs (16 C.F.R. §§ 1700.14(a)(10)) and that are then granted over-the-counter ("OTC") status. If the Commission votes to propose such a rule, the Office of the General Counsel and the staff will prepare a notice of proposed rulemaking for the Commission's consideration.

Please indicate your vote on the following options.

I. PREPARE A DRAFT NPR TO PROPOSE A RULE REQUIRING SPECIAL PACKAGING FOR OTC-SWITCHED ORAL PRESCRIPTION DRUGS FOR THE COMMISSION'S CONSIDERATION.

_____ (Signature) _____ (Date)

NOTE: This document has not been reviewed or accepted by the Commission.
Initial rh Date 5/16/00



CPSA 6 (b)(1) Cleared 5/16/00
No Mfrs/PrivLblrs or Products Identified
Excepted by
Firms Notified

II. DO NOT PROPOSE A RULE REQUIRING SPECIAL PACKAGING FOR OTC-SWITCHED ORAL PRESCRIPTION DRUGS.

_____ _____
(Signature) (Date)

III. TAKE OTHER ACTION (please specify).

_____ _____
(Signature) (Date)

Attachment

Comments/Instructions:

# BRIEFING PACKAGE

# PROPOSED RULE TO REQUIRE SPECIAL PACKAGING FOR ORAL PRESCRIPTION DRUGS THAT ARE GRANTED OVER-THE-COUNTER STATUS BY THE FOOD AND DRUG ADMINISTRATION


**For Information Contact**
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NOTE: This document has not been reviewed or accepted by the Commission.
Initial [illegible] Date 5/16/00

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## Executive Summary

The regulations of the Poison Prevention Packaging Act (PPPA) require child-resistant packaging of most oral prescription drugs When the Food and Drug Administration (FDA) allows an oral prescription drug to be sold over-the-counter, child-resistant packaging of that drug is no longer required The staff recommends that the Commission propose a rule to require that the child-resistant packaging requirements of an oral prescription drug continue when the active chemical is granted OTC status by the FDA This potential rule will require that children have the same protection when the drugs are more widely available as OTC preparations as they did when the drugs were available only by prescription

Those companies that do not need to use child-resistant packaging can provide information to the Commission, as they do currently under the PPPA oral prescription drug rule, to demonstrate that the drug products will not injure children if they are marketed in non-child-resistant packaging The staff recommends that the Commission revoke 16 CFR 1702 16(b) to allow petitions for exemptions from child-resistant packaging to be submitted and considered by the Commission before the NDAs are approved by the FDA This would decrease the potential financial and regulatory burdens to the drug company associated with a post-marketing package change

Child-resistant packaging for these products is technically feasible, practicable, and appropriate These drugs are supplied in child-resistant packaging as prescription drugs It is anticipated that this potential rule would not create a financial burden on small companies

UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

**Memorandum**

Date MAY 16 2000

TO The Commission
Sadye E Dunn, Secretary

THROUGH Michael S Solender, General Counsel
Pamela Gilbert, Executive Director PG

FROM Ronald L Medford, Assistant Executive Director for Hazard Identification and Reduction RLM
Suzanne Barone, Ph D Project Manager for Poison Prevention, Directorate for Health Sciences

SUBJECT Oral Prescription Drugs That Are Granted Over-The-Counter Status by the Food and Drug Administration

This memorandum presents the staff's recommendation to propose that child-resistant packaging requirements for oral prescription drugs continue when such drugs are granted over-the-counter (OTC) status by the Food and Drug Administration The recommended rule would help ensure that children have the same protection when drugs are widely available as OTC preparations as they did when the drugs were available only by prescription

## BACKGROUND

The Poison Prevention Packaging Act of 1970 (PPPA) was established to protect children from serious personal injury or illness resulting from handling, using, or ingesting hazardous substances Under the PPPA, the U S Consumer Product Safety Commission (CPSC) can require child-resistant packaging of hazardous household chemicals, including drugs The CPSC currently requires child-resistant packaging of oral prescription medications, unless they have been specifically exempted from the packaging requirements (16 CFR § 1700 14(a)(10)) In contrast, OTC drugs, which are also called nonprescription drugs because they can be sold to consumers without a prescription from a licensed medical practitioner, are not regulated under the PPPA as a class However, regulations have been issued to require several individual OTC products to have child-resistant packaging

To date, 12 OTC drugs have been regulated individually under the PPPA The drugs and the effective dates of these PPPA requirements are aspirin (1972), liquid methyl salicylate (1972), iron-containing drugs (1978), acetaminophen (1980), diphenhydramine (1984), ibuprofen (1992), loperamide (1993), lidocaine

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(1996), dibucaine (1996), naproxen (1996), ketoprofen (1997), and minoxidil (1999)

Several of the OTC drugs listed above have been sold only as nonprescription products However, diphenhydramine, ibuprofen, loperamide, naproxen, and ketoprofen were oral drugs available originally only by prescription These drugs therefore required child-resistant packaging under the oral prescription drug regulation (16 CFR § 1700(a)(10)) The Food and Drug Administration (FDA) subsequently granted these drugs OTC status at specific dosage levels, thus removing them from the child-resistant packaging requirements of the oral prescription drug regulation After each of these substances was granted OTC status, the Commission promulgated a separate regulation to require the child-resistant packaging of the drug

## THE ROLE OF THE FDA

The FDA regulates which drugs and combinations of drugs can be sold in the United States This includes determining which drugs can be sold directly to the consumer in OTC preparations The primary concern of the FDA is to provide drug products to the consumer that will be safe and effective when self-administered in a proper manner The FDA does not base granting OTC status on whether the drug would be toxic to a child if the drug is unintentionally ingested The FDA stated in a letter to CPSC staff that "approval of an OTC switch does not in any way imply that FDA has concluded that the product does not continue to need child-resistant packaging " A copy of this letter is at Tab A

## OTC "SWITCHES"

Since 1976, the FDA has permitted many drugs to be sold OTC According to the Consumer Healthcare Products Association (CHPA) website, "more than 600 OTC products on the market today use ingredients or dosages available only by prescription just 20 years ago " Trade press articles speculate that this trend will continue.[1] A table listing 80 drugs that have been granted OTC status since 1976 compiled by the Consumer Healthcare Products Association (CHPA) is at Tab B It should be noted that of the 80 listings in the table, 22 are different oral drugs that were previously available by prescription The other listings are topical drugs, new uses, or new formulations for existing OTC drugs, or new approved OTC drugs that were not previously prescription products

The intent of the current staff proposal is to maintain child-resistant packaging of oral drug products when those products are switched from prescription to OTC status by the FDA[2]. Therefore, oral drugs that are switched

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[1] Levy, S , *Several Prescription Candidates Reported Ripe for OTC Switching*, Drug Topics, November 16, 1998, p 51

[2] This would not apply to topical drugs because as a class, topical prescription drugs do not require child-resistant packaging Topical drugs, either prescription or OTC, would have to be regulated separately

from prescription to OTC status would still be subject to a child-resistant packaging requirement.

