UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

VOTE SHEET

DATE: July 2, 2001

TO: The Commission
Todd A. Stevenson, Acting Secretary

FROM: Michael S. Solender, General Counsel MSJ
Stephen Lemberg, Assistant General Counsel
Lowell F. Martin, Attorney, GCRA (ext. 2217)

SUBJECT: Final PPPA Rule to Maintain Child-Resistant Packaging for Oral Prescription Drugs That Have Been Granted Over-The-Counter ("OTC ") Status by the Food and Drug Administration ("FDA")

VOTE SHEET

The attached staff briefing package recommends that the Commission approve a final rule to maintain child-resistant packaging for oral prescription drugs that have been granted OTC status by the FDA ("OTC switched" drugs). The rule would apply prospectively to any OTC drug approved by the Food and Drug Administration (FDA) that contains an active ingredient of a prescription drug subject to the Commission's existing CR packaging requirement at 16 C.F.R. § 1700.14(a)(10). The draft final rule that would require CR packaging pursuant to authority granted to the CPSC by the Poison Prevention Packaging Act of 1970, as amended, (PPPA) is attached for Commission consideration. The new regulation would appear at 16 C.F.R. § 1700.14(a)(30).

The final rule would go into effect 180 days after publication. It would not apply to any OTC drug with an approval application submitted to the FDA before the effective date. It would apply only to oral dosage formulations of OTC drugs, as is the case with the Commission's current CR packaging regulation for prescription drugs.

The rule also would eliminate the current requirement of the Commission's regulations at 16 C.F.R. § 1702.16(b) that FDA approval for a new drug be obtained prior to seeking an exemption from any otherwise applicable CPSC child-resistant packaging requirement. Where justified, this would allow a prospective OTC drug marketer to obtain an exemption from the CR packaging requirement prior to submission of the new drug application to the FDA, thus providing assurance that the proposed packaging would not need to be changed subsequent to FDA approval.

NOTE: This document has not been reviewed or accepted by the Commission.
Initial mh Date 7/2/01

CPSA 6 (b)(1) Cleared 7/2/01
No ... Privileged ...
Product ... Exception ...

Staff recommends that the Commission delegate to staff the responsibility to periodically issue by *Federal Register* notice a list of those drugs for which the FDA has approved an OTC switch making them subject to the CR packaging requirement of the final rule.

Please indicate your vote on the following options.

I. APPROVE THE FINAL RULE AS DRAFTED.

_____ _____

(Signature) (Date)

II. APPROVE THE FINAL RULE WITH THE FOLLOWING CHANGES (PLEASE SPECIFY).

_____

_____

_____

_____ _____

(Signature) (Date)

III. DO NOT APPROVE THE FINAL RULE AS DRAFTED

_____ _____

(Signature) (Date)

IV. DELEGATE TO STAFF THE RESPONSIBILITY TO PERIODICALLY ISSUE BY *FEDERAL REGISTER* NOTICE A LIST OF THOSE DRUGS FOR WHICH THE FDA APPROVES AN OTC SWITCH MAKING THEM SUBJECT TO THE CR PACKAGING REQUIREMENT OF THE FINAL RULE.

_____ _____

YES NO

_____ _____

(Signature) (Date)

V. TAKE OTHER ACTION (PLEASE SPECIFY).

_____

_____

_____

_____ _____

(Signature) (Date)

Attachments

Staff briefing package

Draft final rule

BRIEFING PACKAGE

FINAL 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
Suzanne Barone, Ph.D.
Directorate for Health Sciences
(301) 504-0477 ext. 1196

CPSA 6 (b)(1) Cleared
7/2/01
No Mfrs/Prvtlblrs or Products Identified
Excepted by
Firms Notified.
Comments Processed.

NOTE: This document has not been reviewed or accepted by the Commission.
Initial HN Date 7/2/01

TABLE OF CONTENTS

Executive Summary

The Commission proposed to require child-resistant packaging of oral prescription drugs that are granted OTC status by the FDA in the future (65 FR 52678). The regulations of the Poison Prevention Packaging Act (PPPA) require child-resistant packaging of most oral prescription drugs. However, 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 issue the rule as proposed 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 rule will ensure 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. None of the public comments provided any basis for changing the staff recommendation.

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 earlier in the process, before the New Drug Applications (NDA) are submitted or 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 oral prescription products that are granted OTC status is technically feasible, practicable, and appropriate since these drugs are already supplied in child-resistant packaging as prescription drugs. It is anticipated that this rule would not create a financial burden on small companies.

UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

Memorandum

Date: JUL 2 2001

TO: The Commission
Todd A. Stevenson, Acting Secretary

THROUGH: Michael S. Solender, General Counsel MSS TM
Thomas W. Murr Jr., Acting Executive Director

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 issue child-resistant packaging requirements for oral prescription drugs when such drugs are granted over-the-counter (OTC) status by the Food and Drug Administration (FDA). The memorandum addresses the comments received in response to the Notice of Proposed Rulemaking (NPR).

BACKGROUND

The Poison Prevention Packaging Act of 1970 (PPPA) was established to protect children from serious personal injury or serious 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 as a class under the PPPA.

Regulations have been issued to require child-resistant packaging of several individual OTC products including diphenhydramine, ibuprofen, loperamide, naproxen, and ketoprofen. Theses oral drugs were available originally only by prescription and therefore required child-resistant packaging under the oral prescription drug regulation (16 CFR § 1700.14(a)(10)). The Food and Drug Administration (FDA) subsequently granted OTC status to these drugs,

NOTE: This document has not been reviewed or accepted by the Com... Initial ph Date 7/2/01

CPSA 6 (b)(1) Cleared 7/2/01 No Mfrs/Prvtlrs or Products Identified

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.

On August 30, 2000, the Commission proposed to require child-resistant packaging of oral prescription drugs that are granted OTC status by the FDA in the future (65 FR 52678) (Tab A). This rule would ensure that children continue to be protected after oral prescription drugs are granted OTC status. The NPR outlined that the potential rule would include oral drug entities that are granted OTC status by the FDA even if the usage, dosages, oral forms, and drug combinations differ from those products that were available as prescription drugs. The NPR also proposed that notice be published in the Federal Register following FDA approval of a "switched" oral drug to help consumers and industry identify which drugs would require child-resistant packaging under this rule.

The NPR also proposed revocation of 16 CFR 1702.16(b), which mandates that the Commission deny a petition requesting an exemption from the requirement of child-resistant packaging unless the FDA has approved the drug for marketing. Elimination of this provision would provide manufacturers with the opportunity to request an exemption and to have a decision by the Commission before the new drug application is submitted to the FDA for review and approval.

Five commenters submitted information response to the NPR (Tab B). The staff's response to the comments, a discussion of the findings, and the staff recommendation are presented below.

COMMENTS

Three of the five commenters supported the rulemaking (CP01-1, 2,5).

Comment: Several commenters questioned whether the PPPA permits imposing child-resistant packaging requirements on a category of drugs and then placing the burden on the manufacturer to seek exemption of individual drugs. (CP01-1-3, 4)

Response: The PPPA authorizes regulation of a category of substances where the required findings can be made for that category. In fact, a number of entries under the CPSC regulation imposing the PPPA child-resistant packaging requirement, 16 CFR § 1700.14(a), are defined as broad categories. (See, for example: controlled *drugs* -- "any preparation for human use that consists in whole or in part of any substance subject to control under the Comprehensive Drug Abuse Prevention and Control Act...;" *prescription drugs* – "any drug for human use that is in a dosage form intended for oral administration...;")

All members of the class that would be required to be in child-resistant packaging by an OTC-switch rulemaking were previously covered by the PPPA child-resistant packaging

requirement for oral prescription drugs (16 CFR § 1700.14(a)(10)). The statutory findings for that class were made by the FDA in the 1972-1973 rulemaking that imposed child-resistant packaging on oral prescription drugs.

The ability of a drug to cause serious injury to a child does not change when it is sold OTC. Child-resistant packaging remains technically feasible, practicable, and appropriate for the OTC version, just as was the case when it was required for the prescription formulation. Furthermore, the continued need for child-resistant packaging is not a factor considered by the FDA when making its decision to approve the switch of a drug from prescription to OTC status. Under the proposed rule, the responsibility/burden on a manufacturer to justify an exemption for an OTC-switched drug would be the same as it was before the drug was switched.

Comment: One commenter requested that OTC products be available in both child-resistant packaging and non child-resistant packaging for the elderly and disabled (CP01-1).

Response: The opportunity for the use of both child-resistant and non child-resistant packaging exists under the PPPA. Section 4 of the PPPA allows manufacturers to package products in one size that does not meet the child-resistant packaging standards. This product must carry a labeling statement warning that it is not recommended for use in households with young children. There is no requirement that manufacturers have a non child-resistant size.

It is the manufacturer's decision whether to market a noncomplying size. Manufacturers who market one size of their product in nonchild-resistant packaging must also supply the product in popular-sized packages that are child-resistant. If the manufacturer does not comply with this provision, the Commission can require that the product be packaged exclusively in child-resistant packaging if such packaging is necessary to accomplish the purposes of the PPPA (15 U.S.C. 1473(c)).

Child-resistant packaging is also more "adult-friendly." In 1995, the Commission issued a revised test method that tests adult participants aged 50 to 70 rather than 18 to 45 years of age to ensure that most adults can use child-resistant packaging properly.

Comment: One commenter requested that manufacturers and sellers have 18-months advance notice of the effective date of these packaging changes and that these measures only be implemented for newly manufactured packages (CP01-2).

Response: The proposed packaging regulations would only apply to drugs granted OTC status in which the new drug applications (NDAs) are submitted to the FDA on or after the effective date of a final OTC-switch rule. The rule would not affect any product that is approved for OTC sale before that date. The rule would not impact the current production or sale of previously switched products. Therefore the proposed effective date of 180 days after issuance of a final rule should be adequate for companies currently preparing NDA submissions requesting OTC status for oral prescriptions.

Comment: One commenter requested that a comprehensive list of affected products and ingredients be made available in advance of the effective date (CP01-2).

Response: The CPSC will publish a list of drugs that are affected by the rule as soon as the Agency becomes aware of them. CPSC will work with the FDA to obtain timely notification of approval of oral prescription drugs that are granted OTC status. Since no oral prescription drug approved for OTC sale before the effective date would be affected by the rule, the list would address OTC switches granted by the FDA on or after that date.

Comment: One commenter questioned the efficiency of the potential rule to save staff resources because of the resources used to consider requests for exemptions. The commenter states that it may be just as efficient to continue the practice of considering the need for child-resistant packaging on a case-by-case basis (CP01-3).

Response: The primary goal of this rulemaking is not to save staff resources but to continue to protect children from serious injury from ingesting oral prescription drugs when those drugs are granted OTC status and become widely available. This rulemaking would eliminate the potential for newly switched oral OTC drugs to be packaged and sold without child-resistant packaging before a decision about their continued need for child-resistant packaging is made by the Commission. The staff cannot estimate how many petitions for exemption from the child-resistant packaging requirements the Commission will receive. Some companies voluntarily use child-resistant packaging for their "switched" OTC products.