## CHILD-RESISTANT PACKAGING STATUS OF "SWITCHED" DRUGS

To date, the Commission has required child-resistant packaging of 6 of the 22 oral prescription drugs that have been approved for OTC sale The six OTC-switched drugs that currently require child-resistant packaging, the date of OTC approval by the FDA, and the effective date of the child-resistant packaging requirements are listed in Table 1 The other 16 drugs are discussed below

**Table 1: Prescription Drugs Switched to OTC Status that Require Child-Resistant Packaging**

| DRUG | Year OTC | Year CRP Effective |
|---|---|---|
| *Diphenhydramine HCL* | *1982* | *1984* |
| *Diphenhydramine monocitrate* | *1982* | *1985* |
| *Ibuprofen* | *1984* | *1992* |
| *Loperamide* | *1988* | *1993* |
| *Naproxen sodium* | *1994* | *1996* |
| *Ketoprofen* | *1995* | *1997* |

## HISTORY OF CPSC STAFF APPROACH TO "SWITCHED" ORAL DRUGS

In the past, the staff focused primarily on ingestion data to recommend what products should be in child-resistant packaging In the late 1970s the FDA allowed the OTC sale of several antihistamines that were previously available only by prescription In 1982, the CPSC staff evaluated the possibility of requiring child-resistant packaging of OTC antihistamines Ingestion data and medical literature reports were reviewed This effort to require child-resistant packaging of all OTC antihistamines was discontinued because, at that time, limited available ingestion data showed that diphenhydramine was the antihistamine associated with several deaths and the most serious injuries to children. Diphenhydramine hydrochloride was the first OTC-switched drug to be regulated under the PPPA by CPSC FDA permitted the monocitrate salt of diphenhydramine to be sold OTC in 1982 The diphenhydramine hydrochloride packaging regulation was then amended to cover all diphenhydramine salts

In 1984, the CPSC staff evaluated the ingestion data related to ibuprofen Ibuprofen was granted OTC status during that year At that time, the poisoning

data were limited and the staff did not recommend child-resistant packaging The two companies that first marketed OTC ibuprofen used child-resistant packaging voluntarily on some package sizes In 1989, the CPSC staff revisited ibuprofen toxicity because ibuprofen had become widely available Not all companies were using child-resistant packaging and serious injuries to children resulted. The staff recommended child-resistant packaging for these products and the Commission issued the rule Companies that were marketing their products in non-child-resistant packaging changed their packaging to comply

The experience with diphenhydramine and ibuprofen resulted in a change in the staff's approach to recommendations for child-resistant packaging for "switched" OTC products Rather than wait for deaths or injuries to children, the staff has become more proactive in recommending child-resistant packaging requirements for the OTC drugs For the past several years the staff has focused on the potential toxicity of drugs that are going to be switched instead of waiting for poisonings to occur after the drug is released and marketed The staff has made the evaluation of potential switched drugs the first priority. As a result, separate regulations for loperamide, naproxen, and ketoprofen were considered by the Commission shortly after OTC status for each drug was granted by the FDA

The CPSC staff monitors FDA's activities concerning approval of switched OTC drugs The staff attends FDA advisory panel meetings when possible, to better understand any issues about a potential drug and the likelihood of approval of OTC status by the FDA The FDA is not bound to accept the panel's recommendations regarding OTC switches, though in most cases the FDA does The review of the potential toxicity of the drug to young children then becomes a priority for the CPSC staff For example, the FDA Nonprescription Drug Advisory Panel and the Arthritis Advisory Panel met jointly in July 1999 to discuss the proposed OTC switch of a current prescription drug used for muscle spasms The CPSC staff attended this meeting and continues to follow the status of this drug If it appears that the drug may receive OTC approval, completion of a toxicity review will become a priority for HS staff The staff waits for FDA approval before proceeding with a review, to avoid expending the CPSC's limited resources if the FDA does not approve the OTC sale of the drug This rulemaking would eliminate the lag between OTC approval and the requirement for child-resistant packaging

As a result of the staff's focus on newly switched drugs, many of the earlier switched drugs have not been formally reviewed to determine if they should be in child-resistant packaging. The 16 oral prescription drugs that were switched to OTC status and do not require child-resistant packaging are listed in Table 2 The fact that these drugs do not currently require child-resistant packaging is not the result of an affirmative determination that these drugs do not **need** to be in child-resistant packaging to protect children The staff has preliminarily assessed the toxicity of eight of these drugs Based on the toxicity of these products, the staff would recommend child-resistant packaging for four of the drugs (indicated with a plus sign) Five of the antihistamine drugs identified by a question mark are

currently under preliminary review by the staff These drugs are related in structure and activity to diphenhydramine, which currently requires child-resistant packaging

**Table 2: Oral Prescription Drugs that Switched to OTC Status**

| DRUG | Type of Drug | Toxicity | Year OTC |
|---|---|---|---|
| Brompheniramine maleate | Antihistamine | ? | 1976 |
| Chlorpheniramine maleate | Antihistamine | ? | 1976 |
| Pseudoephedrine HCl | Decongestant | + | 1976 |
| Pseudoephedrine sulfate | Decongestant | + | 1976 |
| Doxylamine succinate | Antihistamine | ? | 1978 |
| Phenylpropanolamine HCl | Decongestant | + | 1981 |
| Dexbrompheniramine maleate | Antihistamine | ? | 1982 |
| Triprolidine HCl | Antihistamine | ? | 1982 |
| Pyrantel pamoate | Antihelmintic | ? | 1985 |
| Chlophedianol HCl | Antitussive | ? | 1987 |
| Clemastine fumarate | Antihistamine | + | 1992 |
| Dexchlorpheniramine maleate | Antihistamine | ? | 1992 |
| Famotidine | $H_2$ Antihistamine | - | 1995 |
| Cimetidine | $H_2$ Antihistamine | - | 1995 |
| Ranitidine | $H_2$ Antihistamine | - | 1995 |
| Nizatidine | $H_2$ Antihistamine | - | 1996 |

+Toxicity of the drug is such that the staff would recommend CR packaging
- Toxicity of the drug is such that the staff would not recommend CR packaging
? Review of the toxicity of the drug has not been completed.

The four drugs listed that the staff would not recommend child-resistant packaging for are antihistamines used to reduce stomach acid These drugs do not have the same toxicity associated with antihistamines used to treat cold symptoms The staff would have recommended that the Commission exempt these drugs from the child-resistant packaging requirements, had the companies petitioned the Commission when the drugs were only available by prescription.