Comment: Two commenters requested revisions to PPPA regulations that define child-resistant unit packaging (CP01-3, 4).

Response: The child-resistant unit packaging regulations are not the subject of this rulemaking.

Comment: One commenter requested clarification that the Commission will accept and act on a petition for exemption early in the process, before a new drug application (NDAs) is submitted to the FDA.

Response: In the proposed rule, the Commission stated that, "...the Commission is proposing to revoke 16 CFR 1702.16(b) so that exemption petitions can be submitted and considered by the Commission earlier in the process, i.e., before FDA approval." If 16 CFR 1702.16(b) were revoked there would be no restriction on the timing for the Commission to consider a petition request. This would enable manufacturers to seek an exemption from the child-resistant packaging requirements and have a Commission decision prior to submitting an application to the FDA for approval of an OTC or prescription drug product.

The exemption process involves rulemaking. This process can be expedited if the manufacturers meet with the CPSC staff to discuss the process before filing a petition for exemption with the Commission as outlined in 16 CFR Pt.1702.

Comment: *One commenter expressed a concern that if a petition is submitted* before the NDA is submitted, it could prematurely signal a company's business plans. They believed that a confidential exemption procedure may be necessary but stated the concern that it would not be compatible with the current rulemaking approach to exemptions. (CP01-3)

Response: The commenter is correct that the child-resistant packaging exemption procedure involves public notice and comment. The petitioner must be willing to have toxicity and safety information available for Commission and public review.

There are many factors that a company considers when deciding to pursue OTC status for an oral drug. These may include safety of use and potential misuse, ability of a consumer to self-treat using the medication or new market for a drug at the end of its patent, etc. There is much speculation in the press about drugs that may be "switched" based upon these factors. The commenter (Consumer Healthcare Products Association) publishes a list of potential switches that have been named in the trade or popular press[1]. The FDA requested comments and held a public meeting last year to discuss potential OTC drugs[2]. Much of the discussion from the public hearing focused on classes of drugs that may or may not be appropriate for OTC sale. With this current speculation and discussion about potential candidates for OTC switches, it seems less likely that a petition for exemption from child-resistant packaging will signal the company's business plans prematurely.

A manufacturer of an oral prescription drug that is contemplating seeking OTC approval could request an exemption from child-resistant packaging for the prescription drug. It is the active ingredient itself at a defined level that will be exempted. Under the rule as proposed, an exempted oral prescription drug would be exempted from child-resistant packaging when it is granted OTC status. For example, if an oral contraceptive or colestipol were made available OTC, it would not require child-resistant packaging if the OTC preparation met the same conditions as the exempted oral prescription drugs (16 CFR § 1700.14(a)(10)(iv) and (xv)).

A manufacturer would still have the option of petitioning the Commission for exemption after the drug is approved for OTC sale.

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[1] Available on the CHPA website, www.chpa-info.org
[2] 65 FR 24704

FINDINGS

Hazard to Children

The Commission preliminarily found 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 serious illness from handling, using, or ingesting the drugs (15 U.S.C. 1472(a)(1)). This finding was previously made for oral prescription drugs in the 1972-1973 FDA rulemaking now appearing at 16 CFR § 1700.14(a)(10).

There were no comments received that directly questioned the potential toxicity of oral prescription drugs that are granted OTC status. These drugs have the same toxicity whether they are prescription or OTC. Toxicity of the drugs still exists even when the OTC dosage is lower than prescription strength. In addition, 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 personal injury or serious illness from ingesting oral prescription drugs that have been granted OTC status.

Technical Feasibility, Practicability, and Appropriateness

The Commission must also find that child-resistant packaging for OTC-switched drugs is technically feasible, practicable, and appropriate. No commenter questioned the ability to produce child-resistant packaging for these products. 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 like the anti-inflammatory drugs such as ibuprofen or naproxen are sold in bottles. There are child-resistant designs of reclosable packaging and unit packaging that are commercially available and in widespread use in the OTC market.

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 application to the FDA requesting the "switch," the staff recommends that this rule apply to OTC-switched drugs subject to a new drug application (NDA) or abbreviated new drug application (ANDA) submitted to the FDA 180 days or more 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 Commission proposed an effective date of 180 days after publication of the final rule. 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. The commenter requesting a further delayed effective date seemed not to understand that the proposed rule would only apply to oral prescription drugs for which the NDA requesting OTC status was submitted to the FDA after the effective date. Previously "switched" OTC products would not be affected by this rule. Therefore, the staff recommends retaining the 180-day effective date as proposed.

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.

No comments were received that addressed economic issues related to this potential rule. 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 same 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 already widely 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 present the same environmental effects as non child-resistant packaging.

OPTIONS

The Commission has several options:

1. The Commission may issue the rule as proposed, if the Commission finds that child-resistant packaging is necessary to continue to protect children from serious injury or serious illness from oral prescription drugs that are granted OTC status. The Commission may delegate to the staff the responsibility to publish a Federal Register notice naming the drugs affected by the rule when they are granted OTC status by the FDA.

2. The Commission may revoke 16 CFR § 1702.16(b) so that petitions for exemption from child-resistant packaging can be submitted and considered by the Commission before FDA approval.

3. The Commission may decline to issue the rule.

RECOMMENDATION AND DISCUSSION

The staff recommends that the Commission issue the rule as proposed to require that the child-resistant packaging requirement on an oral prescription drug remain when the active chemical in that drug is granted OTC status by the FDA. No comment provided any basis for changing this staff recommendation.

This rule would give children the same protection when the drugs are more widely available as OTC preparations as they had when the drugs were available only by prescription. The rule would eliminate the possibility of a drug being available in non child-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 on the basis of 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 recommends that the Commission delegate to the CPSC staff the responsibility to publish a notice to identify the drugs that would be affected by this rule following the FDA approval of an OTC switched oral drug. This drug would then be listed in an appendix to the switched regulation at 16 CFR §1700.14.

The staff also recommends that the Commission revoke 16 CFR 1702.16(b) to allow a petition for exemption from child-resistant packaging to be submitted and considered by the Commission before the NDA is approved by the FDA. This would decrease the potential financial and regulatory burden 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 currently supplied in child-resistant packaging as prescription drugs. It is anticipated that this rule would not create a financial burden on small companies or the environment.

TAB A

activated. Additional review has found that the AFM's of Model 35A and 36A series airplanes also do not contain appropriate flightcrew actions when the cabin altitude aural warning is activated. However, the AFM's do *contain an abnormal procedure that* allows the flightcrew to troubleshoot the pressurization system prior to donning the oxygen masks after the cabin altitude warning sounds. Troubleshooting may delay donning of the oxygen masks to the point that flightcrews may become incapable of donning their oxygen masks.

The SCR findings indicated that the most likely cause for incapacitation was hypoxia (lack of oxygen). The only other plausible cause of incapacitation is exposure to toxic substances. However, no evidence was found to support the existence of toxic substances.

Delayed response of the flightcrew in donning oxygen masks upon the activation of the cabin altitude warning horn could lead to incapacitation of the flightcrew and loss of control of the airplane.

A review of the emergency procedures in the AFM for Lockheed Model 188A and 188C series airplanes revealed that those AFM's also did not contain the requirement for the flightcrew to immediately don emergency oxygen masks. Therefore, all Lockheed Model 188A and 188C series airplanes may be subject to the same unsafe condition as described above.

Explanation of Requirements of Proposed Rule

Since an unsafe condition has been identified that is likely to exist or develop on other products of this same type design, the proposed AD would require revising the Emergency Procedures Section of the AFM to provide the flightcrew with appropriate and timely actions in response to activation of the cabin altitude warning horn.

Cost Impact

There are approximately 75 Model 188A and 188C series airplanes of the affected design in the worldwide fleet. The FAA estimates that 32 airplanes of U.S. registry would be affected by this proposed AD, that it would take approximately 1 work hour per airplane to accomplish the proposed actions, and that the average labor rate is $60 per work hour. Based on these figures, the cost impact of the proposed AD on U.S. operators is estimated to be $1,920, or $60 per airplane.

The cost impact figure discussed above is based on assumptions that no operator has yet accomplished any of the proposed requirements of this AD action, and that no operator would accomplish those actions in the future if this proposed AD were not adopted. The cost impact figures discussed in AD rulemaking actions represent only the time necessary to perform the specific actions actually required by the *AD*. These figures typically do not include incidental costs, such as the time required to gain access and close up, planning time, or time necessitated by other administrative actions.

Regulatory Impact

The regulations proposed herein would not have a substantial direct effect on the States, on the relationship between the national Government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, it is determined that this proposal would not have federalism implications under Executive Order 13132.

For the reasons discussed above, I certify that this proposed regulation (1) Is not a "significant regulatory action" under Executive Order 12866; (2) is not a "significant rule" under the DOT Regulatory Policies and Procedures (44 FR 11034, February 26, 1979); and (3) if promulgated, will not have a significant economic impact, positive or negative, on a substantial number of small entities under the criteria of the Regulatory Flexibility Act. A copy of the draft regulatory evaluation prepared for this action is contained in the Rules Docket. A copy of it may be obtained by contacting the Rules Docket at the location provided under the caption **ADDRESSES.**

List of Subjects in 14 CFR Part 39

Air transportation, Aircraft, Aviation safety, Safety.

The Proposed Amendment

Accordingly, pursuant to the authority delegated to me by the Administrator, the Federal Aviation Administration proposes to amend part 39 of the Federal Aviation Regulations (14 CFR part 39) as follows:

PART 39—AIRWORTHINESS DIRECTIVES

1. The authority citation for part 39 continues to read as follows:

Authority: 49 U.S.C. 106(g), 40113, 44701.

§ 39.13 [Amended]

2. Section 39.13 is amended by adding the following new airworthiness directive:

Lockheed: Docket 2000–NM–265–AD.

Applicability: All Model 188A and 188C series airplanes, certificated in any category.

Compliance: Required as indicated, unless accomplished previously.

To prevent incapacitation of the flightcrew and consequent loss of control of the airplane due to delays in donning oxygen masks in response to the activation of the cabin altitude warning horn; accomplish the following:

Revision to the Airplane Flight Manual

(a) Within 90 days after the effective date of this AD, revise the Emergency Procedures Section of the FAA–Approved Airplane Flight Manual (AFM) to include the following. This may be accomplished by inserting a copy of this AD in the AFM.

"Low Cabin Pressure Warning Light Comes On and Horn Starts Blowing

a. Oxygen Masks—Don. Select 100% oxygen.
b. If conditions dictate, initiate emergency descent.
c. Check cabin differential pressure gage.
   1. If differential pressure is below 13.34 + 0.30 in. Hg, lower cabin altitude selector wheel.
   2. If differential pressure is at 13.34 + 0.30 in. Hg, descend to lower aircraft altitude.

Note: Warning horn can be silenced with cabin altitude warning horn switch."

Alternative Methods of Compliance

(b) An alternative method of compliance or adjustment of the compliance time that provides an acceptable level of safety may be used if approved by the Manager, Atlanta Aircraft Certification Office (ACO), FAA. Operators shall submit their requests through an appropriate FAA Principal Maintenance Inspector, who may add comments and then send it to the Manager, Atlanta ACO.

Note 1: Information concerning the existence of approved alternative methods of compliance with this AD, if any, may be obtained from the Atlanta ACO.

Special Flight Permit

(c) Special flight permits may be issued in accordance with §§ 21.197 and 21.199 of the Federal Aviation Regulations (14 CFR 21.197 and 21.199) to operate the airplane to a location where the requirements of this AD can be accomplished.

Issued in Renton, Washington, on August 24, 2000.

Donald L. Riggin,

Acting Manager, Transport Airplane Directorate, Aircraft Certification Service.

[FR Doc. 00–22123 Filed 8–29–00; 8:45 am]

BILLING CODE 4910–13–U

CONSUMER PRODUCT SAFETY COMMISSION

16 CFR Part 1700

Child-Resistant Packaging for Certain Over-The-Counter Drug Products

AGENCY: Consumer Product Safety Commission.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Consumer Product Safety Commission (CPSC or Commission) is proposing a rule to require child-resistant (CR) packaging on drugs approved by the Food and Drug Administration (FDA) for over-the-counter (OTC) sale that contain active ingredients previously available only in prescription drugs. Current Commission regulations require CR packaging for most oral drug products containing prescription-only active ingredients. However, at present, there is no general requirement for CR packaging of such drug products in forms subsequently approved by the FDA for OTC sale.

The Commission is also proposing to revoke the current prohibition on granting a petition for an exemption from a CR packaging requirement prior to FDA approval of the drug product in question.

The Commission takes these actions under authority of the Poison Prevention Packaging Act of 1970, as amended.

DATES: The Office of the Secretary must receive comments on this proposal on or before November 13, 2000.

ADDRESSES: Mail comments to the Office of the Secretary, Consumer Product Safety Commission, Washington, D.C. 20207, or hand deliver them to the Office of the Secretary, Consumer Product Safety Commission, Room 502, 4330 East-West Highway, Bethesda, Maryland 20814–4408, telephone (301) 504–0800. Comments may also be filed by telefacsimile to (301) 504–0127 or by email to cpsc-os@cpsc.gov.

FOR FURTHER INFORMATION CONTACT: Suzanne Barone, Directorate for Health Sciences, Consumer Product Safety Commission, Washington, D.C. 20207; telephone (301) 504–0477 ext. 1196.

SUPPLEMENTARY INFORMATION:

A. Background

1. Current Approach to CR Packaging Requirements

The Poison Prevention Packaging Act, 15 U.S.C. 1471–1476, was enacted to protect children from serious personal injury or illness resulting from handling, using, or ingesting hazardous substances. Under the PPPA the CPSC can require CR packaging of hazardous household chemicals, including drug products. The CPSC regulations currently require CR packaging of all oral prescription drug products that have not been specifically exempted from that requirement. 16 CFR 1700.14(a)(10).

In contrast, OTC drug products, also referred to as nonprescription drug products, are not now regulated as a class under the PPPA. However, a number of specific OTC drug products have been required by Commission regulation to have CR packaging. These drug products and the effective dates of the CR requirements are: (1) Aspirin (1972), (2) liquid methyl salicylate (1972), (3) iron-containing drug products (1978), (4) acetaminophen (1980), (5) diphenhydramine (1984), (6) ibuprofen (1992), (7) loperamide (1993), (8) lidocaine (1996), (9) dibucaine (1996), (10) naproxen (1996), (11) *ketoprofen (1997), and (12) minoxidil* (1999).

Diphenhydramine, ibuprofen, loperamide, naproxen, and ketoprofen were active ingredients available originally only in oral dose prescription drug products.[1] Drug products containing them therefore required CR packaging under the Commission's general oral prescription drug product CR packaging regulation. The FDA subsequently approved these active ingredients for use in OTC drug products at specific dosage levels. The OTC forms were not subject to the Commission's CR packaging requirement for oral prescription drug products. The CPSC conducted a rulemaking and promulgated a separate regulation to require CR packaging for OTC products containing each of these active ingredients.

2. The Limited Effect of FDA Approval of an OTC-Switch

The FDA approves drug products containing a single active ingredient or a combination of active ingredients for sale in the United States. This includes approval for sale directly to the consumer in OTC product formulations. The primary responsibility of the FDA with respect to OTC drug products is to assure that they are safe and effective when self-administered by a consumer in a proper manner. The FDA does not base granting of OTC status on whether a drug product would be toxic to a child if unintentionally ingested. The FDA confirmed this in a letter to CPSC staff dated October 7, 1998 stating 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 the FDA letter is available in the docket for this rulemaking.

3. Frequency of OTC-Switches

Since 1976, the FDA has permitted many drug products 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."[2] Trade press articles speculate that this trend will continue.[3] The CHPA has compiled a table listing 80 drug products that have been granted *OTC status since 1976.*[4] *Of the 80* listings in the table, 22 are oral drug products that were previously available by prescription. The other listings are topical drug products, new uses, or new formulations for existing OTC drug products, or OTC-approved drug products that were not previously available as prescription products.

The FDA is currently evaluating whether other drug products or drug product categories should be OTC-switched. That agency conducted a two-day public hearing in late June of this year on a spectrum of OTC issues, including OTC switches. In the April 27, 2000 Federal Register notice announcing the hearing, 65 FR 24704–6, the FDA stated that it had "received comments suggesting that a number of other types of drugs should be considered for OTC status." The FDA notice indicated that the types of drug products suggested for OTC status include diuretics, antihypertensive agents, cholesterol-lowering drug products, antidiabetic drug products, treatments for osteoporosis, drug products for stomach problems, *etc.*

4. OTC-Switched Drug Products Currently Subject to CR Packaging Requirements

To date, the Commission has required CR packaging for OTC products containing 6 of the 22 oral prescription active ingredients that have also been approved for sale in OTC products. The six active ingredients that currently

[1] The meanings of the terms active ingredient and drug product as used in this rulemaking are the same as the meanings assigned to those terms in the drug product regulations of the FDA. The FDA drug product regulations define active ingredient as "any component (of a drug product) that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the body of humans, but does not include intermediates used in the synthesis of such ingredient." 21 CFR 201.66 (1999). The FDA regulations define drug product as "a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance (active ingredient), generally, but not necessarily, in association with one or more other ingredients." 21 CFR 314.3 (1999). Drug product also encompasses a product containing more than one active ingredient. 21 CFR 300.50 (1999).

[2] The Uniform Resource Locator (URL) for the CHPA website is: www.ndmainfo.org

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

[4] The CHPA Table is available on that organization's website at: www.ndmainfo.org/pdfs/Switch%20List/pdf

require CR packaging in OTC products, the date of OTC approval by the FDA, and the effective date of the CR packaging requirements are listed in Table 1. The other 16 active ingredients are discussed below.

TABLE 1: PRESCRIPTION ACTIVE INGREDIENTS SWITCHED TO OTC STATUS THAT REQUIRE CR PACKAGING

Active ingredient	Year OTC-switched	Year CR packaging effective
Diphenhydramine HCL	1982	1984
Diphenhydramine monocitrate	1982	1985
Ibuprofen	1984	1992
Loperamide	1988	1993
Naproxen sodium	1994	1996
Ketoprofen	1995	1997

5. History of CPSC Regulation of OTC–Switched Oral Drug Products

In the past, CPSC staff focused primarily on ingestion data to recommend to the Commission what products should be in CR packaging. In the late 1970s the FDA allowed the OTC sale of several antihistamines that were previously available only by prescription. Of these, diphenhydramine hydrochloride was the first OTC-switched active ingredient regulated by the CPSC under PPPA authority. Then, in 1982, the FDA approved the monocitrate salt of diphenhydramine for OTC sale. The existing diphenhydramine hydrochloride CR packaging regulation was then amended to cover all diphenhydramine salts.

In 1984, the CPSC staff evaluated ingestion data related to ibuprofen. Products containing ibuprofen were granted OTC status during that year. At that time, the poisoning data were limited and Commission staff did not recommend CR packaging. The two companies that first marketed OTC ibuprofen products used CR packaging voluntarily on some package sizes.

In 1989, CPSC staff revisited ibuprofen toxicity because ibuprofen had become widely available. Not all companies were using CR packaging and serious injuries to children resulted. The Commission issued a rule requiring CR packaging for all of these products. 16 CFR 1700.14(a)(20). Companies that had been marketing their products in non-CR packaging changed their packaging accordingly.

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

CPSC staff monitors FDA's activities concerning approval of switched OTC drug products. The staff attends FDA advisory panel meetings when possible, to better understand any issues about a potential switch 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 to young children of the active ingredient or ingredients in the product then becomes a priority for the CPSC staff.

To avoid expending the CPSC's limited resources if the FDA does not approve OTC sale of the drug product, Commission staff waits for FDA approval before proceeding with a review. The proposed rule would eliminate this lag between FDA approval of an OTC-switch and the CPSC requirement to maintain CR packaging.

The 16 oral prescription active ingredients that were switched to OTC status and are not currently required to have CR packaging are pseudoephedrine HCL, pseudoephedrine sulfate, phenylpropanolamine HCL, clemastine fumarate, brompheniramine maleate, chlorpheniramine maleate, dexbrompheniramine maleate, triprolidine HCL, dexchlorpheniramine maleate, doxylamine succinate, pyrantel pamoate, chlophedianol HCL, famotidine, cimetidine, ranitidine, and nizatidine. In conjunction with this rulemaking, CPSC staff has preliminarily assessed the toxicity of eight of these. Based on their toxicity, the staff would recommend CR packaging for drug products containing pseudoephedrine HCL, pseudoephedrine sulfate, phenylpropanolamine HCL, and clemastine fumarate.

The four active ingredients for which the CPSC staff would not recommend CR packaging are members of the same family of antihistamines used to reduce stomach acid. These are famotidine, cimetidine, ranitidine, and nizatidine. These substances do not have the degree of toxicity associated with antihistamines used to treat cold symptoms.

Five antihistamine active ingredients that are currently under preliminary review by Commission staff are brompheniramine maleate, chlorpheniramine maleate, dexbrompheniramine maleate, triprolidine HCL, and dexchlorpheniramine maleate. These antihistamines are related in structure and activity to diphenhydramine, which is currently subject to a CR packaging requirement.