The staff does not recommend that the Commission retrospectively require child-resistant packaging of the 16 OTC-switched drugs listed in Table 2 Many of

these products are already in child-resistant packaging because they are sold in combination with other drugs that already require child-resistant packaging, for example pseudoephedrine with ibuprofen or an antihistamine with acetaminophen or aspirin In addition, staff is aware of some OTC products that are packaged voluntarily in child-resistant packaging The staff continues to evaluate these OTC drugs as time and priority permit More staff time would be available to review these previously released products if a rule to maintain packaging on future switched OTCs is adopted by the Commission

## ISSUES RELATED TO SCOPE OF THE CURRENT PROJECT

The staff recommends that this potential rule extend to oral OTC drugs that contain an ingredient that originally required a prescription As described below, variables such as dosages, uses, new oral formulations, and combinations with other drugs should not affect the requirement for child-resistant packaging

### Additional Uses, Forms, and Combinations of OTC-Switched Drugs

The FDA can approve a new usage or a new dosage form of an existing OTC product The staff recommends that the new use or new dose automatically require child-resistant packaging even if the new use or dose was not approved when the drug was only available by prescription Currently, a new use for an oral OTC product that is already PPPA-regulated does not affect the child-resistant packaging requirement. For example, after February 11,1985, any oral product that contained more than the equivalent of 66 mg diphenhydramine base was required to be in child-resistant packaging At that time, diphenhydramine was in OTC sleep aids and hay fever preparations In 1987, when diphenhydramine was allowed by the FDA to be sold OTC as an oral antiemetic drug, no further PPPA regulation was necessary This same focus on the drug entity itself rather than the approved usage is necessary for the recommended rule to be successful If an oral prescription drug were granted OTC status by the FDA it would automatically require child-resistant packaging under the recommended rule If the FDA then approved another OTC use for that same drug it would also automatically require child-resistant packaging

The current project would not extend child-resistant packaging requirements to switched OTC products that are not oral formulations, even if they contain the same drug as an oral preparation. Formulations other than oral, such as topical preparations, or transdermal patches would still have to be regulated separately

In some cases, after a prescription drug is approved for OTC sale by the FDA, other forms, dosages, or combinations containing that drug will also be approved for OTC sale These combinations or forms may not have existed when the drug was available by prescription only. This current project would cover these situations if, as we recommend, any proposed rule is not limited to the specifically

switched preparation, but extends to all oral products that contain a drug that was originally switched For example, loperamide was granted OTC status in 1988 The CPSC required the packaging of any oral product that contained more than 0.045 mg of loperamide in 1993 In 1997, the FDA approved the combination of loperamide and simethicone in an OTC product This was never a prescription combination product. However, the combination product currently requires child-resistant packaging because the loperamide PPPA rule is not limited to the original prescription formulation It is important that this rulemaking include all future oral OTC combinations that contain the switched drug

**Change in Dosage Between Prescription and OTC Drugs**

The prescription version of a drug may be available in different dosages, strengths, and forms However, the FDA may place restrictions on the allowed level of a drug available for OTC use Several different scenarios exist First, the drug may be sold OTC at the lowest prescription dosage This is true for many of the switched drugs, including the antihistamines Second, the drug may be sold OTC at the prescription strength but the total daily allowable dose is lower for the OTC drug This is the case for OTC loperamide Lastly, a lower dosage may be developed for the OTC preparation OTC ibuprofen and naproxen are examples of this

The staff recommends that the Commission propose including any OTC oral drug containing the chemical entity that was available by prescription even if the OTC dosage is lower than the prescription strengths. This is consistent with the PPPA oral prescription drug regulation, which does not specify a dose for the individual prescription drugs In addition, the Commission has issued rules for OTC drugs that are available at a lower dose than the prescription strength The Commission's experience with ibuprofen and naproxen demonstrate that toxic amounts of the drugs are available even at these new lower dosages The utility of the current potential rulemaking would decrease substantially if drugs such as ibuprofen and naproxen had to be regulated individually.

**Identification of Switched Drugs**

If this potential rulemaking includes switched drugs and any future combination, dosage, oral formulation, etc without individual action by the Commission as the staff recommends, it may be difficult for CPSC staff and the drug industry to identify which drugs would require child-resistant packaging Therefore, the staff recommends that after the FDA approves an oral prescription drug for OTC sale, the CPSC publish an FR notice identifying the drug as requiring special packaging under the "OTC switched" regulation in 16 CFR § 1400.14 This would not involve rulemaking, it would merely consist of CPSC identifying products that already would require child-resistant packaging under the existing regulation.

## EXEMPTIONS

An exemption procedure exists for PPPA-regulated products that do not pose a risk of serious injury or illness to children or for which child-resistant packaging is not technically feasible, practicable, or appropriate (16 CFR § 1702) Companies petition the Commission to exempt products by submitting data, described in 16 CFR § 1702, to support either that the drug will not cause serious injury or that it is not technically possible to develop and produce child-resistant packaging for the drug product The exemption procedure involves rulemaking Currently, 18 oral prescription drugs (16 CFR §1700 14(a)(10)(i)-(xx)) and several OTC formulations of aspirin (16 CFR § 1700 14(a)(1)(i)-(ii)), acetaminophen (16 CFR § 1700 14(a)(16)(i)-(ii)), and iron (16 CFR § 1700 14(a)(13)(i)-(ii)) have been exempted from the child-resistant packaging requirements.

This exemption procedure would be available to manufacturers of OTC switch products if the products continued to require child-resistant packaging when the status changed to OTC Two issues related to the petition process for exemptions that need to be considered are staff resources and timing

The first issue relates to the potential expenditure of staff resources to process petitions requesting exemptions of switched drugs The staff believes that the number of exemptions that may be requested in the future for switched drugs would not be high None of the 22 drugs that have switched to OTC status requested an exemption from the child-resistant packaging standards when they were prescription drugs Therefore, we should not assume that the makers of the 16 switched OTC drugs that do not currently require child-resistant packaging would have petitioned for exemption if their drugs had required child-resistant packaging at the time of the switch As stated above, many of these drugs are already marketed in child-resistant packaging, either voluntarily or because they are in combination with another PPPA-regulated substance In addition, current child-resistant packaging is easier for adults to use because of the 1995 revisions to the child-resistant packaging test protocols Also, companies have the option of marketing one OTC package size that is non-child-resistant, as long as it is properly labeled and other popular sizes of child-resistant OTC packaging are available (15 USC 1473)

The second issue is one of the timing of the submission of petitions for exemption. The PPPA regulations currently specify that the Commission shall deny a petition if the FDA has not approved the new drug application (NDA) (16 CFR § 1702 16(b)) Applications to switch drugs from prescription to OTC status are handled by the FDA as NDAs. Therefore, if the Commission does not grant a petition before a drug is approved, companies would have to either market in child-resistant packaging, delay marketing the approved OTC drug until the Commission acts, or request a stay of enforcement to allow marketing in non-child-resistant packaging while the Commission considers the petition.