This rulemaking proposal would not retrospectively require CR packaging of FDA-approved drug products containing the 16 OTC-switched active ingredients not currently subject to CR packaging requirements. CPSC staff continues to evaluate these substances as time and other priorities permit. Many drug products containing these active ingredients are in CR packaging because they contain other active ingredients that require CR packaging, for example pseudoephedrine with ibuprofen or an antihistamine with acetaminophen or aspirin. In addition, the Commission is aware of some OTC products that are voluntarily marketed in CR packaging.

B. Relevant Statutory and Regulatory Provisions

The Poison Prevention Packaging Act authorizes the Commission to establish standards for the "special packaging" of any household substance if: (1) 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; and (2) the special packaging is technically feasible, practicable, and appropriate for such substance. 15 U.S.C. § 1472(a).

CR or "special" packaging must be designed or constructed to be: (1) Significantly difficult for children under 5 years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time; and (2) not difficult for "normal adults" to use properly. 15 U.S.C. 1471(4). Household substances for which the Commission may require CR

packaging include (among other categories) foods, drugs, or cosmetics as these terms are defined in the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 321. 15 U.S.C. 1471(2)(B). The Commission has promulgated performance requirements for special packaging. 16 CFR 1700.15 and 1700.20.

Section 4(a) of the PPPA, 15 U.S.C. 1473(a), allows the manufacturer or packer to package a nonprescription product subject to special packaging standards in one size of non-CR packaging only if the manufacturer (or packer) also supplies the product in CR packages of a popular size, and the non-CR package bears conspicuous labeling stating "This package for households without young children." 15 U.S.C. 1473(a), 16 CFR 1700.5.

C. The Proposed Rule

1. General Approach

The Commission is proposing a rule to require that CR packaging requirements applicable to any oral prescription drug product continue to apply when that drug product or any other drug product containing an active ingredient of that product is granted OTC status by the FDA. This rule will provide children with the same protection when a drug product is more widely available as an OTC preparation that they had when it was available only by prescription. The rule would eliminate the possibility of a drug product being available in non-CR packaging for an extended time before the CR packaging requirement is reimposed by Commission rulemaking. The need to continue to protect children does not diminish when an oral prescription drug product is granted OTC status. As noted above, a decision by the FDA to grant OTC status for a prescription drug product does not include a finding that there is a lack of toxicity to a child if the drug product is accidentally ingested in an unpredictable amount, which could be the entire contents of the OTC product package. The active ingredient(s) in the drug product still have the same toxicity, whether the drug product is in prescription or OTC form.

2. Additional Uses, Forms, and Combinations of OTC-Switched Drug Products

The FDA can approve a new usage or a new dosage form of a previously-approved OTC-switched drug product. The proposed rule would require that the new use or new dose be sold in CR packaging even if the new use or dose was not approved when the drug product was only available by prescription. This is consistent with the current regulatory approach for a new use for an oral OTC product that is already subject to a CR packaging requirement. For example, after February 11, 1985, any oral product that contained more than the equivalent of 66 mg. of diphenhydramine base was required to be in CR packaging. At that time, diphenhydramine was in OTC sleep aids and hay fever preparations. In 1987, when diphenhydramine was approved by the FDA for OTC sale as an oral antiemetic drug product, no further CPSC regulatory action was necessary. This same focus on the active ingredient itself rather than the approved usage is the approach of the proposed rule. If an oral prescription drug product were granted OTC status by the FDA it would automatically be subject to a CR packaging requirement under the proposed rule. If the FDA then approved another OTC drug product containing some or all of the active ingredients in that drug product, the new drug product would also automatically be subject to the CR packaging requirement.

The proposed rule would not extend CR packaging requirements to OTC-switched products that are not oral formulations, even if they contain any of the same active ingredients as an oral preparation. Formulations other than oral, such as topical preparations, or transdermal patches would still be regulated individually and therefore not affected by this proposed rule.

In some cases, after a prescription drug product is approved for OTC sale by the FDA, other forms, dosages, or combinations containing some or all of the active ingredients in that drug product will also be approved for OTC sale. These combinations or forms may not have existed when the drug was available by prescription only. This proposal would cover these situations. For example, loperamide was granted OTC status by the FDA in 1988. In 1993, the CPSC required CR packaging for any oral product that contained more than 0.045 mg of loperamide. In 1997, the FDA approved the combination of loperamide and simethicone in an OTC product. This combination was never a prescription product. However, the combination OTC product is subject to the CR packaging requirement because the loperamide rule is not limited to the original prescription formulation.

3. Change in Dosage Between Prescription and OTC Drugs

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

This proposal would require CR packaging for any OTC oral drug product containing an active ingredient that was available by prescription even if the OTC dosage is lower than the prescription strength. This is consistent with the approach of the CPSC's oral prescription drug product CR packaging regulation, which applies to all dosages approved by the FDA for prescription sale. This recognizes the reality that absent CR packaging, the "dose" potentially available to a child is the entire package contents.

The Commission has issued rules for individual OTC switched drug products that are only available at a lower dose than the prescription strength product. The Commission's experiences with ibuprofen and naproxen demonstrate that toxic amounts of the active ingredients are available from a single OTC product container even at these new lower dosages.

4. 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 CR packaging is not technically feasible, practicable, or appropriate. 16 CFR Part 1702. Companies petition the Commission to exempt products by submitting data, described in 16 CFR Part 1702, to support a conclusion either that: (1) the drug product will not cause serious injury or illness, or (2) it is not technically possible to develop and produce CR packaging for the drug product. An exemption petition is processed by informal, notice and comment rulemaking. Currently, 18 oral prescription drug products and several OTC formulations of aspirin, acetaminophen, and iron have been exempted from the CR packaging requirements. 16 CFR 1700.14. Under the proposed rule, this exemption procedure would remain available to manufacturers of OTC-switched products.

5. Timing of Exemption Petitions

The Commission's current CR packaging regulations specify that the Commission shall deny an exemption petition if the FDA has not approved the new drug product. 16 CFR 1702.16(b). Therefore,at present, a company seeking an exemption for a newly approved drug product must either market in CR packaging, delay marketing until the Commission acts on the petition, or request a stay of enforcement to allow marketing in non-CR packaging while the Commission considers the petition.

A post-marketing change in packaging of an approved OTC drug product may be more complex for the manufacturer than simply buying different packaging and modifying the packaging equipment. In some cases, the FDA must approve the new packaging before the drug product can be marketed.[5] Stability testing of the product in the new package must be completed and the results approved by the FDA before the product can be marketed in the new package.

Accordingly, the Commission is proposing to revoke 16 C.F.R. 1702.16(b) so that exemption petitions can be submitted and considered by the Commission earlier in the process, *i.e.*, before FDA approval. This would enable manufacturers to seek an exemption from the CR packaging requirements and have a Commission decision prior to submitting an application to the FDA for approval of an OTC or prescription drug product.

6. Listing of OTC-Switched Drug Products Subject to CR Packaging

To assist consumers and industry in identifying which OTC-switched drug products require CR packaging, the Commission intends to maintain a list of such drug products as an appendix to the regulations at 16 CFR 1700.14. As the FDA approves OTC-switches, the list would be updated periodically by publishing a revised appendix in the **Federal Register**.

D. Findings

1. Hazard to Children

Before issuing a rule requiring CR packaging, the Commission must find that the degree or nature of the hazard to children in the availability of OTC-switched drug products 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 drug products. 15 U.S.C. 1472(a)(1). These statutory findings were made when the rule requiring CR packaging for oral prescription drug products was promulgated in 1973. 38 Fed. Reg. 9,431.

OTC-switches did not begin to occur until several years after the 1973 rule requiring CR packaging for oral prescription drug products was promulgated. The first such switches were carried out in response to recommendations from an FDA Advisory Panel's review of over-the-counter drug products.

The need to continue to protect children remains when oral prescription drug products are granted OTC status. As noted previously, a decision by the FDA to grant OTC status for a prescription drug product is not a determination that there is no toxicity to a child if the drug product is accidentally ingested. The active ingredient(s) contained in the drug product have the same toxicity whether in prescription or OTC form. The issue is whether drug products switched to OTC status at a lower dosage than was available by prescription are still hazardous to young children. This is the case since absent CR packaging, the "dose" available to a child can be the entire contents of the OTC product package. The Commission's experiences with ibuprofen and naproxen demonstrate that toxic amounts of the active ingredients are available even when lower dosages are approved for OTC product sale.

Another important consideration is that OTC drug products are more readily available to consumers and therefore more accessible to children than prescription products containing the same active ingredient(s). The CPSC concludes that the available data support the finding that maintaining CR packaging is necessary to protect children from serious injury or illness from ingesting oral prescription drug products that have been granted OTC status.

2. Technical Feasibility, Practicability, and Appropriateness

As a prerequisite to a CR packaging rule, the Commission must also find that the special packaging is "technically feasible, practicable, and appropriate." 15 U.S.C. 1472(a)(2). Technical feasibility may be found when technology exists or can be readily developed and implemented by the effective date to produce packaging that conforms to the standards. Practicability means that special packaging complying with the standards can utilize modern mass production and assembly line techniques. Packaging is appropriate when complying packaging will adequately protect the integrity of the active ingredient(s) in the product and not interfere with its intended storage or use.

In some cases the same packaging can be used for the OTC product as for the prescription product. However, companies must modify the labels since FDA labeling requirements for OTC drug products differ from the labeling requirements for prescription drugs. Also, most companies develop new packaging specifically for the OTC market. Unit dose packaging is popular for the OTC market especially for drug products such as antihistamines that are sold in limited quantities. Other products containing active ingredients such as the anti-inflammatory compounds ibuprofen and naproxen are sold in bottles. CR designs of this sort of unit and reclosable packaging are commercially available. The change in status of the drug from prescription-only to OTC does not change the availability of the CR packaging in mass-produced quantities, or detract from its ability to maintain the shelf life of switched drug products. Therefore, the Commission concludes that CR packaging for OTC-switched drug products is technically feasible, practicable, and appropriate.

3. Other Considerations

Section 3(b) of the PPPA requires that the Commission consider the following in establishing a special packaging standard:

a. The reasonableness of the standard;

b. Available scientific, medical, and engineering data concerning special packaging and concerning childhood accidental ingestions, illness, and injury caused by household substances;

c. The manufacturing practices of industries affected by the PPPA; and

d. The nature and use of the household substance. 15 U.S.C. 1472(b).

The Commission has considered these factors with respect to the various determinations made in this notice, and preliminarily finds no reason to conclude that the rule is unreasonable or otherwise inappropriate.

E. Applicability

The packaging configuration for a drug product to be switched is determined before a company submits the OTC-switch application to the FDA. Accordingly, the Commission is proposing that this rule apply prospectively to drug products for

[5] *Guidance for Industry, Changes to An Approved NDA or ANDA.* Food and Drug Administration, Drug Information Branch, Center for Drug Evaluation and Reserech, November 1999. This document is available on the FDA website at: www.fda.gov/cder/guidance/index.htm

Copies can also be obtained by calling the FDA Drug Information Branch at (301) 827–4573.

which the application for the OTC-switch is submitted to the FDA on or after the effective date of the final rule (180 days after publication).