A post-marketing change in packaging of an approved new or generic OTC drug may be more complex for the drug manufacturer than simply buying different packaging and modifying the packaging equipment In some cases, the FDA must approve the new packaging before the drug can be marketed[3] Stability testing of the product in the new package must be completed and the results submitted to the FDA for approval before the product can be marketed in the new package

The staff recommends that 16 CFR 1702 16(b) be revoked to allow petitions to be submitted and considered by the Commission earlier in the process, before the NDAs are approved by the FDA This would provide manufacturers with the opportunity to request an exemption from the child-resistant packaging requirements and have a decision by the Commission prior to the NDA submission and approval

## FINDINGS

### Hazard to Children

Before issuing a rule, the Commission must find that the degree or nature of the hazard to children in the availability of these OTC drugs by reason of their packaging is such that special packaging is required to protect children from serious injury or illness from handling, using, or ingesting the drugs (15 U S C 1472(a)(1)) The Commission made this finding previously for oral prescription drugs The oral prescription drug regulation does not specify a dose for the individual prescription drugs

The need to continue to protect children remains when oral prescription drugs are granted OTC status A decision by the FDA to grant OTC status for a prescription drug is not determined by the lack of toxicity to a child if the drug is accidentally ingested (Tab A). The drugs have the same toxicity whether they are prescription or OTC The issue is whether drugs switched to OTC status at a lower dosage than was available by prescription are still hazardous to young children The Commission has previously issued rules for OTC drugs that are available at a lower dose than the prescription strength The Commission's experiences with ibuprofen and naproxen demonstrate that toxic amounts of the drugs are available even at the lower dosages

Another important consideration is that OTC drugs are more readily available to consumers and therefore more accessible to children. The CPSC staff concludes that the available data support the finding that child-resistant packaging is necessary to protect children from serious injury or illness from ingesting oral prescription drugs that have been granted OTC status

[3] Guidance for Industry, Changes to An Approved NDA or ANDA Food and Drug Administration, CMC, November 1999

## Technical Feasibility, Practicability, and Appropriateness

The Commission must also find that child-resistant packaging is technically feasible, practicable, and appropriate The Commission made these findings previously for oral prescription drugs The change in status from prescription to OTC does not change the ability of child-resistant packaging to be made, to be mass-produced, and to maintain the shelf life of these drugs.

In some cases the same packaging can be used for the OTC product as the prescription product However, companies must modify the labels since the FDA labeling requirements for OTC drugs are different than the prescription drug requirements Most companies develop new packaging specifically for the OTC market because prescription drugs are typically repackaged by the pharmacist from containers of bulk drugs Unit dose packaging is popular for the OTC market especially for drugs that are sold in limited quantities like antihistamines Other products are sold in bottles like the anti-inflammatory drugs such as ibuprofen or naproxen There are child-resistant designs of reclosable packaging and unit packaging that are commercially available

The CPSC staff concludes that the available data support the finding that it is technically feasible, practicable, and appropriate to produce special packaging for oral OTC products that were originally sold by prescription

## APPLICABILITY

Since the packaging of OTC-switched drugs is determined before the company submits the information requesting the "switch" to the FDA, the staff recommends that this rule only apply to OTC-switched drugs subject to a new drug application (NDA) or abbreviated new drug application (ANDA) submitted to the FDA more than 180 days after the publication of the final rule This proposed regulation would not affect any oral prescription drug that is already approved by the FDA for OTC sale

## EFFECTIVE DATE

The PPPA provides that no regulation shall take effect sooner than 180 days or later than one year from the date such final regulation is issued, except that, for good cause, the Commission may establish an earlier effective date if it finds that it is in the public interest to do so For the reasons discussed in the preceding section, the staff recommends a 180-day effective date.

## ECONOMIC CONSIDERATIONS

Before issuing a rule, in addition to complying with the requirements in the PPPA, the Commission must either assess the impact of a regulation on small

entities or certify that there will not be a significant economic effect on a substantial number of small entities.

Historically, marketers of a drug that transferred to OTC status develop packaging with "shelf appeal" to attract consumers and compete with other products in the therapeutic category The incremental costs of providing child-resistant packaging is small ($0 005 - $0 02) depending on the choice of packaging In addition, child-resistant packaging is readily available It is unlikely that this proposal will have a substantial effect on a significant number of small businesses A more detailed discussion is at Tab C

## ENVIRONMENTAL CONSIDERATIONS

A special packaging requirement will have no significant effects on the environment, since these products required child-resistant packaging before the change in status to OTC In addition, the manufacture, use, and disposal of child-resistant packaging will present the same environmental effects as nonchild-resistant packaging

## RECOMMENDATION AND DISCUSSION

The staff recommends that the Commission propose a rule to require that the child-resistant packaging requirements of an oral prescription drug continue when the active chemical is granted OTC status by the FDA This potential rule will require that children have the same protection when the drugs are more widely available as OTC preparations as they did when the drugs were available only by prescription The potential rule would eliminate the possibility of a drug being available in nonchild-resistant packaging for an extended time before child-resistant packaging is required The need to continue to protect children does not diminish when oral prescription drugs are granted OTC status A decision by the FDA to grant OTC status for a prescription drug is not determined by the lack of toxicity to a child if the drug is accidentally ingested The drugs are still toxic, whether they are prescription or OTC

The staff does not recommend that the rule include drugs previously switched to OTC To the extent existing OTC-switched drugs are not already in child-resistant packaging, the staff will continue to review these drugs and where appropriate recommend that the Commission issue separate PPPA regulations for those products

The CPSC staff believes that the number of OTC switches is likely to increase in the future With this rule, child-resistant packaging of the switched oral drugs will be maintained without a separate evaluation of each switched product CPSC staff resources that would have been used to review each of these drugs would be saved and could be directed towards other Commission activities.

The potential rule should extend to all future oral OTC drugs containing an ingredient that originally required a prescription even if the dosage or formulation for the OTC product differs from the original prescription drugs The PPPA rules for ibuprofen and naproxen demonstrate the need for this provision Without it, the utility of such a rule decreases because drugs such as ibuprofen and naproxen would still have to be regulated separately

In order to identify the drugs that would be affected by this rule, the staff recommends that the CPSC publish an FR notice following the FDA approval of an OTC switched oral drug This drug would then be listed under the switched regulation in 16 CFR §1700 14 Since this process would not involve rulemaking, the staff recommends that the Commission delegate to the CPSC staff the authority to publish the notice listing the drugs

This potential rulemaking will make it easier for the drug industry to develop packaging for switched OTC drugs Changing packaging in the post-marketing stage will be unnecessary The industry will know that the drugs require child-resistant packaging Those companies that do not need to use child-resistant packaging can provide information to the Commission, as they do currently under the PPPA oral prescription drug rule, to demonstrate that the drug products will not injure children if they are marketed in non-child-resistant packaging The staff recommends that the Commission revoke 16 CFR 1702 16(b) to allow petitions for exemptions from child-resistant packaging to be submitted and considered by the Commission before the NDAs are approved by the FDA. This would decrease the potential financial and regulatory burdens to the drug company associated with a post-marketing package change

Child-resistant packaging for these products is technically feasible, practicable, and appropriate These drugs are supplied in child-resistant packaging as prescription drugs It is anticipated that this potential rule would not create a financial burden on small companies.

# TAB A

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

GENERAL COUNSEL OFFICE

'98 OCT 14 A7:35

OCT 7 1998

Jeffrey S. Bromme, Esq.
General Counsel
Consumer Product Safety Commission
Washington, DC 20207-0001

Dear Mr Bromme:

This letter responds to your inquiry regarding whether the Food and Drug Administration (FDA) uses as a condition of approval for switching orally administered drugs for human use from prescription to over-the-counter (OTC) status. a determination that a child who ingests an accidental overdose of the product would not sustain a serious injury or illness or that children would not have access to the product.