F. Effective Date

The PPPA provides that no regulation shall take effect sooner than 180 days or later than one year after the date such final regulation is issued, except that, for good cause, the Commission may establish an earlier effective date if it determines an earlier date to be in the public interest. 15 U.S.C. 1471n.

CR packaging is currently available commercially for most, if not all, types of oral prescription drug products that would be subject to this rulemaking. Thus, the Commission is proposing that the final rule take effect 180 days after its publication.

G. Regulatory Flexibility Act Certification

When an agency undertakes a rulemaking proceeding, the Regulatory Flexibility Act (RFA), as amended by the Small Business Regulatory Enforcement Fairness Act of 1996, 5 U.S.C. 601 *et seq.*, generally requires the agency to prepare initial and final regulatory flexibility analyses describing the impact of the rule on small businesses and other small entities. Section 605 of the RFA provides that an agency is not required to prepare a regulatory flexibility analysis if the head of an agency certifies that the rule will not have a significant economic impact on a substantial number of small entities.

The Commission's Directorate for Economic Analysis prepared a preliminary assessment of the impact of a rule to maintain CR packaging for OTC-switched drug products. A copy of the preliminary analysis is available for inspection in the docket for this rulemaking. The assessment reports that the incremental cost of providing basic CR packaging is usually small ($0.005-$0.02/per package). The assessment also notes that the incremental cost may be somewhat higher if the marketer provides more elaborate packaging in the effort to create "shelf appeal" to attract consumers and compete with other OTC products in the same therapeutic category.

At present, the Commission does not have quantitative information on the number of small businesses that might be affected by the OTC-switch proposal. However, the staff assessment concludes that because the incremental cost of CR packaging is minimal, and because these costs (if any) are likely to be passed on to consumers, it is unlikely that the proposal will have a substantial effect on a significant number of small businesses. The Commission requests comment from companies that supply OTC-switched drug products. The Commission is particularly interested in information on the likely effect of this proposed rule on small businesses.

Many OTC-switched drug products are already in CR packaging. In some instances, for example with certain oral dosage formulations of acetaminophen, ibuprofen and loperamide, this is because the Commission has affirmatively required CR packaging. In other cases, the marketer has elected voluntarily to use CR packaging.

This notice proposes revocation of the existing requirement at 16 CFR 1702.16(b) that new drug approval be obtained from the FDA prior to Commission approval of a petition seeking exemption from a CR packaging requirement. Allowing for advance consideration and approval of any legitimate CR packaging exemption petition should minimize or eliminate any unwarranted economic impact that would otherwise result from maintaining the CR packaging requirement on OTC-switched oral prescription drug products or from requiring a change to CR packaging post-marketing.

Based on the foregoing assessment, the Commission certifies that the rule to maintain CR packaging for OTC-switched drug products, if promulgated in final form as proposed, would not have a significant impact on a substantial number of small businesses or other small entities.

H. Environmental Considerations

Pursuant to the National Environmental Policy Act, and in accordance with Council on Environmental Quality regulations and CPSC procedures for environmental review, the Commission has assessed the possible environmental effects associated with the proposed PPPA requirements for OTC-switched drug products.

The Commission's regulations state that rules requiring special packaging for consumer products normally have little or no potential for affecting the human environment. 16 CFR 1021.5(c)(3). Nothing in this proposed rule alters that expectation. Therefore, because the rule would have no adverse effect on the environment, neither an environmental assessment nor an environmental impact statement is required.

I. Executive Orders

As provided for in Executive Order 12,988 the CPSC states the preemptive effect of this proposed regulation as follows.

The PPPA provides that, generally, when a special packaging standard issued under the PPPA is in effect, "no State or political subdivision thereof shall have any authority either to establish or continue in effect, with respect to such household substance, any standard for special packaging (and any exemption therefrom and requirement related thereto) which is not identical to the [PPPA] standard." 15 U.S.C. 1476(a). A State or local standard may be excepted from this preemptive effect if (1) the State or local standard provides a higher degree of protection from the risk of injury or illness than the PPPA standard; and (2) the State or political subdivision applies to the Commission for an exemption from the PPPA's preemption clause and the Commission grants the exemption through procedures specified at 16 CFR part 1061. 15 U.S.C. 1476(c)(1). In addition, the Federal government, or a State or local government, may establish and continue in effect a non-identical special packaging requirement that provides a higher degree of protection than the PPPA requirement for a household substance for the Federal, State or local government's own use. 15 U.S.C. 1476(b).

Thus, with the exceptions noted above, the proposed rule requiring CR packaging for OTC-switched drug products would preempt non-identical state or local special packaging standards for such drug products.

J. Trade Secret or Proprietary Information

Any person responding to this notice who believes that any information submitted is trade secret or proprietary should specifically identify the exact portions of the document claimed to be confidential. The Commission's staff will receive and handle such information confidentially and in accordance with section 6(a) of the Consumer Product Safety Act (CPSA), 15 U.S.C. 2055(a). Such information will not be placed in the public docket for the rulemaking and will not be made available to the public simply upon request. If the Commission receives a request for disclosure of the information or concludes that its disclosure is necessary to discharge the Commission's responsibilities, the Commission will inform the person who submitted the information and provide that person an opportunity to present additional information and views concerning the confidential nature of the information. 16 CFR 1015.18(b) (1999).

The Commission's staff will then make a determination of whether the information is trade secret or proprietary information that cannot be released. That determination will be made in accordance with applicable provisions of the CPSA; the Freedom of Information Act (FOIA), 5 U.S.C. 552b; 18 U.S.C. 1905; the Commission's procedural regulations at 16 CFR part 1015 governing protection and disclosure of information under provisions of FOIA; and relevant judicial interpretations. If the Commission concludes that any part of the information that has been submitted with a claim that the information is a trade secret or proprietary is disclosable, it will notify the person submitting the material in writing and provide at least 10 calendar days from the receipt of the letter to allow for that person to seek judicial relief. 15 U.S.C. 2055(a)(5) and (6); 16 CFR 1015.19(b).

List of Subjects in 16 CFR Part 1700

Consumer protection, Drugs, Infants and children, Packaging and containers, Poison prevention, Toxic substances, Reporting and recordkeeping requirements.

For the reasons set forth above, the Commission proposes to amend 16 CFR part 1700 as follows:

PART 1700—POISON PREVENTION PACKAGING ACT OF 1970 REGULATIONS

1. The authority citation for part 1700 continues to read as follows:

Authority: 15 U.S.C. 1471–76. Secs. 1700.1 and 1700.14 also issued under 15 U.S.C. 2079(a).

2. Section 1700.14 is amended by republishing paragraph (a) introductory text and by adding new paragraph (a)(32) to read as follows:

§ 1700.14 Substances requiring special packaging.

(a) *Substances.* The Commission has determined that the degree or nature of the hazard to children in the availability of the following substances, by reason of their packaging, is such that special packaging meeting the requirements of § 1700.20(a) is required to protect children from serious personal injury or serious illness resulting from handling, using, or ingesting such substances, and the special packaging herein required is technically feasible, practicable, and appropriate for these substances:

* * * * *

(32) *Over-the-Counter Drug Products.* (i) Any over-the-counter drug product in a dosage form intended for oral administration that contains an active ingredient also contained in a drug product that is or was a prescription drug product required by paragraph (a)(10) of this section to be in special packaging shall be packaged in accordance with the provisions of § 1700.15 (a), (b), and (c). This requirement applies whether or not the amount of the active ingredient in the over-the-counter drug product is different from the amount of that active ingredient in the prescription drug product. This requirement does not apply to a drug product for which an application for over-the-counter marketing has been submitted to the FDA before [insert date 180 days after promulgation of final rule] or which has been granted over-the-counter status by the FDA before [insert date 180 days after promulgation of final rule]. Notwithstanding the foregoing, any special packaging requirement under this § 1700.14 otherwise applicable to an over-the-counter drug product remains in effect.

(ii) For purposes of this paragraph (a)(32), active ingredient means any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the body of humans; and drug product means a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance (active ingredient), generally, but not necessarily, in association with one or more other ingredients. (These terms are intended to have the meanings assigned to them in the regulations of the Food and Drug Administration appearing at 21 CFR 201.66 and 21 CFR 314.3, respectively.)

§ 1702.16 [Amended]

3. Section 1702.16 is amended by removing paragraph (b) thereof in its entirety.

Dated: August 23, 2000.

Sadye E. Dunn,

Secretary, Consumer Product Safety Commission.

List of Relevant Documents

1. Briefing memorandum from Suzanne Barone, Ph.D., EH, to the Commission, "Proposed Rule to Require Special Packaging for Oral Prescription Drugs that are Granted Over-the-Counter Status by the Food and Drug Administration," May 16, 2000.

2. Letter from Debra L. Bowen, M.D., Acting Director, Division of Over-the-Counter Drug Products, Food and Drug Administration, to Jeffrey S. Bromme, Esq., General Counsel, Consumer Product Safety Commission, October 7, 1998.

3. Memorandum from Marcia P. Robins, EC, to Suzanne Barone, Ph.D., EH, "Economic considerations: Proposal to Maintain Child-Resistant Packaging Requirements for Oral Prescription Drugs that Have Been Granted OTC Status by the FDA," April 7, 2000.

4. Memorandum from Suzanne Barone, Ph.D., Project manager for Poison prevention, Directorate for Health Sciences, to Sadye E. Dunn, Secretary, Consumer Product Safety Commission, "Responses to Questions from Commissioner Moore on Over-the-Counter Switches," June 23, 2000.

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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 2

[FRL–6860–9]

RIN 2025–AA02

Elimination of Special Treatment for Category of Confidential Business Information: Reproposal

AGENCY: Environmental Protection Agency.

ACTION: Proposed rule.

SUMMARY: The Environmental Protection Agency (EPA or Agency) published a document in the **Federal Register** on October 25, 1999 (64 FR 57421), proposing to amend its regulations to eliminate the special treatment of a category of confidential business information (CBI). This category of CBI includes comments received from businesses that substantiate their claims of confidentiality for previously submitted information. In response to requests from interested parties, EPA extended the comment period on the proposed rule from December 27, 1999, to January 26, 2000 (64 FR 71366, December 21, 1999). EPA is now reproposing the rule to address some of the comments that it received.

DATES: Comments on this proposed rule must be submitted by October 30, 2000.

ADDRESSES: Send written comments on this proposed rule to Docket Number EC–1999–015, Enforcement and Compliance Docket and Information Center (ECDIC), U.S. Environmental Protection Agency, 1200 Pennsylvania Ave., NW, Room 4033, Mail Code 2201A, Washington, DC 20460; Phone, 202–564–2614 or 202–564–2119; Fax, 202–501–1011; Email, *docket.oeca@epa.gov.* Documents related to this proposed rule are available for public inspection and viewing by contacting the ECDIC at this same address.