As you are aware, with some enumerated exceptions, orally administered drugs when required by law to be dispensed by prescription are subject to a special packaging standard issued by the FDA under the Poison Prevention Packaging Act of 1970 (PPPA), which is now administered by the U.S Consumer Product Safety Commission (CPSC) 16 C.F.R. § 1700 14(a) (10). When the special packaging requirement was issued, the standard was premised on a statutory finding that special packaging is required to protect children from serious personal injury or serious illness resulting from handling, using, or ingesting orally administered prescription drug products. 15 U.S.C. § 1472(a) (1). When such drugs are switched from prescription to OTC status, that special packaging requirement no longer expressly applies.

The FDA does not condition OTC status on a determination that a child who ingests an accidental overdose of the product would not sustain a serious injury or illness or that children would not have access to the product Approval of an OTC switch does not in any way imply that FDA has concluded that the product does not continue to require child-resistant packaging.

I hope this discussion addresses your concerns. Please contact me if you have any questions

Sincerely,

Debra Bowen

Debra L. Bowen, M.D.
Acting Director
Division of Over-the-Counter
Drug Products

# TAB B

Consumer Healthcare Products Association

**Ingredients & Dosages Transferred From Rx-to-OTC Status (or New OTC Approvals) by the Food and Drug Administration Since 1975**

March 21, 2000

| INGREDIENT | ADULT DOSAGE | PRODUCT CATEGORY | DATE OF OTC APPROVAL | PRODUCT EXAMPLES |
|---|---|---|---|---|
| brompheniramine maleate | 4 mg /4-6 hours (oral) | antihistamine | September 9, 1976 | Dimetane (A H Robins) |
| chlorpheniramine maleate | 4 mg /4-6 hours (oral) | antihistamine | September 9, 1976 | Allerest (Pharmacraft), Chlor-Trimeton (Schering), Contac (SmithKline), Sudafed Plus (Warner-Lambert) |
| oxymetazoline hydrochloride | 0 05% aqueous solution (topical) | nasal decongestant | September 9, 1976 | Afrin (Schering), Duration (Plough) Dristan Long Lasting (Whitehall), Neo-Synephrine-12 Hour (Bayer) |
| pseudoephedrine hydrochloride | 60 mg /4 or 4-6 hours (oral) 240 mg max /24 hours | nasal decongestant | September 9, 1976 | Sudafed (Warner-Lambert), Neo-Synephrinol (Bayer) |
| pseudoephedrine sulfate | 60 mg /4 or 4 6 hours (oral) | nasal decongestant | September 9, 1976 | Afrinol (Schering), Chlor-Trimeton (Schering) |
| *xylometazoline hydrochloride* | *01% aqueous solution (topical)* | *nasal decongestant* | *September 9, 1976* | *Ornivin (Ciba)* |
| doxylamine succinate (NDA) | 25 mg single dose only (oral) | sleep-aid | October 18, 1978 | Unisom (Pfizer) |
| hydrocortisone | 0 25 to 0 50% (topical) | antipruritic (anti-itch) | December 4, 1979+ | Cortaid (Upjohn), Lanacort (Combe) |
| hydrocortisone acetate | 0 25 to 0 50% (topical) | antipruritic (anti-itch) | December 4, 1979+ | Bactine (Miles), Caldecort (Pharmacraft) |
| acidulated phosphate fluoride rinse | 0 02% fluoride in aqueous solution | dental rinse | March 28, 1980 | |
| sodium fluoride rinse | 0 05% aqueous solution (topical) | dental rinse | March 28, 1980 | Fluorigard (Colgate-Palmolive) |
| stannous fluoride gel | 0 4% gel (topical) | anticaries gel | March 28, 1980 | GelKam Gel (Colgate-Palmolive) |
| stannous fluoride rinse | 0 1% aqueous solution (topical) | dental rinse | March 28, 1980 | Stan Care (Block) |
| ephedrine sulfate | 0 1 to 1 25% (topical) | anorectal/vasoconstrictor | May 27 1980 | Pazo Ointment (Bristol-Myers) |
| epinephrine hydrochloride | 0 005 to 0 01% (topical) | anorectal/vasoconstrictor | May 27 1980 | |
| phenylephrine hydrochloride | 0 25% (topical) | anorectal/vasoconstrictor | May 27 1980 | |
| chlorpheniramine maleate (NDA) | 12 mg /12 hours (oral timed-release) | antihistamine | July 23 1981 | Triaminic 12 (Sandoz) |
| phenylpropanolamine hydrochloride (NDA) | 75 mg /12 hours (oral timed-release) | nasal decongestant | July 23 1981 | Triaminic 12 (Sandoz) |
| diphenhydramine hydrochloride (NDA) | 25 mg /4 hours (oral) | antitussive | August 7, 1981 | Benylin (Parke-Davis) |
| haloprogin | 1 0% (topical) | antifungal | March 23, 1982 | |
| miconazole nitrate | 2 0% (topical) | antifungal | March 23 1982 | Micatin (Ortho) |
| diphenhydramine hydrochloride | 50 mg single dose only (oral) | sleep aid | April 23 1982 | Sominex 2 (Beecham), Sleep-eze 3 (Whitehall) |
| diphenhydramine monocitrate | 76 mg single dose only (oral) | sleep aid | April 23 1982 | Excedrin PM (Bristol-Myers) |
| dyclonine hydrochloride | 0 05 to 0 1% solution or suspension, 1 to 3 mg as lozenge | oral anesthetic | May 25 1982 | Sucrets Maximum Strength (SmithKline) |
| dexbrompheniramine maleate (NDA) | 6 mg /12 hours (oral timed-release) | antihistamine | September 3 1982 | Drixoral (Schering) |
| pseudoephedrine sulfate (NDA) | 120 mg /12 hours (oral timed-release) | nasal decongestant | September 3 1982 | Afrinol Repetabs (Schering) |
| triprolidine hydrochloride | 2 5 mg /4-6 hours | antihistamine | November 26 1982 | Actifed Capsules (Warner-Lambert) Actidil Syrup and Capsules (Warner-Lambert) |