FOR FURTHER INFORMATION CONTACT: Rebecca Moser, Office of Information

TAB B

6a6h OK 11/15/00

United States
CONSUMER PRODUCT SAFETY COMMISSION
Washington, D.C. 20207

MEMORANDUM

DATE : November 15, 2000

TO : HS

Through: Sadye E. Dunn, Secretary

FROM : Martha Kosh

SUBJECT: Child-Resistant Packaging for Certain Over-The-Counter Drug Products; Notice of Proposed Rulemaking; 65 Fed. Reg 52678, August 30, 2000

ATTACHED ARE COMMENTS ON THE CP 01-1

COMMENT	DATE	SIGNED BY	AFFILIATION
CP 01-1	9/19/00	Students	Florida International University 6520 SW 44 Street Miami, FL 33155
CP 01-2	10/13/00	John Coster Ph.D, R.Ph. Vice President Federal and State Programs	National Association of Chain Drug Stores 413 North Lee Street P.O. Box 1417-D49 Alexandria, VA 22313
CP 01-3	11/10/00	Eve Bachrach Senior Vice President, General Counsel & Secretary & William W. Bradley Vice President - Technical Affairs	Consumer Healthcare Products Association 1150 Connecticut Ave., NW Washington, DC 20036
CP 01-4	11/13/00	Peter Mayberry Exec. Director	Healthcare Compliance Packaging Council 7799 Leesburg Pike Suite 900N Falls Church, VA 22043

Child-Resistant Packaging for Certain Over-The-Counter Drug Products; Notice of Proposed Rulemaking; 65 Fed. Reg 52678, August 30, 2000

CP 01-5	11/5/00	John Armitstead Director of Pharmacy Services Clinical Assoc. Professor	University of Kentucky Hospital Chandler Medical Center 800 rose St, Rm C114C Lexington, KY 40536

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TAB C

UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

Memorandum

Date: May 31, 2001

TO : Suzanne Barone
Project Manager for Poison Prevention
Directorate for Health Sciences

THROUGH: Warren Prunella
Associate Executive Director
Directorate for Economic Analysis

FROM : Robert Franklin
Economist
Directorate for Economic Analysis

SUBJECT : Economic Considerations Related to the Rule 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) regulations issued by the Food and Drug Administration and now administered by the Consumer Product Safety Commission ("CPSC" or "Commission") require child-resistant (CR) packaging for all oral drugs dispensed by a prescription, unless they have been specifically exempted from the packaging requirements. Drug ingredients sold over-the-counter (OTC) are not required to be in CR packaging unless the CPSC requires CR packaging for the specific ingredients. Therefore, when the Food and Drug Administration (FDA) approves OTC marketing for drug ingredients formerly available only by prescription, the OTC product does not require CR packaging unless the CPSC has issued a regulation requiring CR packaging for the drug ingredients. The CPSC has issued regulations that require several OTC drug products to be in CR packaging, including those containing aspirin, ibuprofen, loperamide, naproxen, and ketoprofen.

The effect of the rule before the Commission now is to require firms to maintain CR packaging for oral prescription drugs switched to OTC status, except when the Commission votes to exempt a specific drug product. This action would ensure that the same level of protection against accidental ingestion is provided after the drug product is switched to OTC status as before the switch. The rule will not apply to non-oral drug products or to oral drug products switched or in the process of being switched to OTC status prior to the rule's effective date.

The staff prepared a briefing package for the proposed rule and sent it to the Commission on 16 May 2000. The Commission voted to issue a notice of proposed rulemaking, which was

published in the Federal Register on 30 August 2000. Although the Commission received several comments on the proposed rule, no comment directly addressed economic issues.

Economic Considerations Related to Packaging Costs

Although prescription drugs that are switched to OTC status were sold in CR packaging as prescription drugs, there may some costs associated with the switch to OTC status. Whereas prescription drugs are often dispensed in generic bottles supplied by the pharmacy, manufacturers of OTC drugs often try to package their products in ways that enhance their "shelf appeal" to attract consumers and compete with other products in the same therapeutic category. However, the incremental cost of providing CR packaging (i.e., over and above the other costs of packaging drugs for sale over the counter) is usually small, typically in the range of $0.005 to $0.02 per unit. The incremental cost may be somewhat higher if the manufacturer chooses more elaborate packaging.

It is unlikely that closure manufacturers will have difficulty supplying the needed CR packaging for OTC switched drugs for several reasons. There are a wide variety of CR packaging designs for both prescription and non-prescription oral drug products already in use. These include drugs in liquid, capsule, and tablet form. Most packaging firms already produce both CR and non-CR packaging. And, because the production differences between the CR and non-CR packages are minimal, packaging manufacturers should be able to increase the relative production of CR packages within a short period of time. Finally, based on past experience, only a small number of ingredients for oral prescription drugs is likely to be transferred to OTC status in any given year. For example, from 1975 to May 1996 an estimated 63 ingredients and dosages were transferred from being available by prescription only to OTC status. This number includes topical as well as oral preparations.[1] The rule covers only oral preparations. Consequently, manufacturers should not have difficulty finding CR packaging for newly switched products even if there is an increase in the number of products switched each year.

Small Business Effects (Regulatory Flexibility Act)

In the notice of proposed rulemaking the Commission certified that the rule (if promulgated as proposed) would not have a significant impact on a substantial number of small businesses or other small entities. The notice included justification for the certification.[2] The Commission did not receive any comments related to this certification.

The CPSC does not know how many small businesses will be affected by the rule. However, as described above, since the incremental cost of CR packaging [illegible] because these costs (if any) are likely to be passed on to consumers, it is unlikely that the rule will have a substantial impact on a significant number of small businesses.

[1] Pharmaceutical and Medical Packaging News, September 1996.
[2] Federal Register, Vol. 65, No. 169 (30 August 2000), p. 52683.

Environmental Assessment

The staff has assessed the possible environmental effects that would be associated with the rule maintaining CR packaging requirements for oral prescription drugs that have been granted OTC status by the FDA. A preliminary environmental assessment was published with the notice of proposed rulemaking.[3] The Commission did not receive any public comments concerning the preliminary environmental assessment.

The Commission's regulations at 16 CFR Sec. 1021 (5)(C)(3) state that rules requiring special packaging for consumer products normally have little or no potential for affecting the human environment. The staff's assessment indicates that maintaining CR packaging requirements for prescription oral drug products switched to being available over-the-counter will have no significant effects on the environment. Generally, the manufacture, use, and disposal of CR packaging for drug products has the same environmental effects as does the manufacture, use, and disposal of non-CR packaging.

[3] Ibid.

DRAFT

Billing Code 6355-01-P

CONSUMER PRODUCT SAFETY COMMISSION

16 CFR Part 1700

Child-Resistant Packaging for Certain Over-The-Counter Drug Products

AGENCY: Consumer Product Safety Commission.

ACTION: Final Rule.

SUMMARY: The Consumer Product Safety Commission (CPSC or Commission) is issuing a rule to require child-resistant (CR) packaging on drugs (OTC switched drugs) approved by the Food and Drug Administration (FDA) for over-the-counter (OTC) sale that contain active ingredients previously available only in prescription drugs. Current Commission regulations require CR packaging for most oral drug products containing prescription-only active ingredients. However, prior to issuance of this rule there was no general requirement to maintain CR packaging of such drug products in forms subsequently approved by the FDA for OTC sale.

The Commission is also revoking the current prohibition on granting a petition for an exemption from a CR packaging requirement prior to FDA approval of the drug product in question.

The Commission takes these actions under authority of the Poison Prevention Packaging Act of 1970, as amended.

DATES: The rule will become effective on [INSERT DATE THAT IS 180 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER], and applies only to products for which the new drug application

(NDA) or abbreviated new drug application (ANDA) for the OTC switch is submitted to the FDA on or after that date.

FOR FURTHER INFORMATION CONTACT: Suzanne Barone, Ph.D., Directorate for Health Sciences, Consumer Product Safety Commission, Washington, D.C. 20207; telephone (301)504-0477 ext. 1196 or Geri Smith, Office of Compliance, Consumer Product Safety Commission, Washington, D.C. 20207; telephone (301)504-0608 ext. 1160.

SUPPLEMENTARY INFORMATION:

A. Background

1. *Prior Regulatory Approach*

The Poison Prevention Packaging Act of 1970 (PPPA), 15 U.S.C. 1471-1476, was established to protect children from serious personal injury or serious illness resulting from handling, using, or ingesting hazardous substances. Under the PPPA, the 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 prescription by a licensed medical practitioner, have not previously been regulated as a class under the PPPA.

Regulations have been issued to require child-resistant

packaging of several individual OTC products including diphenhydramine, ibuprofen, loperamide, naproxen, and ketoprofen. These oral drugs were available originally only by prescription and therefore required child-resistant packaging under the oral prescription drug regulation. The FDA subsequently granted OTC status to these drugs, thus removing them from the scope of 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.

2. *Relevant Statutory and Regulatory Provisions*

The PPPA authorizes the Commission to establish standards for the "special packaging" of any household substance if: (1) 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; and (2) the special packaging is technically feasible, practicable, and appropriate for such substance. 15 U.S.C. 1472(a).

CR or "special" packaging must be designed or constructed to be: (1) significantly difficult for children under 5 years of age to open or obtain a toxic or harmful amount of the substance contained therein within a

reasonable time; and (2) not difficult for "normal adults" to use properly. 15 U.S.C. 1471(4). Household substances for which the Commission may require CR packaging include (among other categories) foods, drugs, or cosmetics as these terms are defined in the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 321. 15 U.S.C. 1471(2)(B). The Commission has promulgated performance requirements for special packaging. 16 CFR 1700.15 and 1700.20.

Section 4(a) of the PPPA, 15 U.S.C. 1473(a), allows the manufacturer or packer to package a nonprescription product subject to special packaging standards in one size of non-CR packaging only if the manufacturer (or packer) also supplies the product in a CR package of a popular size, and the non-CR package bears conspicuous labeling stating "This package for households without young children." 15 U.S.C. 1473(a), 16 CFR 1700.5.

3. *The Proposed Rule*

On August 30, 2000, the Commission issued a notice of proposed rulemaking (NPR) that would require that CR packaging requirements applicable to an oral prescription drug product continue to apply when that drug product or any other drug product containing an active ingredient of that product is granted OTC status by the FDA. 65 FR 52678. The proposed rule would require that the new use or new dose be sold in CR packaging even if the new use or dose was not approved when the drug product was only available by

prescription. This is consistent with the current regulatory approach for a new use for an oral OTC product that is already subject to a CR packaging requirement.

The proposed rule would not extend CR packaging requirements to OTC-switched products that are not oral formulations, even if they contain any of the same active ingredients as an oral preparation.