*+FDA approval for OTC marketing is on an interim basis pending adoption of a Final Monograph*

| INGREDIENT | ADULT DOSAGE | PRODUCT CATEGORY | DATE OF OTC APPROVAL | PRODUCT EXAMPLES |
|---|---|---|---|---|
| ibuprofen (NDA) | 200 mg /4-6 hours (oral) | internal analgesic/ antipyretic | May 18, 1984 | Advil (Whitehall) Nuprin (Bristol-Myers) |
| dexbrompheniramine maleate | 2 mg /4-6 hours (oral) | antihistamine | January 15, 1985 | |
| diphenhydramine hydrochloride | 25-50 mg /4 6 hours (oral) | antihistamine | January 15, 1985 | Benadryl 25 (Warner-Lambert) |
| pseudoephedrine hydrochloride(NDA) | 120 mg /12 hours (oral timed-release) | nasal decongestant | June 17, 1985 | Actifed (Warner-Lambert) |
| triprolidine hydrochloride (NDA) | 5 mg /12 hours | antihistamine | June 17, 1985 | Actifed 12-hour Capsules (Warner-Lambert) |
| oxymetazoline hydrochloride (NDA) | 0 025% solution/drops (topical) | occular vasoconstrictor | May 30, 1986 | Ocuclear (Schering) |
| pyrantel pamoate | 11 mg /kilo of body weight maximum dose 1 gram (oral) | anthelmintic | August 1, 1986 | Pin-X (Effcon) |
| povidone iodine sponge (NDA) | 10% (new dosage form) | antimicrobial | January 7, 1987 | E-Z Scrub 241 (Deseret) |
| diphenhydramine hydrochloride | 25 50 mg /4-6 hours (oral) | antiemetic | April 30, 1987 | |
| dexbrompheniramine maleate (NDA) | 3 mg /6-8 hours (oral) | antihistamine | May 22, 1987 | Drixoral Plus (Schering) |
| chlophedianol hydrochloride | 25 mg /6 8 hours (oral) | antitussive | August 12, 1987 | |
| doxylamine succinate | 7 5 mg - 12 5 mg /4-6 hours (oral) | antihistamine | August 24, 1987 | Nyquil (Procter & Gamble) |
| loperamide (NDA) | 4 mg , then 2 mg , 8 mg /day (oral) | antidiarrheal | March 3 1988 | Imodium A D (Johnson & Johnson) |
| hydrogenated soybean oil and lecithin | 12 4 gm powder in 2-3 oz water 20 minutes before gall bladder x-rays | cholecystokinetic | February 28, 1989 | Liposperse (Merck) |
| clotrimazole (NDA) | 1% lotion and cream/2 times daily | antifungal | October 23, 1989 | Lotrimin AF (Schering) |
| permethrin (NDA) | 1% cream rinse | pediculicide (head lice) | May 5, 1990 | Nix (Warner-Lambert) |
| clotrimazole (NDA) | 1% cream & 100 mg inserts | anticandidal | November 30, 1990 | Gyne-Lotrimin (Schering), Mycelex-7 (Miles) |
| miconazole nitrate | 2 0% cream and 100 mg inserts | anticandidal | March 13, 1991 | Monistat 7 (Ortho) |
| hydrocortisone | above 0 50% to 1 0% | antipruritic (anti itch) | August 30, 1991+ | |
| hydrocortisone acetate | above 0 50% to 1 0% | antipruritic (anti-itch) | August 30, 1991+ | |
| clemastine fumarate (NDA) | 1 34 mg /12 hours | antihistamine | August 21, 1992 | Tavist-1 (Sandoz Consumer) |
| clemastine fumarate (in combination with phenylpropanolamine HCl (NDA) | 1 34 mg /12 hours decongestant | antihistamine/ | August 21, 1992 | Tavist-D (Sandoz Consumer) |
| dexchlorpheniramine maleate | 2 mg/4-6 hours (oral) | antihistamine | December 9, 1992 | (last monograph switch) |
| naproxen sodium (NDA) | 200 mg/4-6 hours (oral) | internal analgesic/ antipyretic | January 11, 1994 | Aleve (Bayer) |
| pheniramine maleate with naphazoline HCl (NDA) | 0 3%, 0 025% in solution | ophthalmic antihistamine/ decongestant | June 8, 1994 | Naphcon A (Alcon) Opcon A (Bausch & Lomb) Ocuhist (Akorn) |
| antazoline phosphate with naphazoline HCl (NDA) | 0 5%, 0 05% in solution | ophthalmic antihistamine/ decongestant | July 11, 1994 | Vasocon A (Ciba) |
| famotidine (NDA) | 10 mg, up to 20 mg/day | acid reducer | April 28, 1995 | Pepcid AC (J&J Merck) |
| ibuprofen suspension 100mg/5ml for pediatric use (NDA) | 7 5 mg/kg up to 4 times a day | internal analgesic antipyretic | June 16 1995 | Children's Motrin (McNeil Consumer) |
| cimetidine (NDA) | 200 mg up to twice per day | acid reducer | June 19, 1995 | Tagamet HB (SmithKline) |
| ketoprofen (NDA) | 12 5 mg every 4 to 6 hours | Internal analgesic | October 16 1995 | Orudis KT (Whitehall-Robins) Actron (Bayer) |
| ranitidine (NDA) | 75 mg up to twice per day | acid reducer | December 19, 1995 | Zantac 75 (Warner Wellcome) |

| INGREDIENT | ADULT DOSAGE | PRODUCT CATEGORY | DATE OF OTC APPROVAL | PRODUCT EXAMPLES |
|---|---|---|---|---|
| butoconazole nitrate (NDA) | 2 0% cream and applicators (3 days) | anticandidal | December 26, 1995 | Femstat 3 (Procter & Gamble) |
| minoxidil (NDA) | 2 0% topical solution | hair grower | February 9, 1996 | Rogaine (Pharmacia & Upjohn) |
| nicotine polacrilex (NDA) | 2 mg and 4 mg gum | smoking cessation | February 9, 1996 | Nicorette (SmithKline Beecham) |
| nizatidine (NDA) | 75 mg up to twice daily | acid reducer | May 9, 1996 | AXID AR (Whitehall-Robins Healthcare) |
| miconazole nitrate (NDA) | 2 0% cream and 200 mg inserts | anticandidal | April 16, 1996 | Monistat 3 (Ortho) |
| nicotine transdermal system (NDA) | 15 mg patch | smoking cessation | July 3, 1996 | Nicotrol (McNeil Consumer) |
| clotrimazole (NDA)* | 1% cream & 200 mg inserts | anticandidal | July 29, 1996 | Gyne-Lotrimin 3 (Schering-Plough) |
| nicotine transdermal system (NDA) | 21, 14, & 7 mg patch | smoking cessation | August 2, 1996 | Nicoderm CQ (SmithKline Beecham) |
| bentoquatam (NDA)* | 5% lotion | poison ivy protection | August 26 1996 | Habitrol (Novartis) (Nov 12, 1999)<br>Ivy Block (EnviroDerm) |
| cromolyn sodium (NDA) | 4% nasal solution | allergy prevention & treatment | January 6, 1997 | Nasalcrom (McNeil Consumer) |
| tioconazole (NDA) | 6 5% vaginal ointment | anticandidal | February 11, 1997 | Vagistat-1 (Bristol-Myers Squibb), Monistat 1 (McNeil) |
| loperamide/simethicone (NDA)* | 2 mg loperamide, 125 mg simethicone | antidiarrheal/antigas | June 26, 1997 | Imodium Advanced (McNeil Consumer) |
| triclosan (dentifrice) (NDA)* | 0 30% triclosan/0 243% fluoride | antigingivitis | July 11, 1997 | Total (Colgate-Palmolive) |
| ketoconazole (NDA) | 1% shampoo | dandruff shampoo | October 10, 1997 | Nizoral (Johnson & Johnson Consumer Products) |
| minoxidil (NDA)* | 5 0% topical solution | hair grower | November 17, 1997 | Rogaine Extra Strength for Men (Pharmacia & Upjohn) |
| aspirin /caffeine /acetaminophen(NDA)** | 250mg/65mg/250mg | migraine | January 14 1998 | Excedrin Migraine (Bristol-Myers Squibb) |
| ranitidine (NDA)* | 75 mg (effervescent system) | acid reducer | February 26, 1998 | Zantac 75 EFFERdose (Glaxo Wellcome) |
| miconazole nitrate (NDA)* | 4 0% cream | anticandidal | March 30 1998 | Monistat 3 (Advanced Care Products) |
| terbinafine hydrochloride (NDA) | 1 0% cream | antifungal | March 9 1999 | Lamisil AT (Novartis) |
| cimetidine suspension (NDA)* | suspension | acid reducer | July 9, 1999 | Tagamet HB 200 (SmithKline Beecham) |
| naproxen Na, pseudoephedrine HCl* | 220 mg naproxen Na, 120 mg pseudoephedrine HCl | analgesic/decongestant | November 29, 1999 | Aleve Cold & Sinus (Bayer Consumer Care) |
| ibuprofen** | 200 mg | migraine | February 25, 2000 | Motrin Migraine Pain (McNeil Consumer Healthcare) |
| ibuprofen** | 200 mg | migraine | March 16, 2000 | Advil Migraine Liqui-Gels (Whitehall-Robins) |

*DA approval for OTC marketing is on an interim basis pending adoption of a Final Monograph* * *New OTC NDA - Not previously Rx* ** *New OTC indication, product previously OTC*

**II Other Potential OTC Ingredients/Dosages**

*Note CHPA Listing of Potential Switches is Based on Published Sources or Publicly Available Information*

| INGREDIENT | ADULT DOSAGE | PRODUCT CATEGORY | SOURCE OR INTERIM FDA POSITION, IF KNOWN |
|---|---|---|---|
| acamprosate | ------- | alcoholism treatment | Mentioned as hopefully "eventually" an OTC in New York Times, July 31, 1998 |
| acyclovir | 200 mg | antiviral | Adv Cmte voted "No" on 1/12/95 for OTC management of recurrent genital herpes |
| albuterol sulfate | 2 mg | bronchodilator | Mentioned as switch candidate in *Med Ad News*, Dec , 1996 |
| alosetron | -------- | irritable bowel syndrome | Mentioned as switch candidate in *The Tan Sheet* " January 24, 2000 |
| astemizole | -------- | antihistamine | Mentioned as "future switch" in *Switch Newsletter* Feb , 1996 |
| atorvastatin calcium | -------- | cholesterol-lowering agent | Asbury Park Press, July 14, 1999 |
| GREDIENT | ADULT DOSAGE | PRODUCT CATEGORY | SOURCE OR INTERIM FDA POSITION, IF KNOWN |
| ithromycin | - ----- | antibiotic | Mentioned as switch candidate in *Med Ad News* Dec , 1996 |

| | | | |
|---|---|---|---|
| beclomethasone dipropionate | nasal spray 0 042% | allergy prevention & treatment | Scheduled Adv Cmte consideration on Sept 19, 1997 - postponed |
| butenafine | ----- -- | antifungal | Mentioned as switch candidate in *Drug Store News* Sept 7, 1998 |
| celecoxib | ----- -- | non-steroidal anti inflammatory | Mentioned as switch candidate in *PRNewswire/NewsEdge* Nov 9 1999 |
| cetirizine Hcl | -------- | antihistamine | Mentioned as switch candidate in *Drug Topics* Apr 6 1998 |
| cholestyramine | ----- -- | cholesterol-lowering agent | FDA tentative position cholesterol lowering agents not appropriate for OTC use |
| clotrimazole/betamethasone | ----- -- | antifungal | Mentioned as switch candidate in *Drug Store News*, Sept 7, 1998 |
| colestipol hydrochloride | ------- | cholesterol lowering agent | FDA tentative position cholesterol-lowering agents not appropriate for OTC use |
| cyclobenzaprine HCl | 5 mg | muscle spasm treatment | Discussed at NDAC/Arthritis Adv Cmte meeting on July 20 1999 More info requested |
| diclofenac | -------- | non-steroidal anti inflammatory | Mentioned as switch candidate in *'The Tan Sheet,"* March 23, 1998 |
| diflunisal | -------- | non steroidal anti-inflammatory | *FDC Reports*, November 7, 1988 p 10 |
| docosanol | 10% topical cream | antiviral for cold sores | *Scrip* Nov 5, 1999 FDA says clinical data "sufficient for approval' as new OTC |
| econazole nitrate | 1% | antifungal | NDA pending *Progressive Grocer* April, 1995 |
| erythromycin | -------- | antibiotic | *FDC Reports* June 12, 1989, "Potential switch product" in *Med Ad News*, August 1996 |
| etodolac | 200 mg | non steroidal anti-inflammatory | *FDC Reports* - *'The Tan Sheet,"* Sept 30 1996, p 15 |
| fexofenadine | ----- -- | antihistamine | Mentioned as switch candidate in *The Tan Sheet* " August 18 1997 |
| fluconazole | -------- | antifungal | Mentioned as 'future switch' in *Switch Newsletter* Feb , 1996 |
| fluticasone propionate | nasal spray | allergic rhinitis symptoms | Mentioned as switch candidate in *"The Tan Sheet,"* January 24 2000 |
| fluvastatin | -------- | cholesterol-lowering agent | FDA tentative position cholesterol-lowering agents not appropriate for OTC use |
| ibuprofen extended release | -------- | non-steroidal anti-inflammatory | |
| loratadine | -------- | antihistamine | Mentioned as future switch" in *Switch Newsletter* Feb , 1996 |
| lovastatin | -------- | cholesterol lowering agent | FDA tentative position cholesterol lowering agents not appropriate for OTC use |
| methacarbamol | -------- | muscle relaxant | Muscle relaxants discussed by Adv Cmte 3/28/95 Issue of switch unresolved |
| mupirocin | -------- | topical antiviral | "Potential switch product" in *Med Ad News*, August, 1996 |
| nabumetone | -------- | non-steroidal anti-inflammatory | "Potential switch product in *Med Ad News*, August, 1996 |
| nicotine | nasal spray, oral inhaler | smoking cessation | "Near-term switch candidates" in *"The Tan Sheet,"* May 19, 1997 |
| nitrofurantoin monohydrate | -------- | urinary tract antibiotic | "Potential switch candidate" in *"The Tan Sheet* " Dec 16, 1996, p 7 |
| nystatin | -------- | antifungal | Mentioned as switch candidate in *Med Ad News*, Dec , 1996 |
| omeprazole | -------- | antisecretory (heartburn) | OTC launch expected 2nd quarter, 2001, per *"The Tan Sheet,"* Nov 1 1999 |
| penciclovir | -------- | topical antiviral (cold sores) | Narrowly rejected by Adv Cmte 12/1/88 'Tan Sheet" reports still being pursued (5/3/99) |
| piroxicam | -------- | non-steroidal anti-inflammatory | Mentioned as "future switch" in *Switch Newsletter* Feb , 1996 |
| rofecoxib | -------- | non-steroidal anti-inflammatory | Mentioned as switch candidate in *PRNewswire/NewsEdge*, Nov 9 1999 |
| sucralfate | -------- | anti-ulcer | NDA pending, *FDC Reports* January 16, 1989, p 8 |
| sulindac | 300 mg /day | analgesic | *FDC Reports* April 3, 1989, p 7 |
| sumatriptan succinate | ------- | migraine treatment | Mentioned as switch candidate in *"The Tan Sheet* January 24 2000 |
| theophylline | -------- | bronchodilator | Mentioned as switch candidate in *Med Ad News* Dec , 1996 |
| REDIENT | ADULT DOSAGE | PRODUCT CATEGORY | SOURCE OR INTERIM FDA POSITION, IF KNOWN |
| oin | ----- -- | acne treatment | Mentioned as switch candidate in *OTC News*, June 1997 |