The proposed rule would require CR packaging for any OTC oral drug product containing an active ingredient that was available by prescription even if the OTC dosage is lower than the prescription strength. This recognizes the reality that absent CR packaging, the "dose" potentially available to a child is the entire package contents.

4. 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 CR packaging is not technically feasible, practicable, or appropriate. 16 CFR part 1702. Under the proposed rule, this exemption procedure would remain available to manufacturers of OTC-switched products.

The proposed rule would revoke 16 CFR 1702.16(b) so that exemption petitions can be submitted and considered by the Commission earlier in the process, i.e., before FDA approval. This would enable manufacturers to seek an exemption from the CR packaging requirements and have a

Commission decision prior to submitting an application to the FDA for approval of an OTC or prescription drug product.

To assist consumers and industry in identifying which OTC-switched drug products require CR packaging, the preamble to the proposal indicated that the Commission intended to maintain a list of OTC-switched drug products subject to the regulation as an appendix to the regulations at 16 CFR 1700.14.

B. Response to Comments

Five comments were received in response to the NPR. Three of the five comments received supported the rule as proposed (CP01-1, 2, 5).

Comment: Several commenters questioned whether the PPPA permits imposing child-resistant packaging requirements on a category of drugs and then placing the burden on a manufacturer to seek exemption of individual drugs. (CP01-1-3, 4)

Response: The PPPA authorizes regulation of a category of substances where the required findings can be made for that category. In fact, a number of entries under the CPSC regulation imposing the PPPA child-resistant packaging requirement, 16 CFR 1700.14(a), are defined as broad categories. (*See*, for example: controlled *drugs* --"any preparation for human use that consists in whole or in part of any substance subject to control under the Comprehensive Drug Abuse Prevention and Control Act…," (16 CFR

1700.14(a)(4); *prescription drugs* - "any drug for human use that is in a dosage form intended for oral administration...," (16 CFR 1700.14(a)(10)).

All members of the class that would be required to be in child-resistant packaging by an OTC-switch rulemaking were previously covered by the PPPA child-resistant packaging requirement for oral prescription drugs (16 CFR 1700.14(a)(10)). The statutory findings for that class were made by the FDA in the 1972-1973 rulemaking that imposed child-resistant packaging on oral prescription drugs. 38 FR 9431 (April 16, 1973).

The ability of a drug to cause serious injury to a child does not change when it is sold OTC. Child-resistant packaging remains technically feasible, practicable, and appropriate for the OTC version, just as was the case when it was required for the prescription formulation. Furthermore, the continued need for child-resistant packaging is not a factor considered by the FDA when making its decision to approve the switch of a drug from prescription to OTC status. Under the OTC-switch rule as proposed, and as issued in final form today, the responsibility/burden on a manufacturer to justify an exemption for an OTC-switched drug via the procedures of 16 CFR 1702 is the same as it was before the drug was switched.

The courts have typically approved the validity of regulatory schemes where a rule addresses a general

situation that is too complex for the rule to be appropriate in every instance, but where an exemption procedure is established to deal with special situations. See, e.g., United States v. Allegheny-Ludlum Steel Corp., 406 U.S. 742 (1972); see also Phillips Petroleum Co. v. EPA, 803 F.2d 545, 562 (10th Cir. 1986)(upholding a regulation applying a "generic streamlined approach or procedure" on the grounds of "feasibility and practicality" where the plaintiff argued that the statute required a case-by-case review).

In a case that addressed the Commission's Flammable Fabrics Act regulatory authority, which is analogous to that under the PPPA, the First Circuit affirmed the categorical approach to regulation. Bunny Bear v. Peterson, 473 F.2d 1002 (1st Cir. 1973). The Bunny Bear court also addressed the "burden" issue by stating that when the regulatory agency "plausibly opts for the inclusion of a particular product [in a regulatory scheme], it is not unreasonable to require affected manufacturers to point out with particularity those features which make special treatment [i.e., exemption] necessary." Bunny Bear at 1007.

Comment: One commenter requested that OTC products be available in both child-resistant packaging and non child-resistant packaging for the elderly and disabled (CP01-1).

Response: The PPPA provides for the use of both child-resistant and non child-resistant packaging. Section 4 of the Act allows manufacturers to package a product in one

size that does not meet the child-resistant packaging standards. 15 U.S.C. 1473. A product so packaged must carry a labeling statement warning that it is not recommended for use in households with young children. There is no requirement that manufacturers have a non child-resistant size.

It is the manufacturer's decision whether or not to market a noncomplying size. Manufacturers who market one size of their product in non child-resistant packaging must also supply the product in popular-sized packages that are child-resistant. If the manufacturer does not comply with this provision, the Commission can require that the product be packaged exclusively in child-resistant packaging. 15 U.S.C. 1473(c).

Child-resistant packaging has also become more "adult-friendly." In 1995 the Commission issued a revised test method that tests participants aged 50 to 70, rather than 18 to 45 years of age, to ensure that most adults can use child resistant packaging properly. 16 CFR § 1700.20(a)(3)(i).

Comment: One commenter requested that manufacturers and sellers have 18-months advance notice of the effective date of these packaging changes and that they only be implemented for newly manufactured packages (CP01-2).

Response: The packaging regulation as proposed and as issued in final form applies only to a drug granted OTC status as a result of a new drug applications (NDA) or abbreviated new

drug application (ANDA) submitted to the FDA on or after the effective date of the final OTC-switch rule. The rule does not affect any product that is approved for OTC sale before that date. The rule does not impact the current production or sale of previously switched products. Therefore the effective date of 180 days after issuance of a final rule should be adequate for companies currently preparing NDA or ANDA submissions requesting OTC status for oral prescriptions.

Comment: One commenter requested that a comprehensive list of affected products and ingredients be made available in advance of the effective date (CP01-2).

Response: The CPSC will publish a list of drugs that are affected by the rule as soon as the Agency becomes aware of them. CPSC will work with the FDA to obtain timely notification of approval of oral prescription drugs that are granted OTC status. No oral prescription drug approved for OTC sale (or for which the NDA or ANDA for an OTC switch was submitted) before the effective date is affected by the rule. The list will include only OTC switched drugs for which the NDA or ANDA was submitted on or after the effective date of the final rule.

Comment: One commenter questioned the efficiency of the proposed rule in saving staff resources because of the resources potentially needed to consider requests for exemptions. The commenter stated that it may be just as

efficient to continue the practice of considering the need for child-resistant packaging on a case-by-case basis (CP01-3).

Response: The primary goal of this rulemaking is not to save staff resources but to continue to protect children from serious injury from ingesting oral prescription drugs that are granted OTC status and become widely available. This rule eliminates the potential for newly switched oral OTC drugs to be packaged and sold without child-resistant packaging before a decision concerning the continued need for child-resistant packaging is made by the Commission. Furthermore, these drugs were already required to be in child-resistant packaging in their prior, prescription-only form. Finally, it is worth noting that some companies already voluntarily use child-resistant packaging for their "OTC switched" products.

The staff cannot estimate how many petitions for exemption from the child-resistant packaging requirements the Commission will receive.

Comment: Two commenters requested revisions to the Commission's PPPA regulations that define child-resistant *unit packaging* (CP01-3, 4).

Response: The child-resistant unit packaging regulations are not part of this rulemaking. Therefore the comment is beyond the scope of this rulemaking. Accordingly, the Commission is not required to respond to it. See, e.g.,

American Iron & Steel Institute v. EPA, 886 F.2d 390, 398 (D.C.Cir. 1989), cert. denied, 497 U.S. 1003 (1990).

Comment: One commenter requested clarification that the Commission will accept and act on a petition for exemption early in the process, before a NDA or ANDA is submitted to the FDA.

Response: In the preamble to the proposed rule, the Commission stated that, "...the Commission is proposing to revoke 16 CFR 1702.16(b) so that exemption petitions can be submitted and considered by the Commission earlier in the process, *i.e.*, before FDA approval. This would enable manufacturers to seek an exemption from the child-resistant packaging requirements and have a Commission decision prior to submitting an application to the FDA for approval of an OTC or prescription drug product." 65 FR 52682. Since 16 CFR 1702.16(b) is revoked by today's rule, there is no longer any restriction on the timing of Commission consideration of a petition for exemption from an otherwise applicable child-resistant packaging requirement.

The exemption process involves rulemaking. This process can be expedited if the manufacturer meets with the CPSC staff to discuss the process before filing a petition for exemption with the Commission as outlined in 16 CFR part 1702.

Comment: One commenter expressed a concern that if a petition is submitted before the NDA is submitted, it could

prematurely signal a company's business plans. They believed that a confidential exemption procedure might be necessary but stated the concern that it would not be compatible with the current rulemaking approach to exemptions. (CP01-3)

Response: The commenter is correct that the child-resistant packaging exemption procedure involves public notice and comment. A petitioner must be willing to make toxicity and safety information available for Commission and public review.

There are many factors that a company considers when deciding to pursue OTC status for an oral prescription drug. These may include safety of use and potential misuse, ability of a consumer to self-treat using the medication, or a new market for a drug at the end of its patent, etc. There is much speculation in the press about drugs that may be "switched" based upon these factors. The commenter (Consumer Healthcare Products Association) publishes a list of potential switches that have been named in the trade or popular press.[1] The FDA requested comments and held a public meeting last year to discuss potential OTC drugs.[2] Much of the discussion at the public hearing focused on classes of drugs that may or may not be appropriate for OTC sale.

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[1] Available on the CHPA website: www.chpa-info.org
[2] 65 FR 24704

A manufacturer of an oral prescription drug that is contemplating seeking approval for an OTC switch could request an exemption for the prescription drug. It is the active ingredient itself at a defined level that would then be exempted. Under the rule as proposed, an exempted oral prescription drug would remain exempted from child-resistant packaging when it is granted OTC status. For example, if an oral contraceptive or colestipol were made available OTC, it would not require child-resistant packaging if the OTC preparation met the same conditions as the exempted oral prescription form. (16 CFR 1700.14(a)(10)(iv) and (xv)). A manufacturer would still have the option of petitioning the Commission for exemption after the drug is approved for OTC sale.

C. Statutory Considerations

1. Hazard to Children

Before issuing a rule requiring CR packaging, the Commission must find that the degree or nature of the hazard to children in the availability of OTC-switched drug products 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 drug products. 15 U.S.C. 1472(a)(1). These statutory findings were made when the rule requiring CR packaging for oral prescription drug products was promulgated in 1973. 38 Fed. Reg. 9431 (April 16, 1973).

OTC-switches did not begin to occur until several years after the 1973 rule requiring CR packaging for oral prescription drug products was promulgated. The first such switches were carried out in response to recommendations resulting from an FDA Advisory Panel's review of over-the-counter drug products.