| | | | |
|---|---|---|---|
| valacyclovir | 500 mg | antiviral | Mentioned as switch candidate in *"The Tan Sheet,"* August 18, 1997 |
| zanamivir | inhalant | influenza treatment prophylaxis | Mentioned as switch candidate in *"The Tan Sheet"* May 12, 1997, p 15 |

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# TAB C

UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

**Memorandum**

Date: April 7, 2000

TO : Suzanne Barone, Ph D Project Manager, HS

THROUGH Warren J. Prunella, AED, EC

FROM Marcia P. Robins, EC

SUBJECT : Economic Considerations: Proposal to Maintain Child-Resistant Packaging Requirements for Oral Prescription Drugs That Have Been Granted OTC Status by the FDA

The Directorate for Economic Analysis reviewed the economic, small business, and environmental effects of the subject proposal Attached are the finds of these reviews.

Attachment (s)

## Economic Considerations: Proposal to Maintain Child-Resistant Packaging Requirements for Oral Prescription Drugs That Have Been Granted OTC Status by the FDA

The Poison Prevention Packaging Act (PPPA) requires child-resistant (CR) packaging for all oral drugs dispensed by prescription (Rx), unless they have been specifically exempted from packaging requirements CR packaging is provided either by the drug supplier pre-packaging the drug, or by the dispensing pharmacist repackaging the prescribed amount of the drug for the consumer Packaging requirements can be waived based on a request by the physician prescribing the drug or by the purchaser When over-the-counter (OTC) marketing approval for drug ingredients originally available Rx-only is granted by the Food and Drug Administration (FDA), the PPPA oral prescription drug requirements no longer apply The ultimate packaging of a product then becomes the responsibility of the drug marketer, and the pharmacist is no longer a secondary packager.

CPSC can promulgate packaging requirements for OTC products if the Commission finds that the degree or nature of the hazard to children in the availability of such substance, by reason of its packaging, is such that special packaging is required to protect children from serious personal injury or serious illness resulting from handling, using, or ingesting such substance The Commission made such findings for products formerly marketed as oral Rx drugs and now available OTC that contain ingredients such as ibuprofen, loperamide, naproxen, and ketoprofen The staff recommends that the Commission propose the continuation of PPPA requirements for oral drug products containing ingredients transferred by the FDA from Rx to OTC marketing status.

### FDA Procedures for Transferring Drugs from Rx to OTC Status

The FDA transfers ingredients from Rx to OTC marketing status through the approval of a New Drug Application (NDA) initiated by the manufacturer and,with the concurrence of an Advisory Panel. Approvals are for specific ingredient dosages and specific therapeutic usage An ingredient can be transferred for multiple purposes The ingredient review program started in 1972; the first Rx/OTC transferred ingredients were marketed in 1976. An estimated 63 ingredients and dosages were transferred from 1975 to May 1996, including ingredients used in topical preparations.[1] No one knows exactly how many ingredients/dosages are in, or may soon enter, the transfer "pipeline" However, a July 1998 article in the trade press citing Consumer Healthcare Products Association (CHPA) data listed 28 potential transfers, including some for topical use as well as for oral use.[2]

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[1] *Pharmaceutical and Medical Packaging News, September 1996.*
[2] *Drug Topics, July 20, 1998.*

## Packaging Rx/OTC Transferred Products

Historically, when a drug product's ingredients transfer from Rx to OTC status, the marketer provides packaging with "shelf appeal" in an effort to attract consumers and compete with other products in the therapeutic category. Marketers must chose some form of packaging but are no longer bound by PPPA requirements and can provide nonCR packaging for transferred products The incremental cost of providing basic CR packaging is usually small ($0 005-$0 02) depending upon the choice of package. The cost may be somewhat higher if more elaborate packaging is provided. Marketers are required to perform one-time stability and other testing to meet FDA requirements when changes in packaging are made.

It is unlikely that packaging manufacturers would have difficulty supplying the needed CR packaging that might result from this rule Based on past experience, there is only a relatively small number of ingredients for oral prescription drugs that would be transferred from Rx to OTC in any given year. Consequently, CR packaging for newly transferred drug ingredients is expected to be readily available for new product introductions. Moreover, because most packaging firms already produce both CR and nonCr packaging, and because the production differences between CR and nonCR packages are minimal, packaging manufacturers would, if necessary, be able to increase the relative production of CR packages within a short time.

## Small Business Effects

The proposal to continue PPPA requirements for ingredients transferred by the FDA from Rx to OTC marketing status will affect an unknown number of small businesses. However, as described above, packagers of products with transferred ingredients will have to choose some form of packaging Since the incremental cost of CR packaging is minimal, and because these costs (if any) are likely to be passed on to consumers, it seems unlikely that the proposal will have a substantial effect on a significant number of small businesses.

**Preliminary Environmental Assessment of the Proposal to Maintain Child-Resistant Packaging Requirements for Oral Prescription Drugs That Have Been Granted Over-the-Counter Status by The Food And Drug Administration**

Pursuant to the National Environmental Policy Act, and in accordance with the Council on Environmental Quality regulations and CPSC procedures for environmental review, the Commission has preliminarily assessed the possible environmental effects associated with the proposed Poison Prevention Packaging Act (PPPA) packaging requirements for maintaining child-resistant (CR) packaging requirements for oral prescription drugs that have been granted over-the-counter (OTC) status by the Food and Drug Administration.

The Commission's regulations at 16 CFR Sec. 1021 5 [C] [3] state that the rules requiring special packaging for consumer products normally have little or no potential for affecting the human environment Preliminary analysis of the impact of this proposed rule indicates that maintaining CR packaging requirements for the production of marketers of oral prescription drug ingredients under the proposed rule will have no significant effects on the environment The continued manufacture, use, and disposal of CR packaging will not present environmental effects.