The need to continue to protect children remains when oral prescription drug products are granted OTC status. As noted previously, a decision by the FDA to grant OTC status for a prescription drug product is not a determination that there is no toxicity to a child if the drug product is accidentally ingested. The active ingredient(s) contained in the drug product have the same toxicity whether in prescription or OTC form. The issue is whether drug products switched to OTC status at a lower dosage than was available by prescription are still hazardous to young children. This is the case since absent CR packaging, the "dose" available to a child can be the entire contents of the OTC product package. The Commission's experiences with ibuprofen and naproxen demonstrate that toxic amounts of the active ingredients are available even when lower dosages are approved for OTC product sale.

Another important consideration is that OTC drug products are more readily available to consumers and therefore more accessible to children than prescription products containing the same active ingredient(s). The

Commission concludes that the available data support the finding that maintaining CR packaging is necessary to protect children from serious injury or illness from ingesting oral prescription drug products that have been granted OTC status.

2. Technical Feasibility, Practicability, and Appropriateness

As a prerequisite to a CR packaging rule, the Commission must also find that the special packaging is "technically feasible, practicable, and appropriate." 15 U.S.C. 1472(a)(2). Technical feasibility may be found when technology exists or can be readily developed and implemented by the effective date to produce packaging that conforms to the standards. Practicability means that special packaging complying with the standards can utilize modern mass production and assembly line techniques. Packaging is appropriate when complying packaging will adequately protect the integrity of the active ingredient(s) in the product and not interfere with its intended storage or use. *See* S. Rep. No. 91-845, at 10 (1970).

In some cases the same packaging can be used for the OTC product as for the prescription product. However, companies must modify the labels since FDA labeling requirements for OTC drug products differ from the labeling requirements for prescription drugs. Also, most companies develop new packaging specifically for the OTC market. Unit

dose packaging is popular for the OTC market, especially for drug products such as antihistamines that are sold in limited quantities. Other products containing active ingredients such as the anti-inflammatory compounds ibuprofen and naproxen are sold in bottles. CR designs of this sort of unit and reclosable packaging are commercially available. The change in status of the drug from prescription-only to OTC does not change the availability of the CR packaging in mass-produced quantities, or detract from its ability to maintain the shelf life of switched drug products. Therefore, the Commission concludes that CR packaging for OTC-switched drug products is technically feasible, practicable, and appropriate.

3. *Other Considerations*

Section 3(b) of the PPPA requires that the Commission consider the following in establishing a special packaging standard:

a. The reasonableness of the standard;

b. Available scientific, medical, and engineering data concerning special packaging and concerning childhood accidental ingestions, illness, and injury caused by household substances;

c. The manufacturing practices of industries affected by the PPPA; and

d. The nature and use of the household substance. 15 U.S.C. 1472(b).

The Commission has considered these factors with respect to the various determinations made in this rulemaking, and finds no reason to conclude that the rule is unreasonable or otherwise inappropriate.

D. Applicability

The packaging configuration for a drug product to be switched is determined before a company submits the NDA or the ANDA for the OTC-switch to the FDA. Accordingly, this rule applies prospectively to drug products for which the application for the OTC-switch is submitted to the FDA on or after the effective date of the final rule (180 days after publication).

E. Effective Date

The PPPA provides that no regulation shall take effect sooner than 180 days or later than one year after the date such final regulation is issued, except that, for good cause, the Commission may establish an earlier effective date if it determines an earlier date to be in the public interest. 15 U.S.C. 1471n. The NPR proposed an effective date of 180 days after publication of the final rule. The commenter suggesting a further delayed effective date seemed to believe that the proposed rule might apply to an oral prescription drug for which an NDA or ANDA had been submitted to the FDA prior to the effective date or for which the OTC switch had been approved by the FDA prior to the effective date. This is not the case. The rule as

proposed and as issued today applies only to drugs for which the NDA or ANDA for the OTC switch is submitted on or after the effective date. Thus the final rule takes effect 180 days after publication.

F. Regulatory Flexibility Act Certification

When an agency undertakes a rulemaking proceeding, the Regulatory Flexibility Act (RFA), as amended by the Small Business Regulatory Enforcement Fairness Act of 1996, 5 U.S.C. 601 *et seq.*, generally requires the agency to prepare initial and final regulatory flexibility analyses describing the impact of the rule on small businesses and other small entities. Section 605 of the RFA provides that an agency is not required to prepare a regulatory flexibility analysis if the head of the agency certifies that the rule will not have a significant economic impact on a substantial number of small entities.

The Commission's Directorate for Economic Analysis prepared an assessment of the impact of a rule to maintain CR packaging for OTC-switched drug products. A copy of the analysis is available for inspection in the docket for this rulemaking. The assessment reports that the incremental cost of providing basic CR packaging is usually small ($0.005-$0.02/per package). The assessment notes that the incremental cost may be somewhat higher if the marketer elects to provide more elaborate packaging in an effort to create "shelf appeal" to attract consumers and compete with

other OTC products in the same therapeutic category.

Because these costs (if any) are likely to be passed on to consumers, it is unlikely that the rule will have a substantial effect on a significant number of small businesses.

Many previously OTC-switched drug products are already sold in CR packaging. In some instances, for example with certain oral dosage formulations of acetaminophen, ibuprofen and loperamide, this is because the Commission has affirmatively required CR packaging. In other cases, the marketer has elected voluntarily to use CR packaging.

This rule revokes the existing requirement at 16 CFR 1702.16(b) that new drug approval be obtained from the FDA prior to Commission approval of a petition seeking exemption from a CR packaging requirement. Allowing for advance consideration and approval of any legitimate CR packaging exemption petition should minimize or eliminate any unwarranted economic impact that would otherwise result from maintaining the CR packaging requirement on OTC-switched oral prescription drug products or from requiring a change to CR packaging post-marketing.

Based on the foregoing assessment, the Commission certifies that this rule to maintain CR packaging for OTC-switched drug products does not have a significant impact on a substantial number of small businesses or other small entities.

G. Environmental Considerations

Pursuant to the National Environmental Policy Act, and in accordance with Council on Environmental Quality regulations and CPSC procedures for environmental review, the Commission has assessed the possible environmental effects associated with the proposed PPPA requirements for OTC-switched drug products.

The Commission's regulations state that rules requiring special packaging for consumer products normally have little or no potential for affecting the human environment. 16 CFR 1021.5(c)(3). Nothing in this rule alters that expectation. Therefore, because the rule would have no adverse effect on the environment, neither an environmental assessment nor an environmental impact statement is required.

H. Executive Order No. 12,988

As provided for in Executive Order No. 12,988 the CPSC states the preemptive effect of this proposed regulation as follows.

The PPPA provides that, generally, when a special packaging standard issued under the PPPA is in effect, "no State or political subdivision thereof shall have any authority either to establish or continue in effect, with respect to such household substance, any standard for special packaging (and any exemption therefrom and requirement related thereto) which is not identical to the [PPPA] standard." 15 U.S.C. 1476(a). A State or local

standard may be excepted from this preemptive effect if (1) the State or local standard provides a higher degree of protection from the risk of injury or illness than the PPPA standard; and (2) the State or political subdivision applies to the Commission for an exemption from the PPPA's preemption clause and the Commission grants the exemption through procedures specified at 16 CFR part 1061. 15 U.S.C. 1476(c)(1). In addition, the Federal government, or a State or local government, may establish and continue in effect a non-identical special packaging requirement that provides a higher degree of protection than the PPPA requirement for a household substance for the Federal, State or local government's own use. 15 U.S.C. 1476(b).

Thus, with the exceptions noted above, this rule preempts non-identical state or local special packaging standards for such drug products.

List of Subjects in 16 CFR Part 1700

Consumer protection, Drugs, Infants and children, Packaging and containers, Poison prevention, Toxic substances, Reporting and recordkeeping requirements.

For the reasons set forth above, the Commission amends 16 CFR part 1700 as follows:

PART 1700--POISON PREVENTION PACKAGING ACT OF 1970 REGULATIONS

1. The authority citation for part 1700 continues to read as follows:

Authority: 15 U.S.C. 1471-76. Secs. 1700.1 and 1700.14 also issued under 15 U.S.C. 2079(a).

2. Section 1700.14 is amended by republishing paragraph (a) introductory text and by adding new paragraph (a)(30) to read as follows:

§ 1700.14 Substances requiring special packaging.

(a) *Substances.* The Commission has determined that the degree or nature of the hazard to children in the availability of the following substances, by reason of their packaging, is such that special packaging meeting the requirements of § 1700.20(a) is required to protect children from serious personal injury or serious illness resulting from handling, using, or ingesting such substances, and the special packaging herein required is technically feasible, practicable, and appropriate for these substances:

* * * * *

(30) *Over-the-Counter Drug Products.*

(i) Any over-the-counter drug product in a dosage form intended for oral administration that contains an active ingredient also contained in a drug product that is or was a

prescription drug product required by paragraph (a)(10) to be in special packaging shall be packaged in accordance with the provisions of § 1700.15(a),(b), and (c). This requirement applies whether or not the amount of the active ingredient in the over-the-counter drug product is different from the amount of that active ingredient in the prescription drug product. This requirement does not apply to a drug product for which an application for over-the-counter marketing has been submitted to the FDA before [insert date 180 days after promulgation of final rule] or which has been granted over-the-counter status by the FDA before [insert date 180 days after promulgation of final rule]. Notwithstanding the foregoing, any special packaging requirement under this section 1700.14 otherwise applicable to an over-the-counter drug product remains in effect.

(ii) For purposes of this paragraph (30), *active ingredient* means any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the body of humans; and *drug product* means a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance (active ingredient), generally, but not necessarily, in association with one or more other ingredients. (These terms are intended to have the meanings assigned to them in the regulations of the Food and Drug

Administration appearing at 21 CFR 201.66 (2001) and 21 CFR 314.3 (2000), respectively.)

3. Section 1702.16 is amended by removing subsection (b) thereof in its entirety.

Dated: _____

_____
Todd A. Stevenson, Acting Secretary
Consumer Product Safety Commission

DRAFT

List of Relevant Documents

1. Briefing memorandum from Suzanne Barone, Ph.D., EH, to the Commission, "Final Rule to Require Special Packaging for Oral Prescription Drugs that are Granted Over-the-Counter Status by the Food and Drug Administration," June __, 2001.

2. Letter from Debra L. Bowen, M.D., Acting Director, Division of Over-the-Counter Drug Products, Food and Drug Administration, to Jeffrey S. Bromme, Esq., General Counsel, Consumer Product Safety Commission, October 7, 1998.

3. Memorandum from Robert L. Franklin, EC, to Suzanne Barone, Ph.D., EH, "Economic Considerations Related to the Rule to Maintain Child-Resistant Packaging Requirements for Oral Prescription Drugs that Have Been Granted OTC Status by the FDA," May 31, 2001.

4. Memorandum from Suzanne Barone, Ph.D., Project manager for Poison prevention, Directorate for health Sciences, to Sadye E. Dunn, Secretary, Consumer Product Safety Commission, "Responses to Questions from Commissioner Moore on Over-the-Counter Switches," June 23, 2000.